Biotherapy Journal Review

Volume 3, Number 2; Spring 2017



BioTherapeutics, Education & Research Foundation

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The BTER Foundation's

Biotherapy Journal Review

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Dog Pointer on Brown, Guido Daniele, used with permission from Guido Daniele

From the Editor's Desk:

Dear Readers,



Paradise Fish, Guido Daniele, used with permission from Guido Daniele

This issue of Biotherapy Journal Review could be called a "Special Edition" because of two special features. First, we decided to focus all of this issue's reviews on one small area of biotherapy: service and therapy animals (that is, hippotherapy, pet therapy, service dogs, and the like). This is an application of biotherapy which is relatively new, and quickly growing. Let's face it - even guide dogs are relatively new, compared to hirudotherapy, apitherapy, and many other medicinal animals. As a result, many facilities are ill-prepared to handle their clients' requests to accommodate their service or therapy animals, and some clients are not being adequately trained in how to handle their animals without putting themselves at risk for serious zoonotic infections (infections contracted from animal to human).

Therefore, this issue's in-depth reviews include the study by Gurry et al of how immunocompromised patients are handling their companion animals, as well as the paper by Hardin and associates, which explores how one institution established safeguards against the transmission of zoonotic diseases as part of their pet therapy program. Also reviewed in this issue are two papers that attempt to share new research concerning the benefits of owning a service dog (Hall and colleagues) and the therapeutic effects of horseback riding (Stergiou and associates).

The second reason that we believe this issue is "special" is that we are honored to be able to share with you, scattered throughout the issue, the "Handimal" images of Guido Daniele. Regular readers of BJR will know that we commonly add animal artwork to these pages, but rarely have we had the opportunity to share such a large volume of high quality images. We know you will enjoy viewing them as much as we enjoyed putting it all together for you.

As usual, the rest of the issue is filled with new citations of ***ALL*** of the biotherapy disciplines that we could find. We did not provide internet links to each article this time, since we would not have then been able to meet our deadline had we done so. If you believe that having links directly from each BJR issue is important, then let us know and we will try to find additional staff to help us with that effort in the future.

Of course, we hope that you find ***ALL*** issues of BJR to be "special" in their own right, and worthy of collection. We also hope that you will be inspired to continue to submit your

own photographs, artwork, or reviews. Most of all, we hope that you will continue to be educated in this growing enterprise we call Biotherapy Research.



Ronald A. Sherman, MD, MSc, DTM&H
Director, BTER Foundation

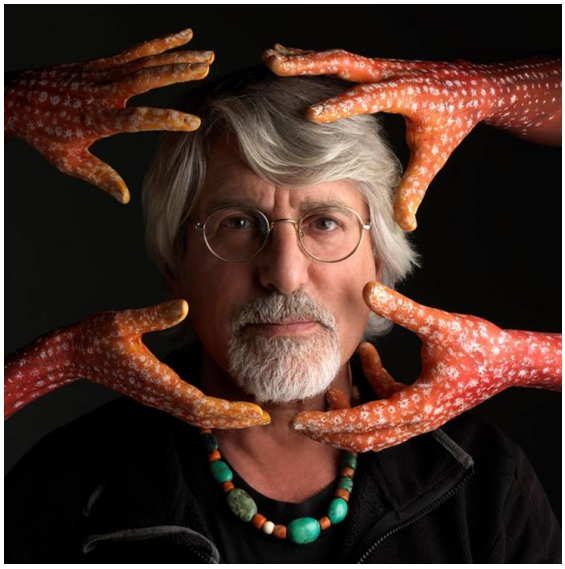
P.S. Don't miss an issue of the Biotherapy Journal Review! To ensure you recieve each quarterly issue via email, please sign up here!



Elephant on Green, Guido Daniele, used with permission from Guido Daniele

FEATURED ARTIST: GUIDO DANIELE

Mr. Daniele's beautiful "handimals" art can be found throughout this issues of the Biotherapy Journal Review as a way of celebrating the beauty and diversity of animal life. Mr. Daniele kindly agreed to allow us to feature his work in our publication - we hope you enjoy it as much as we do. If you are interested in learning more about Mr. Daniele and his work, please visit his website at: http://www.guidodaniele.com/



Guido Daniele; photo retrieved 7/27/17 from http://www.guidodaniele.com/biography.html

Guido Daniele was born in Soverato (CZ - Italy) in 1950 and now lives and works in Milan. From 1964 to 1968 he attended Brera artistic High School. He graduated from Brera School of Arts (major in sculpturing) in 1972.

He lived in India since 1972 to 1974 where he attended the Tankas school in Dharamsala. Since 1968 he has been painting and participating to personal and group art exhibitions. In 1972 he started working as hyper-realistic illustrator, in co-operation with major editing and advertising companies, using and testing different painting techniques.

Since 1986 he has been working and improving his personal usage of airbrush: he paints back-drops in different sizes (the biggest ones can be 400 square metres) for artistic and advertising pictures, tv commercials and tv programmes. He also creates trompe l'oeil, both in private houses and public buildings.

In 1990 he added a new artistic experience to his previous ones: using the body painting technique he creates and paints models bodies for different situations such as advertising pictures and commercials, fashion events and exhibitions.

Its search started in 2000 about "Handimals" maked with the method of body painting on hands has a great international interest.

Daniele is committed to wildlife protection and has become increasingly involved with charities such as WWF, the Jane Goodall Institute, Dolphin Aid, Innocence in Danger, PLAN, APNEEF and Liliane Fonds.

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Section I: Journal Reviews

The BTER Foundation's

Biotherapy Journal Review

Volume 3, Number 2; Spring 2017

Title: High rates of potentially infectious exposures between immunocompromised patients and their companion animals: an unmet need for education.
Authors: Gurry GA, Campion V, Premawardena C, Woolley I, Shortt J, Bowden DK, Kaplan Z, Dendle C.
Reviewer: Ronald Sherman, MD
To view the article review, visit page 7

Title: A survey of the impact of owning a service dog on quality of life for individuals with physical and hearing disability: a pilot study.
Authors: Hall SS, MacMichael J, Turner A, Mills DS.
Reviewer: Ronald Sherman, MD
To view the article review, visit page 10

Title: Prevention of transmitted infections in a pet therapy program: An exemplar.
Authors: Hardin P, Brown J, Wright ME.
Reviewer: Ronald Sherman, MD
To view the article review, visit page 15

Title: Therapeutic Effects of Horseback Riding Interventions: A Systematic Review and Meta-analysis.
Authors: Stergiou A, Tzoufi M, Ntzani E, Varvarousis D, Beris A, Ploumis A
Reviewer: Ronald Sherman, MD
To view the article review, visit page 18

Pet Therapy Reviews

Journal Citation

Gurry GA, Campion V, Premawardena C, Woolley I, Shortt J, Bowden DK, Kaplan Z, Dendle C. **High rates of potentially infectious exposures between immunocompromised patients and their companion animals: an unmet need for education.** Intern Med J. 2017;47(3):333-335.

Published Abstract

A cross-sectional survey of 265 adult patients with haematological malignancy, haemoglobinopathy or human immunodeficiency virus was performed to determine the potential risk of infection from animal exposures. One hundred and thirty-seven (52%) owned an animal; the majority were dogs (74%) and cats (39%), but 14% owned birds and 3% reptiles. Eighty percent engaged in behaviour with their animals that potentially put them at risk of zoonotic infections. The most frequent behaviours were picking up animal faeces 72 (52%), cleaning animal areas 69 (50%) and allowing animals to sleep in the same bed 51 (37%). Twenty-eight percent allowed the animal to lick their face. Of all patients, 80 (30%) had been bitten or scratched by an animal. Only 16% of those who owned pets could recall receiving education regarding safe behaviours around animals. These immunocompromised patients are at risk of infection through exposure to pets. Our study highlights the need for increased education of patients regarding how to remain safe around their pets.

Context

Humans can catch infections from animals ("zoonotic infections"). Increased contact with animals puts people at greater risk of catching those infections. Immunodeficiency (a suppressed immune response) puts people at risk of more invasive and symptomatic illnesses from those infections. Understanding this is important because many people who are ill find solace and companionship in a pet, companion, or service animal. Pets and companion animals are often obtained without medical consultation. This study was aimed to identify the level of knowledge about these risks among animal owners with immunodeficiency diseases, and to identify the extent to which they partake in such risky behaviors.

Findings

A cross-sectional survey was conducted at a large tertiary care hospital in Melbourne, Australia, selecting patients with one of three disease groups: haematological malignancies (chronic lymphocytic leukaemia and lymphoma), haemoglobinopathies requiring transfusion, and patients living with human immunodeficiency virus (HIV). Consecutive adults attending one of these clinics were asked to complete the

anonymous, self-administered questionnaire, consisting of questions about demographic information, animal ownership, types of animal contact, and whether the subject recalled receiving education regarding safe animal contact, from a healthcare worker.

The survey was completed by 275 subjects, with 64% male. The median age was 48 years (range of 17–92 years). Fifty-two percent of the surveyed subjects owned some type of animal (more or less evenly distributed between the three patient populations). Of the animals owned, 74% were dogs, 36% were cats, 14% birds, 3% reptiles, 2% rabbits, 1% rodents, and 19% something else.

Of the subjects who owned animals, 80% engaged in at least one activity that may have exposed them to zoonotic infections, such as picking up animal feces (66% of those engaged in risky behaviors), cleaning animal living areas (63%), or sleeping in the same bed (47%). Thirty percent of the subjects who owned animals reported having been bitten or scratched. Only 17% of subjects who owned animals recalled receiving advice from a healthcare worker regarding safe practices around animals.

Discussion

Pet ownership is quite common throughout much of the world, and this study of immunocompromised subjects informs us that pet and companion animals are commonly owned by these patients as well: Over half of the surveyed subjects owned a companion animal. What's more, approximately 80% of the animal-owning individuals engaged in behavior that placed them at increased risk of contracting a zoonotic infection.

The significance of this is brief but well-summarized and referenced by this study's authors. Contraction of microbes from the dog to the human has been well-documented by several earlier studies of patients who kissed, were licked by, or slept with their dogs or cats, compared to those who simply owned dogs or cats. In fact, in at least one published study, a patient died from their infection, acquired from a dog lick. Animal bites carry an even greater risk of transmitting infection, and there are multiple reports of immunocompromised patients dying as a result. The authors also remind us of the prior study that estimates that 14% of all human illness caused by common enteric (intestinal) pathogens are attributable to animal contact.

Perhaps even more disturbing than the frequency of risky behavior among immunocompromised patients is the lack of needed counseling by their health care providers. Speaking as a health care provider for many immunocompromised patients, I have to admit that I rarely think about this issue during my office visits, which are so commonly monopolized by disease pathology and complications, medication, drug interactions and side effects, etc. This is not intended to be a "cop-out," but rather a confession that our current office-visit protocols will need to change if we are to make room for preventive counseling about safe handling of companion animals.

For me, the take-away message from this article was: Many of my patients – including those with chronic or immunocompromising diseases – own animals, and need to be counseled regarding safe behaviors with those animals.

The take-away question was: How can I do a better job counseling those patients? Printed materials exist, though they are limited in number and scope. Handing out printed materials saves time and is arguably "better than nothing," but probably not much better. Without the doctor or nurse discussing the issue, whatever is written on the brochure - if it is read at all - will not carry as much sway / power / influence. I believe the medical health care provider and the veterinarian both have the obligation to counsel at least at-risk individuals. Even if only one sentence is said (perhaps as the brochure is handed out), the message will likely be considered and remembered more seriously than would be the case of simply handing out a brochure without any verbal communication. Of course, as this study's authors conclude, only a prospective study evaluating the impact of educational interventions on pet-handling behaviors will clearly inform us about the best approach to minimizing the zoonotic infection risk.

-Reviewed by Ron Sherman, MD



Hound Dog, Guido Daniele, used with permission from Guido Daniele

Pet Therapy Reviews (cot'd)

Journal Citation

Hall SS, MacMichael J, Turner A, Mills DS. **A survey of the impact of owning a service dog on quality of life for individuals with physical and hearing disability: a pilot study.** Health Qual Life Outcomes. 2017 Mar 29;15(1):59.

Published Abstract

BACKGROUND: Quality of life refers to a person's experienced standard of health, comfort and happiness and is typically measured using subjective self-report scales. Despite increasing scientific interest in the value of dogs to human health and the growing demand for trained service dogs, to date no research has reported how service dogs may affect client perceptions of quality of life. ***METHOD***: We compared quality of life scores on the 16 item Flanagan quality of life scale from individuals who owned a trained service dog with those who were eligible to receive a dog, but did not yet have one (waiting list control). Data were analysed separately from two groups; those with a service dog trained for individuals with physical disabilities (with physical service dog: n = 72; waiting for a service dog: n = 24; recruited from Dogs for Good database) and those with a hearing service dog (with hearing service dog = 111; waiting for a service dog = 30; recruited from Hearing Dogs for Deaf People database). ***RESULTS***: When controlling for age and gender individuals scored higher on total quality of life scores if they owned a service dog or a hearing service dog, but this was only statistically significant for those with a service dog. Both groups (physical service dog and hearing service dog) scored significantly higher on items relating to health, working, learning and independence if they owned a service dog, in comparison to those on the waiting list. Those with a physical service dog also scored significantly higher on items relating to recreational activities (including items relating to reading/listening to music, socialising, creative expression), and those involving social interactions (including items relating to participating in organisations, socialising, relationship with relatives). Additionally, those with a physical service dog scored higher on understanding yourself and material comforts than those on the waiting list control. In contrast, those with a hearing service dog appeared to receive fewer benefits on items relating to social activities. ***CONCLUSIONS***: Owning a service dog can bring significant specific and potentially general benefits to the quality of life of individuals with physical disabilities and hearing impairments. These benefits may have considerable implications for individuals with disabilities, society and the economy by promoting independence, learning and working abilities.

Context

Physical and medical consequences of an intervention are relatively easy to assess, but what about the consequences like happiness, energy level, and satisfaction with life? These "quality of life" issues are important, but not always very easy to measure. To help

assess changes in quality of life (QOL) issues, several "assessment tools" (questionnaires) have been studied. Using these QOL assessment tools, it is now possible to get a better understanding about how interventions can affect a subject's QOL.

For individuals with physical disabilities, their QOL is often impacted, especially in specific areas (i.e., social interactions, sense of independence, etc). Service animals improve the functioning of such individuals, but do they improve the individual's QOL? In the words of the authors, this study was undertaken to "to assess the impact that owning a service dog (for physical assistance or hearing assistance) may have on a client's perceived quality of life in comparison to the quality of life scores obtained from individuals who need a service dog but do not yet own one." Their starting hypothesis was that "that there would be a significant difference in quality of life scores between those 'with service dogs' in comparison to those 'waiting for a service dog'."

Findings

This investigation was designed as a case-control study of surveys collected from individuals who currently owned a service dog or were waiting to receive one. Participants were self-recruited from databases held by either of two UK charitable organizations: Dogs for Good and Hearing Dogs for Deaf People. The only stipulation for participating in the study was that the individual must be over 18 years of age and meet the criteria for receiving a service dog, set by the organization to which they belonged (either Dogs for Good or Hearing Dogs for Deaf People).

Once enrolled, questionnaires were distributed to contacts by way of postal or electronic mail. Participants were also allowed to elect to read their responses over the telephone, which one participant chose to do. Subjects were given 4 weeks to return the questionnaire. A reminder notice was sent to all participants who did not return their questionnaires within the first 2 weeks.

The questionnaire consisted of demographics questions: age, gender and service dog status, along with a question asking subjects to describe their disability. The second section of the questionnaire consisted of the Flanagan Quality of Life Scale (QOLS) assessment tool, with one additional question, previously tested and validated, to assess independence. As the authors describe it, "Independence was thought to be important in this study because service dogs are often applied for in the belief that they increase their owner's independence and ability to do more without assistance from others." Subjects were asked to answer each of the 16 questions with a response on a 7-point scale: (1 = Terrible, 4 = Mixed, 7 = Delighted). The total quality of life score was obtained by summing the individual scores from each of the 16 items.

The authors evaluated the physically impaired groups and the hearing impaired groups separately, figuring that the difference between physical and hearing disability itself might impact on subjects' quality of life, as because the capacity to impact that QOL might differ between a physical service dog and a hearing assistance dog.

A total of 208 contacts were made through Dogs for Good; 96 (46%) returned the forms: 72 participants had been trained to work with and currently lived with a service dog (53% response rate); 24 had qualified for and were waiting for their service dog, or they had contacted the charity in order to be assessed to see if they qualified for a service dog. Subjects' underlying medical problems included arthritis (n = 7 with dog; n = 2 waiting for dog); wheelchair user due to spinal injury or infection (n = 21 with dog; n = 8 waiting for dog), multiple sclerosis (n = 18 with dog; n = 5 waiting for dog), "impairment from disease/virus such as polio (n = 6 with dog; n = 1 waiting for dog), stroke (n = 3 with dog; n = 2 waiting for dog) and Ehlers danlos syndrome (n = 2 with dog; n = 2 waiting for dog). Impairments mentioned only by the 'with dog' group included muscular injury/wastage (n = 4), spondyloptosis (n = 1), neurological/brain disorders (n = 3), arthrogryposis (n = `), cerebral palsy (n = 1) and spina bifida (n = 1). Impairments mentioned only by those in the waiting list "control" group included seizures (n = 1), dystonia (n = 1), and scleroderma (n = 1). Four subjects in the "with dog" group and 1 in the control group chose not to disclose their disability. There was a significantly larger portion of older subjects in the "have dog" group compared to the "waiting for dog" group. There was no significant difference in the proportion of men and women between the two groups, however.

A total of 667 clients from the Hearing Service Dog agency were similarly contacted. The response rate was 39% (260 individuals), but only 21% (141) actually completed and returned the questionnaire: 111 currently living with a hearing service dog and 30 waiting to receive a dog. There was no significant age or gender difference between these two "have dog" and "waiting for dog" groups.

Analysis of the physical disability subjects' questionnaires revealed a significant effect of Service Dog status on total Quality of Life Scores, when controlling for age and gender; $F(1, 95) = 23.11$, $p = .000$. Those with a service dog had a significantly higher total Quality of Life score than those waiting for a service dog. For individual items, subjects with service dogs scored significantly higher than those waiting for a service dog on the questions of material comforts, general health, relationship with relatives, helping or volunteering, participating in organizations, learning, understanding self, working, creative expression, socializing, active reaction, reading or music, and independence. There was no significant effect on having or rearing children, close relationship with spouse or others, or the question on relationships with close friends. Interestingly, the size of the effects (or the size of the difference between the "have dog" and "waiting for dog" groups) was often greater in men than in women.

Analysis of the questionnaires from the hearing disabled subjects revealed a trend towards an improved total QOL score with ownership of a dog, but this trend could not be considered statistically significant ($p = 0.15$). The only individual QOL questions where there was a significantly higher score among dog owners were: health, learning, working, and independence. There was a trend towards improved QOL score for understanding self ($F = 3.41$, $p = .06$) and active recreation ($F = 3.31$, $p = .06$). Again, effect sizes were generally greater in men than in women.

Discussion

It has long been known that service animals can improve the functioning of many patients with disabilities. It has been demonstrated also that service and companion animals can improve the mental status and emotional state of their owners. In this study, the authors demonstrated an improvement in overall sense of well-being of patients with physical disabilities who own service dogs, as measured by the Quality of Life Score. Most of the individual areas of QOL that the test measures were also significantly improved, with the exception of feelings about having or rearing children or social relationships.

For subjects with hearing impairments, the trend towards improved total QOL score seen in subjects who owned hearing assistance dogs was not statistically significant, but individually, the sense of better health, active learning, working, and independence were all higher in the dog-owning group.

The authors present a thorough discussion of possible explanations, which I will not repeat here. I will offer an example, however, just to give the flavor of the speculation that surrounds these findings:

> "Improved perceptions of physical health with service dog owners may be related to improved perceptions on items relating to personal fulfilment (e.g. independence, learning, engaging in recreational activities) and active interactions with others (e.g. socializing). By leading a fulfilling life, it is possible that participants believe that their health is not holding them back, and hence they report greater health satisfaction. In other words, the person feels able to cope . . . and feelings of coping are directly related to reported health and quality of life. Another possible explanation is that those with service dogs are more likely to go outdoors, which has been shown to improve health, as well as meet others through dog walking; another factor shown to improve wellbeing. However, it is possible that those who are awaiting a service dog report poorer quality of life because they are anticipating the improvement that they believe a service dog will bring. This may result in a negative contrast in their self-perceived quality of life (i.e. they are lacking something which they might soon have which they anticipate will improve their life) or they may be holding off engaging in new health promoting activities until they receive a dog. Therefore, it is plausible that those who are on a waiting list to get a service dog may score lower on quality of life to those who are similarly living with disability who are not awaiting a dog. Nonetheless, it may also be that individuals are holding off taking up activities because without the dog they lack the psychological (e.g. confidence) or physical ability to do so."

While the entire discussion is worth pondering – and definitely worth studying by those who research this field – the fact is that it is all speculation. The authors note as much. They conclude that further research is needed, and that such research should differ in design. For one thing, they propose that subsequent research might use a "three-participant cohort group:" subjects with a service dog, subjects on a waiting list for a service dog, and subjects qualified to receive a service dog but not wishing to do so. Subsequent research also should explore the details behind these general feelings of

satisfaction. Why are subjects more satisfied with their work? Are they performing better, or faster, or more independently? Are they having more social interaction at work, which might be contributing to their overall satisfaction and/or performance at work? These are the sorts of questions that a brief assessment tool cannot answer, but that an in-depth interview might.

For me, the major fault of the study was simply the inability to sort out the control group of subjects who were approved and waiting to receive a physical service dog, from those who were registered but not yet assessed. Clearly, not all of the unassessed subjects would be good case-control matches for the dog-owning group. Though small (especially the hearing-impaired groups), this study was a reasonable way to test the original hypothesis that service dog ownership would improve the owner's sense of well-being, and it points us now in the direction of new questions with new hypotheses, begging to be studied.

-Reviewed by Ronald Sherman, MD



Dog Dalmatian, Guido Daniele, used with permission from Guido Daniele

Pet Therapy Reviews (cot'd)

Journal Citation

Hardin P, Brown J, Wright ME. **Prevention of transmitted infections in a pet therapy program: An exemplar.** Am J Infect Control. 2016 Jul 1;44(7):846-50.

Published Abstract

The focus of the patient experience in health care delivery has afforded the opportunity to integrate pet therapy as a part of patient care. The purpose of this article is to present the implementation of a pet therapy program that includes guidelines for the prevention of transmitted infections. Consideration of infection prevention strategies has resulted in a 16-year program with no documented incidences of transmitted infections, averaging 20,000 pet therapy interactions per year.

Context

Transmission of infections from animals to humans (zoonoses) poses a risk for patients exposed to service and companion animals. The risks rise dramatically when those patients suffer from immunocompromising illnesses, and rises further when the animals are brought into institutions housing other immunocompromised patients, even though they themselves may not participate directly in the animal companion or service program. Therefore, those entertaining the idea of pet therapy in a medical facility must be cognizant of these risks, and implement policies that minimize them.

The Society for Healthcare Epidemiology of America (SHEA) issued guidelines to that effect in 2015. The purpose of the present study was to explore and share the experience of a large pet therapy program that had no transmissions of infection over its 16-year history.

The authors reviewed individual aspects of their pet therapy program (the Pet Therapy Team, preparation of handlers and dogs, policy planning, individual visit process), and then compared their practices with the SHEA guidelines.

Findings

The Pet Therapy Team was interdisciplinary, comprised of veterinarians, infection control staff, physicians, child life specialists, volunteer services, risk management, security and safety officers, and administrators. This interdisciplinary team enacted policies and procedures, in consultation with the existing literature and with pet therapy centers already in operation.

Handler-dog teams must comply with strict requirements set by the facility and by regional and national agencies. The handler-dog team must be registered with either Pet Partners or Therapy Dog Inc, (national animal human bond registration organizations), and the handler must pass an online course and in-person interview by a licensed evaluator. Only then is the human-dog team able to apply for facility privileges. Handler-dog teams applying to the hospital were evaluated through a rigorous set of interviews, background checks and orientations, and then the handler was required to shadow an experienced team before bringing their own dog into the facility. Immunization records were checked and maintained for both the handlers and the dogs. Both were required to wear identification badges while working, and to follow their respective behavior and dress code that included grooming prior to their visits.

In order to receive pet therapy, patients' physicians had to issue an order (prescription) after evaluating the patient for infection risk, which included not only an assessment of their immunological status but also of their pre-or post-surgical status, existing wounds, pet allergies, and the like. At least one member of the Pet Therapy Team also was required to evaluate the patient and give approval. Infection risk was re-evaluated throughout the course of therapy, in case of relevant changes in patient status (i.e. surgical intervention or depressed white blood cell count as a result of chemotherapy).

Pet therapy visits were also highly orchestrated affairs. Treatments were conducted in specific designated areas of the hospital, and each handler-dog team had specific areas and times assigned for their visits. Pet therapy visits began with the patient meeting a program "leash-less volunteer" at the treatment site, at which time the volunteer would review the program and consent the patient. The leash-less volunteer would then go to the hospital lobby to meet the handler-dog team, and escort the team to the treatment area or patient room. Clean sheets were placed on the bed or lap prior to the dog's visit. Alcohol-based hand hygiene solution was used to clean hands before and after petting the dogs. After the visit, the sheet was folded carefully and placed with the dirty linen. Environmental Services followed up to clean the entire area after each animal visit.

This program began with one ward (pediatrics) and grew over the next 16 years to include 28 areas of the hospital. Despite an average of 20,000 contacts per year (counting patients, handlers and staff), not a single infection has been transmitted as a result of this pet therapy program.

Discussion

The authors have reviewed the infection control elements of their pet therapy program in an effort to share their knowledge and experience. They have also provided a table listing the SHEA recommendations alongside their programmatic elements that address those recommendations. This table is very effective in communicating in a concrete way how the recommendations can be put into practice. Overall, the have contributed a useful and inspiring publication to the pet therapy literature.

In reviewing the extreme policies and procedures used by this facility to minimize the risk of infection, some might argue that not all of those procedures are necessary. However, I would remind such opponents that even a single infection could be devastating, and could result in significant health costs and/or financial costs. Those costs far outweigh the costs of all of the time-consuming interventions described. Indeed, the financial and legal costs would be even greater if every manageable effort to prevent such an infection were not taken. This publication gives us all an "exemplar" to inspire us and to guide us in how to best implement pet therapy.

-Reviewed by Ronald Sherman, MD



English Setter Dog, Guido Daniele, used with permission from Guido Daniele

Pet Therapy Reviews (cot'd)

Journal Citation

Stergiou A, Tzoufi M, Ntzani E, Varvarousis D, Beris A, Ploumis A. **Therapeutic Effects of Horseback Riding Interventions: A Systematic Review and Meta-analysis.** Am J Phys Med Rehabil. 2017 Mar 1 [Epub ahead of print].

Published Abstract

OBJECTIVE: Equine-assisted therapies, such as therapeutic riding and hippotherapy, are believed to have positive physical and emotional effects in individuals with neuromotor, developmental, and physical disabilities. The purpose of this review was to determine whether therapeutic riding and hippotherapy improve balance, motor function, gait, muscle symmetry, pelvic movement, psychosocial parameters, and the patients' overall quality of life. ***DESIGN***: In this study, a literature search was conducted on MEDLINE, CINAHL, MBASE, SportDiscus, Cochrane Database of Systematic Reviews, Cochrane Controlled Trials Register, PEDro, DARE, Google Scholar, and Dissertation Abstracts. Only studies with a control / comparison group or self-controlled studies performing preintervention and postintervention assessment were included. Excluded were (1) studies not providing data on baseline score or end-point outcome, (2) single-subject studies, (3) studies providing only qualitative data, and (4) studies that used a mechanical horse. Sixteen trials were included. The methodologic quality of each study was evaluated using Downs and Black quality assessment tool. ***RESULTS***: Most of the studies showed a trend toward a beneficial effect of therapeutic riding and hippotherapy on balance and gross motor function. The meta-analysis showed improvement in both the Berg Balance Scale and the Gross Motor Function Measure in therapeutic riding and hippotherapy programs. ***CONCLUSION***: Programs such as therapeutic riding and hippotherapy are a viable intervention option for patients with balance, gait, and psychomotor disorders.

Context

Let us begin by defining the two terms used in this study to describe therapeutic horseback riding. The terms used in this article to refer to a therapeutic activity with the help of the horse are therapeutic riding (TR) and hippotherapy (HT). Together, they are sometimes referred to as "equine-assisted activities and therapies." The term "therapeutic riding" is used to denote the adaptive or modified sport of equitation (riding on horseback), with the purpose of contributing to the cognitive, physical, emotional, and/or social wellbeing of people with disabilities. The term "hippotherapy" is used to describe a hippotherapy health professional's use of the movement of the horse to address the limitations or disabilities of patients with neuromotor, developmental and physical disabilities. Hippotherapy might be prescribed to address problems with posture, balance, mobility, walking energy expenditure, function, and/or sensory abilities.

Participants in a therapeutic horseback riding program have a wide variety of underlying physical, functional, mental, or emotional disabilities, including central nervous system disease (such as cerebral palsy, stroke, multiple sclerosis, spinal cord injury), lower motor neuron disorders (including spinal muscular atrophy, Charcot-Marie-Tooth disease, myasthenia gravis, muscular dystrophies, sarcopenia), sensory deficits (for example, blindness, deafness) and conditions along the autism spectrum.
It is clear that a wide variety of patients could benefit from equine assisted treatments, if they are effective for the specific deficit of concern. The purpose of this review was to determine whether therapeutic riding and hippotherapy improve balance, motor function, gait, muscle symmetry, pelvic movement, psychosocial parameters, or overall quality of life. The method of addressing this question was a systematic review of well-controlled scientific studies of equine-assisted therapy.

Findings

This literature review was designed in accordance with the Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) statement (for details, see: www.prisma-statement.org/). The literature search included the following databases: MEDLINE, CINAHL, MBASE, SportDiscus, Cochrane Database of Systematic Reviews, Cochrane Controlled Trials Register, PEDro, DARE, Google Scholar, Scopus, ISI Web of Science, and Dissertation Abstracts. The following search algorithm was used: "therapeutic riding" OR "therapeutic horse riding" OR "therapeutic horseback riding" OR "horse riding" OR "horseback riding" OR hippotherapy OR "equine-assisted therapy" OR "equineassisted movement therapy" OR "equine therapy" OR "equine movement therapy" OR "developmental riding therapy" OR "riding for the disabled." Other sources of published papers included hard copies of Pediatric Physical Therapy, Gait and Posture, Developmental Medicine and Child Neurology, American Journal of Physical Medicine & Rehabilitation, Archives of Physical Medicine and Rehabilitation, and Physiotherapy Theory and Practice, and of the Gait and Posture conference and the American Academy of Cerebral Palsy and Developmental Medicine. The reference lists of the included articles were also searched for additional studies.

For inclusion, published articles needed to be in English, and published on or before February 29, 2016. Subjects need to have impairments in motor function and studies needed to be controlled, and focus on the quantitative effects of HT or TR on postural control, balance, gait, and/or spasticity as well as overall quality of life indicators. Studies were excluded if they did not provide data on baseline score or end-point outcome, if they provided only qualitative data, if they did not use a live horse, if they included additional interventions, or if they studied no more than one subject.

The methodologic quality of each study was evaluated using a Downs and Black quality assessment tool (see www.ncbi.nlm.nih.gov/pmc/articles/PMC1756728/pdf/v052p00377.pdf) by two of the coauthors, independently; differences were resolved by a third investigator.

A total of 16 studies were identified and analyzed. Eight studies assessed the effect of HT and TR in children with cerebral palsy, for a total of 343 subjects (170 in the study groups, 158 in the control groups). Four randomized clinical trials assessed the use of equine-assisted therapy for mobility improvement in the elderly, representing a total of 90 participants (43 in the intervention group, 47 in the control group). Three studies focused on subjects with multiple sclerosis, although one of these studies did not include a separate control group. The total number of participants was 52, with 32 in the intervention group and 20 in a separate control group. One randomized clinical trial assessing the effect of HT on post-stroke individuals was identified. That study included 10 subjects in the intervention group and 10 subjects in the control group, for a total of 20 participants. The studies used a variety of measurable and quantified endpoints, but not all studies used the same endpoints. Most commonly used were the Berg Balance Scale, the Pediatric Balance Scale, or the Gross Motor Function Measure.

Of the 16 studies, only 8 included data that could be subjected to further meta-analysis. For all of these studies, subjects in the TR and HT treatment groups demonstrated higher scores on the Berg Balance Scale and the Gross Motor Function Measure than did control subjects; but these differences did not reach statistical significance.

Discussion

Equine-assisted therapy is increasing in use and popularity. Multiple therapists and facilities can be found throughout the country (see the American Hippotherapy Association, www.americanhippotherapyassociation.org/). Several studies do indeed demonstrate improvements in subjects receiving treatment, compared to those not receiving such treatment. The authors note that "all studies and meta-analysis showed increased scores concerning the impact of HT and TR;" but this difference was not statistically significant. As the authors point out, the number of controlled studies is small, and their endpoints vary greatly. So greatly, in fact, that comparing one study to another (as was done in this meta-analysis) is quite difficult. The effort taken by this research team should be commended, based on their exhaustive search of the literature and their detailed evaluating of each study's design.

Current indications for therapy are broad, and the goals of therapy are varied and often quite subtle. As a result, the few studies that are done are understandably dissimilar and not easily compared. Perhaps one of the most important messages to come out of this study, then, is that future researchers should carefully consider the subjects and endpoints that they study in order to focus their energy on demonstrating reliable, statistically sound, and comparable studies. In fact, it might be worth the time and effort of organizations like the AHA to work with researchers to propose meaningful and measurable endpoints, as well as research priorities – populations and disabilities to focus current research efforts. Multi-center trials are another way to add power to a study, but they add cost and complexity which the field may not yet be equipped to bear.

-Reviewed by Ronald Sherman, MD



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Section II: Biotherapy Citations for Spring 2017

A. Apitherapy and Bee Venom Therapy

Awad, K., Abushouk, A. I., AbdelKarim, A. H., Mohammed, M., Negida, A., and Shalash, A. S. Bee venom for the treatment of Parkinson's disease: How far is it possible? Biomed.Pharmacother. 5-3-2017; 91:295-302. PM: 28477460

ABSTRACT: Parkinson's disease (PD) is the second most common neurodegenerative disease, characterized by progressive loss of dopaminergic neurons in the substantia nigra pars compacta leading to depletion of striatal dopamine and motor symptoms as bradykinesia, resting tremors, rigidity, and postural instability. Current therapeutic strategies for PD are mainly symptomatic and may cause motor complications, such as motor fluctuations and dyskinesia. Therefore, alternative medicine may offer an effective adjuvant treatment for PD. Bee venom therapy (BVT) has long been used as a traditional therapy for several conditions, such as rheumatoid arthritis, asthma, and skin diseases. Experimental and clinical studies showed that BVT could be an effective adjuvant treatment for PD. Several mechanisms were suggested for these findings including the ability of BVT to attenuate neuroinflammation, inhibit apoptosis of dopaminergic neurons, protect against glutamate-induced neurotoxicity, and restore normal dopamine levels in the nigrostriatal pathway. In this article, we reviewed and summarized the literature regarding the potential of BVT for the treatment of PD.

Roshan, N., Rippers, T., Locher, C., and Hammer, K. A. Antibacterial activity and chemical characteristics of several Western Australian honeys compared to manuka honey and pasture honey. Arch.Microbiol. 2017; 199(2):347-355. PM: 27785532

ABSTRACT: The physicochemical parameters and antibacterial activity of 10 Western Australian (WA) and two comparator honeys were determined. Honeys showed a pH range of 4.0-4.7, colour range of 41.3-470.7 mAU, methylglyoxal levels ranging from 82.2 to 325.9 mg kg-1 and hydrogen peroxide levels after 2 h of 22.7-295.5 microM. Antibacterial activity was assessed by the disc diffusion assay, phenol equivalence assay, determination of minimum inhibitory and bactericidal concentrations and a time-kill assay. Activity was shown for all honeys by one or more method, however, activity varied according to which assay was used. Minimum inhibitory concentrations for WA honeys against 10 organisms ranged from 4.0 to >32.0% (w/v). Removal of hydrogen peroxide activity by catalase resulted in decreased activity for several honeys. Overall, the data showed that honeys in addition to those derived from Leptospermum spp. have antimicrobial activity and should not be overlooked as potential sources of clinically useful honey.

B. Helminthic Therapy

Bilal, J., Varma, E., Desai, H., and Sudano, D. G. Helminthic Therapy: A New Era in Immune-Mediated Diseases. J.Clin.Rheumatol. 5-11-2017; PM: 28492420

No Abstract Available.

Dige, A., Rasmussen, T. K., Nejsum, P., Hagemann-Madsen, R., Williams, A. R., Agnholt, J., Dahlerup, J. F., and Hvas, C. L. Mucosal and systemic immune modulation by Trichuris trichiura in a self-infected individual. Parasite Immunol. 2017; 39(1); PM: 27743501

ABSTRACT: Helminthic therapy of immune-mediated diseases has gained attention in recent years, but we know little of how helminths modulate human immunity. In this study, we investigated how self-infection with Trichuris (T.) trichiura in an adult man without intestinal disease affected mucosal and systemic immunity. Colonic mucosal biopsies were obtained at baseline, during T. trichiura infection, and after its clearance following mebendazole treatment. Unexpectedly, the volunteer experienced a Campylobacter colitis following T. trichiura clearance, and this served as a positive infectious control. Trichuris trichiura colonization induced equally increased expressions of T-helper (h)1-, Th2-, Th17- and Treg-associated cytokines and transcription factors, measured by quantitative polymerase chain reaction. We observed several indicators of modulation of systemic immunity during the T. trichiura infection. Plasma eosinophils and anti-Trichuris antibodies rose markedly during the inoculation phase, and a shift towards a Th2-dominated T cell response at the expense of the Th1-response was observed in circulating T cells. Taken together, our findings corroborate that helminths modulate regional and systemic human immunity.

Jabbari, Azad F., Kiaee, F., Rezaei, A., Farid, Hosseini R., Soleimani, N., and Borji, H. Downregulation of immune responses in asthmatic humans by ES products of Marshallagia marshalli. Clin.Respir.J. 2017; 11(1):83-89; PM: 25919312

ABSTRACT: BACKGROUND AND AIMS: Helminths and their products are considered to possess therapeutic capability to control or even prevent immune-mediated diseases. Studies suggest that helminths induce a systemic immunomodulatory network, including regulatory T cells and anti-inflammatory interleukin-10 (IL-10), which might play a key role in the protection against the allergic phenotype. Thus, helminthic therapy is becoming of a major interest, and several researchers are enthusiastically tended to explore its role in allergic diseases. *METHODS*: Peripheral blood mononuclear cells (PBMCs) from 25 asthmatic and 25 healthy human were collected. After isolation of PBMCs, they were stimulated with excretory/secretory (ES) antigen of M. marshalli, in incubator with 5% CO2 , 37 degrees C. Total RNA was isolated from all cells from antigen stimulated and non-stimulated control PBMC in asthmatic and healthy human after 6 h. The concentration of Th1 type cytokines [interferon-gamma (IFN-gamma)] and Th2 type cytokines (IL-4) and T-reg cytokines [transforming growth factor-beta (TGF-beta), IL-10] was determined using real-time polymerase chain reaction. *RESULTS*: Results showed that the IFN-gamma expression was significantly decreased in culture condition with ES Ag of M. marshalli in healthy and asthmatic patients ($P < 0.05$). Similar data were obtained for IL-4 expression in both healthy individuals (<0.006) and asthmatic patients (<0.001). The increment of regulatory cytokines IL-10 and TGF-beta expression was considerably increased in our

investigation. *CONCLUSION*: To our knowledge, this is the first report to document the suppressive effect that the M. marshalli ES product has on PBMSC cell culture of asthmatic patients. The present study provides new insights into understanding the immune modulation governed by parasite-derived products and the development of new asthma treatment strategies.

Laan, L. C., Williams, A. R., Stavenhagen, K., Giera, M., Kooij, G., Vlasakov, I., Kalay, H., Kringel, H., Nejsum, P., Thamsborg, S. M., Wuhrer, M., Dijkstra, C. D., Cummings, R. D., and van, Die, I. The whipworm (Trichuris suis) secretes prostaglandin E2 to suppress proinflammatory properties in human dendritic cells. FASEB J. 2017; 31(2):719-731; PM: 27806992

ABSTRACT: Clinical trials have shown that administration of the nematode Trichuris suis can be beneficial in treating various immune disorders. To provide insight into the mechanisms by which this worm suppresses inflammatory responses, an active component was purified from T. suis soluble products (TsSPs) that suppress---- TNF and IL-12 secretion from LPS-activated human dendritic cells (DCs). Analysis by liquid chromatography tandem mass spectrometry identified this compound as prostaglandin (PG)E2. The purified compound showed similar properties compared with TsSPs and commercial PGE2 in modulating LPS-induced expression of many cytokines and chemokines and in modulating Rab7B and P2RX7 expression in human DCs. Furthermore, the TsSP-induced reduction of TNF secretion from DCs is reversed by receptor antagonists for EP2 and EP4, indicating PGE2 action. T. suis secretes extremely high amounts of PGE2 (45-90 ng/mg protein) within their excretory/secretory products but few related lipid mediators as established by metabololipidomic analysis. Culture of T. suis with several cyclooxygenase (COX) inhibitors that inhibit mammalian prostaglandin synthesis affected the worm's motility but did not inhibit PGE2 secretion, suggesting that the worms can synthesize PGE2 via a COX-independent pathway. We conclude that T. suis secretes PGE2 to suppress proinflammatory responses in human DCs, thereby modulating the host's immune response.-Laan, L. C., Williams, A. R., Stavenhagen, K., Giera, M., Kooij, G., Vlasakov, I., Kalay, H., Kringel, H., Nejsum, P., Thamsborg, S. M., Wuhrer, M., Dijkstra, C. D., Cummings, R. D., van Die, I. The whipworm (Trichuris suis) secretes prostaglandin E2 to suppress proinflammatory properties in human dendritic cells.

Liu, J., Morey, R. A., Wilson, J. K., and Parker, W. Practices and outcomes of self-treatment with helminths based on physicians' observations. J.Helminthol. 2017; 91(3):267-277; PM: 27240605

ABSTRACT: The successful use of helminths as therapeutic agents to resolve inflammatory disease was first recorded 40 years ago. Subsequent work in animal models and in humans has demonstrated that the organisms might effectively treat a wide range of inflammatory diseases, including allergies, autoimmune disorders and inflammation-associated neuropsychiatric disorders. However, available information regarding the therapeutic uses and effects of helminths in humans is limited. This study probes the practices and experiences of individuals 'self-treating' with helminths through the eyes of their physicians. Five physicians monitoring more than 700 self-treating patients were interviewed. The results strongly support previous indications that helminth therapy can effectively treat a wide range of allergies, autoimmune conditions and neuropsychiatric disorders, such as major depression and anxiety disorders. Approximately 57% of the self-treating patients observed by physicians in the study had autism. Physicians reported that

the majority of patients with autism and inflammation-associated co-morbidities responded favourably to therapy with either of the two most popular organisms currently used by self-treaters, Hymenolepis diminuta and Trichuris suis. However, approximately 1% of paediatric patients experienced severe gastrointestinal pains with the use of H. diminuta, although the symptoms were resolved with an anti-helminthic drug. Further, exposure to helminths apparently did not affect the impaired comprehension of social situations that is the hallmark of autism. These observations point toward potential starting points for clinical trials, and provide further support for the importance of such trials and for concerted efforts aimed at probing the potential of helminths, and perhaps other biologicals, for therapeutic use.

Matisz, C. E., Faz-Lopez, B., Thomson, E., Al, Rajabi A., Lopes, F., Terrazas, L. I., Wang, A., Sharkey, K. A., and McKay, D. M. Suppression of colitis by adoptive transfer of helminth antigen-treated dendritic cells requires interleukin-4 receptor-alpha signaling. Sci.Rep. 1-17-2017; 7:40631PM:28094779¶

ABSTRACT: Infection with helminth parasites has been explored as a treatment for autoimmune and inflammatory diseases. As helminth antigens have potent immunomodulation properties capable of inducing regulatory programs in a variety of cell types, transferring cells treated with helminth antigens represents a novel extension to helminth therapy. Previous work determined that transfer of bone marrow-derived dendritic cells (DC) pulsed with a crude extract of the tapeworm Hymenolepis diminuta (HD) can suppress colitis in recipient mice. The present study explored the mechanism of disease suppression and the importance of interleukin (IL)-4 signaling. Transfer of HD-DCs suppressed dinitrobenzene sulfonic acid (DNBS)-induced colitis through activation of recipient IL-4 receptor-alpha. The transferred HD-DCs required IL-4Ralpha and the capacity to secrete IL-10 to drive IL-4 and IL-10 production and to suppress colitis in recipient mice. Treatment of DCs with IL-4 evokes an alternatively activated phenotype, but adoptive transfer of these cells did not affect the outcome of colitis. Collectively, these studies demonstrate the complexity between IL-4 and IL-10 in donor cells and recipient, and the requirement for parasite- and host-derived factors in this novel form of cell therapy. Thus IL-4Ralpha signaling is revealed as a pathway that could be exploited for helminth antigen cell-based therapy.

Parande, Shirvan S., Ebrahimby, A., Dousty, A., Maleki, M., Movassaghi, A., Borji, H., and Haghparast, A. Somatic extracts of Marshallagia marshalli downregulate the Th2 associated immune responses in ovalbumin-induced airway inflammation in BALB/c mice. Parasit.Vectors. 5-12-2017; 10(1):233; PM: 28494800

ABSTRACT: BACKGROUND: Recently the role of gastrointestinal nematodes in modulating the immune responses in inflammatory and immune-mediated conditions such as allergy and autoimmune diseases has been introduced. This is mainly due to the suppressive effects of somatic and excretory secretory (ES) products of nematodes on the immune responses. In this study, we evaluated the immunomodulatory potentials of somatic products of Marshallagia marshalli, a gastrointestinal nematodes of sheep, to suppress the immune-mediated responses in a murine model of allergic airway inflammation. BALB/c mice were intraperitoneally (IP) sensitized with ovalbumin (OVA)/Alum and then challenged with 1% OVA. Somatic products of M. marshalli were administered during each sensitization. The effects of somatic products on development of allergic airway inflammation were evaluated by analyzing inflammatory cells recruitment,

histopathological changes, cytokines production (IL-4, IL-13, IL-10, TGF-beta) and serum antibody titers (IgG1, IgG2a). *RESULTS*: Somatic products of M. marshalli were able to suppress the induction of allergic airway inflammation in mice. Modulation of Th2 type responses (IL-4, IL-13, IgG1) via upregulations of IL-10 and TGF-beta production was observed after injection of somatic products of M. marshalli. In addition, inflammatory cells infiltration and pathological disorders were significantly diminished following administration of somatic products. *CONCLUSIONS*: Our data raised the possibility that helminths could be a potential therapeutic candidate to alleviate the inflammatory conditions in allergic asthma. According to these results, we concluded that M. marshalli may contain immune-modulatory molecules that attenuate allergic airway inflammation via induction of regulatory cytokines. Further investigations are required to identify molecules that might have potentials for development of novel therapeutic targets.

Smallwood, T. B., Giacomin, P. R., Loukas, A., Mulvenna, J. P., Clark, R. J., and Miles, J. J. Helminth Immunomodulation in Autoimmune Disease. Front Immunol. 2017; 8:453; PM: 28484453

ABSTRACT: Helminths have evolved to become experts at subverting immune surveillance. Through potent and persistent immune tempering, helminths can remain undetected in human tissues for decades. Redirecting the immunomodulating "talents" of helminths to treat inflammatory human diseases is receiving intensive interest. Here, we review therapies using live parasitic worms, worm secretions, and worm-derived synthetic molecules to treat autoimmune disease. We review helminth therapy in both mouse models and clinical trials and discuss what is known on mechanisms of action. We also highlight current progress in characterizing promising new immunomodulatory molecules found in excretory/secretory products of helminths and their potential use as immunotherapies for acute and chronic inflammatory diseases.



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C. Ichthyotherapy

No New Publications for Spring 2017

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D. Leech Therapy

Herlin, C., Bertheuil, N., Bekara, F., Boissiere, F., Sinna, R., and Chaput, B. Leech therapy in flap salvage: Systematic review and practical recommendations. Ann.Chir Plast.Esthet. 2017; 62(2):e1-e13; PM: 27427444

ABSTRACT: INTRODUCTION: Medicinal leeches have been part of the therapeutic armamenterium of plastic surgeons for more than 50 years. While their use in hand surgery is a matter of course, their use in salvage of flaps with venous congestion remains facultative depending on teams. *MATERIALS AND METHODS*: We conducted a systematic review of leech therapy for flap salvage between 1960 and 2015, analyzing 121 articles and subsequently taking into consideration 41 studies. In parallel, we collected data from 43 patients for whom leach therapy had recently been applied in treatment of venous insufficiency in pedicled or free flaps after revision surgery had failed to improve flap vascularization, or in cases where flap revision was not appropriate. The data collected pertained to relevant indications, treatment procedure, efficacy, adjuvant therapies, side effects and complications. *RESULTS*: For this indication, the success rate of leech therapy ranged from 65 to 85% (83.7% in our series) according to the situations encountered. Optimal frequency of application ranged from 2 to 8hours, while average overall duration ranged from 4 to 10 days. The number of leeches to be applied can be determined depending on volume of the flap. In 50% of the cases reported in the literature, the patients required transfusion. Antibiotic prophylaxis against Aeromonas is highly advisable. A ciprofloxacin and trimethoprim-sulfametoxazole combination currently appears as the most relevant prophylactic antibiotherapy. *CONCLUSION*: Hirudotherapy is a reliable treatment in cases of patent venous insufficiency of pedicled or free flaps (or when revision surgery is not recommended). Even though the relevant literature is highly heterogeneous, we have attempted to put forward a specific protocol bringing together dosage, delivery route, frequency of administration and appropriate prophylactic antibiotherapy. An algorithm for treatment and management of venous congestion and a practical information sheet have been placed at the disposal of plastic surgery teams.

Iqbal, A., Jan, A., Wajid, M. A., and Tariq, S. Management of Chronic Non-healing Wounds by Hirudotherapy. World J.Plast.Surg. 2017; 6(1):9-17; PM: 28289608

ABSTRACT: A chronic wound is a wound that does not heal in an orderly set of stages and in a predictable amount of time or wounds that do not heal within three months are often considered chronic. Chronic wounds often remain in the inflammatory stage for too long and may never heal or may take years. Chronic wound patients often report pain as dominant in their lives. Persistent pain is the main problem for patients with chronic ulcers. Many wounds pose no challenge to the body's innate ability to heal; some wounds, however, may not heal easily either because of the severity of the wounds themselves or because of the poor state of health of the individual. Any wound that does not heal within a few weeks should be examined by a healthcare professional because it might be infected, might reflect an underlying disease.

E. Mammals- Service & Therapeutic Animals

Berns, G. S., Brooks, A. M., Spivak, M., and Levy, K. Functional MRI in Awake Dogs Predicts Suitability for Assistance Work. Sci.Rep. 3-7-2017; 7:43704; PM: 28266550

ABSTRACT: The overall goal of this work was to measure the efficacy of fMRI for predicting whether a dog would be a successful service dog. The training and imaging were performed in 49 dogs entering service training at 17-21 months of age. 33 dogs completed service training and were matched with a person, while 10 were released for behavioral reasons (4 were selected as breeders and 2 were released for medical reasons.) After 2 months of training, fMRI responses were measured while each dog observed hand signals indicating either reward or no reward and given by both a familiar handler and a stranger. Using anatomically defined ROIs in the caudate, amygdala, and visual cortex, we developed a classifier based on the dogs' subsequent training outcomes. The classifier had a positive predictive value of 94% and a negative predictive value of 67%. The area under the ROC curve was 0.91 (0.80 with 4-fold cross-validation, P = 0.01), indicating a significant predictive capability. The magnitude of response in the caudate was positively correlated with a successful outcome, while the response in the amygdala depended on the interaction with the visual cortex during the stranger condition and was negatively correlated with outcome (higher being associated with failure). These results suggest that, as indexed by caudate activity, successful service dogs generalize associations to hand signals regardless who gives them but without excessive arousal as measured in the amygdala.

Champagne, D., Corriveau, H., and Dugas, C. Effect of Hippotherapy on Motor Proficiency and Function in Children with Cerebral Palsy Who Walk. Phys.Occup.Ther.Pediatr. 2017; 37(1):51-63; PM: 26930110

ABSTRACT: AIMS: To evaluate the effects of hippotherapy on physical capacities of children with cerebral palsy. *METHODS*: Thirteen children (4-12 years old) with cerebral palsy classified in Gross Motor Function Classification System Level I or II were included in this prospective quasi-experimental ABA design study. Participants received 10 weeks of hippotherapy (30 min per week). Gross motor function and proficiency were measured with the Bruininks-Oseretski Motor Proficiency short form [BOT2-SF]) and the Gross Motor Function Measure-88 [GMFM-88] (Dimension D and E) twice before the program (T1 and T1'), immediately after (T2), and 10 weeks following the end of the program (T3). *RESULTS*: Mean scores for dimensions D and E of the GMFM-88 Dimension scores (p = .005) and three out of the eight items of the BOT2-SF (fine motor precision (p = .013), balance (p = .025), and strength (p = .012) improved between baseline and immediately after intervention; mean scores immediately following and 10 weeks following intervention did not differ. *CONCLUSIONS*: Hippotherapy provided by a trained therapist who applies an intense and graded session for 10 weeks can improve body functions and performance of gross motor and fine motor activities in children with cerebral palsy.

Fecteau, S. M., Boivin, L., Trudel, M., Corbett, B. A., Harrell, F. E., Jr., Viau, R., Champagne, N., and Picard, F. Parenting stress and salivary cortisol in parents of children with autism spectrum disorder: Longitudinal variations in the context of a service dog's presence in the family. Biol.Psychol. 2017; 123:187-195; PM: 27986514

ABSTRACT: A significant portion of parents of children with autism spectrum disorder

report high levels of stress related to parenting responsibilities, which have been linked to abnormal cortisol patterns. This study seeks to better understand the parents' adaptation to caregiving demands and use of a service dog, by taking into account longitudinal variations in salivary cortisol and perception of parental stress. Salivary cortisol was collected one day per week for 15 weeks by 98 primary caregivers of children with ASD. Overall, parents perceived high levels of stress at baseline. Mean morning cortisol increase was below expected levels for healthy adults, and perception of stress predicted morning cortisol activity. Hypocorticolism related to chronic stress may be present in parents of children with ASD. Longitudinal analysis revealed that the presence of a service dog in the family had an effect on parenting stress, wakening and morning cortisol levels.

Fjeldstad, C. and Pardo, G. Immediate Effect of a Service Dog on Walking Speed in Individuals with Multiple Sclerosis and Gait Dysfunction: A Pilot Study. Int.J.MS Care. 2017; 19(1):40-41; PM: 28243185

No Abstract available.

Glintborg, C. and Hansen, T. G. B. How Are Service Dogs for Adults with Post Traumatic Stress Disorder Integrated with Rehabilitation in Denmark? A Case Study. Animals.(Basel). 4-25-2017; 7(5); PM: 28441333

ABSTRACT: A severe mental illness like Post Traumatic Stress Disorder (PTSD) is known to have psychosocial consequences that can lead to a decreased quality of life. Research in Animal-Assisted Therapy (AAT) has revealed that the presence of a dog can have a positive effect on health, e.g., increase quality of life and lessen depression and anxiety. However, canine companionship is not a catch-all solution. Previous research has revealed methodological limitations that prohibit any clear conclusions, as well as a sparsity of critical reflection in anecdotal reports and case studies, which means that more research is needed to contextualize the findings. There has been an increasing interest in animal-assisted intervention in Denmark in recent years. Previously, authorities could only grant service dogs to adults with physical disabilities, but now this has been extended to adults with mental illnesses. Therefore, it has become important to explore how these service dogs are incorporated into rehabilitation practices in mental health, and how rehabilitation professionals react to the use of service dogs. This paper is a case study of a person who suffers from PTSD. This study examines how the person describes the significance of having a dog during her rehabilitation process, and how this is integrated with existing rehabilitation. The case study has been developed based on a semi-structured interview. A Thematic Content analysis was used to reveal dominant patterns and categories. This study revealed a lack of communication and collaboration between public administration (social service), service dog providers, health rehabilitation services, and providers of psychological treatment. It also revealed limited access for the dog to public services, limited success in incorporating the dog into goal-directed treatment and rehabilitation procedures, a strongly felt emotional support from the dog, and a perceived stigma by having the dog wearing a vest with the words "mentally ill" printed on it.

Hall, S. S., MacMichael, J., Turner, A., and Mills, D. S. A survey of the impact of owning a service dog on quality of life for individuals with physical and hearing disability: a pilot study. Health Qual.Life Outcomes. 3-29-2017; 15(1):59; PM: 28356121

ABSTRACT: BACKGROUND: Quality of life refers to a person's experienced standard of health, comfort and happiness and is typically measured using subjective self-report scales. Despite increasing scientific interest in the value of dogs to human health and the growing demand for trained service dogs, to date no research has reported how service dogs may affect client perceptions of quality of life. *METHOD*: We compared quality of life scores on the 16 item Flanagan quality of life scale from individuals who owned a trained service dog with those who were eligible to receive a dog, but did not yet have one (waiting list control). Data were analysed separately from two groups; those with a service dog trained for individuals with physical disabilities (with physical service dog: n = 72; waiting for a service dog: n = 24; recruited from Dogs for Good database) and those with a hearing service dog (with hearing service dog = 111; waiting for a service dog = 30; recruited from Hearing Dogs for Deaf People database). *RESULTS*: When controlling for age and gender individuals scored higher on total quality of life scores if they owned a service dog or a hearing service dog, but this was only statistically significant for those with a service dog. Both groups (physical service dog and hearing service dog) scored significantly higher on items relating to health, working, learning and independence if they owned a service dog, in comparison to those on the waiting list. Those with a physical service dog also scored significantly higher on items relating to recreational activities (including items relating to reading/listening to music, socialising, creative expression), and those involving social interactions (including items relating to participating in organisations, socialising, relationship with relatives). Additionally, those with a physical service dog scored higher on understanding yourself and material comforts than those on the waiting list control. In contrast, those with a hearing service dog appeared to receive fewer benefits on items relating to social activities. *CONCLUSIONS*: Owning a service dog can bring significant specific and potentially general benefits to the quality of life of individuals with physical disabilities and hearing impairments. These benefits may have considerable implications for individuals with disabilities, society and the economy by promoting independence, learning and working abilities.

Hsieh, Y. L., Yang, C. C., Sun, S. H., Chan, S. Y., Wang, T. H., and Luo, H. J. Effects of hippotherapy on body functions, activities and participation in children with cerebral palsy based on ICF-CY assessments. Disabil.Rehabil. 2017; 39(17):1703-1713; PM: 27440177

ABSTRACT: PURPOSE: To evaluate the effects of hippotherapy on body functions, activities, and participation in children with CP of various functional levels by using the International Classification of Functioning, Disability and Health-Children and Youth (ICF-CY) checklist. *METHODS*: Fourteen children with cerebral palsy (CP) (3-8 years of age) were recruited for a 36-week study composed of baseline, intervention, and withdrawal phases (12 weeks for each phase, ABA design). Hippotherapy was implemented for 30 min once weekly for 12 consecutive weeks during the intervention phase. Body Functions (b) and Activities and Participation (d) components of the ICF-CY checklist were used as outcome measures at the initial interview and at the end of each phase. *RESULTS*: Over the 12 weeks of hippotherapy, significant improvements in ICF-CY qualifiers were found in neuromusculoskeletal and movement-related functions (b7), mobility (d4) and major life areas (d8) and, in particular, mobility of joint functions (b710), muscle tone functions (b735), involuntary movement reaction functions (b755), involuntary movement functions

(b765), and play (d811) (all p < 0.05) when compared with baseline. *CONCLUSION*: This study demonstrated the beneficial effects of hippotherapy on body functions, activities, and participation in children with CP. Implications for Rehabilitation ICF-CY provides a comprehensive overview of functioning and disability and constitutes a universal language for identifying the benefits of hippotherapy in areas of functioning and disability in children with CP. In children with CP, hippotherapy encourages a more complementary approach that extends beyond their impairments and limitations in body functions, activities, and participation. The effect of hippotherapy was distinct from GMFCS levels and the majority of improvements were present in children with GMFCS levels I-III.

Leveille, A., Rochette, A., and Mainville, C. Perceived risks and benefits of hippotherapy among parents of children currently engaged in or waiting for hippotherapy: A pilot study. Physiother.Theory.Pract. 2017; 33(4):269-277; PM: 28379061

ABSTRACT: OBJECTIVE: Explore the perceived risks and benefits of hippotherapy among parents of children currently engaged in or waiting rehabilitation using hippotherapy. *METHOD*: Phenomenological qualitative exploratory pilot study. An interview guide validated by experts was used to conduct the interviews. Summaries were written to capture first impressions. One team member coded the transcripts and the coding was validated by the research team through discussion until consensus was reached. *RESULTS*: The average age of the participants (n = 4) was 37.3 +/- 6.6 years. The few risks they perceived related to physical injuries. Lack of knowledge of contraindications, lack of fear, minimization of risks, and risk-attenuation factors also emerged as important themes. Benefits accounted for a large part of the content of the interviews and were grouped under 13 themes, including motor and postural control, enjoyment and the development of a special relationship. *CONCLUSION*: Minimization of the perceived risks compared to the numerous perceived benefits could create clinical issues such as the client putting self at risk of injuries (e.g., bites, falls, and kicks) if not cautious enough or complications insufficiently prevented, which suggests the need to develop educational activities for an informed consent to this type of rehabilitation.

mmann-Reiffer, C., Bastiaenen, C. H., Meyer-Heim, A. D., and van Hedel, H. J. Effectiveness of robot-assisted gait training in children with cerebral palsy: a bicenter, pragmatic, randomized, cross-over trial (PeLoGAIT). BMC.Pediatr. 3-2-2017; 17(1):64; PM: 28253887

ABSTRACT: BACKGROUND: Walking ability is a priority for many children with cerebral palsy (CP) and their parents when considering domains of importance regarding treatment interventions. Partial body-weight supported treadmill training has become an established therapeutic treatment approach to address this demand. Further, new robotic rehabilitation technologies have increasingly been implemented in the clinical setting to allow for longer training sessions with increased step repetitions while maintaining a consistent movement pattern. But the current evidence about its clinical effectiveness in pediatric rehabilitation is weak. The aim of this research project is therefore to investigate the effectiveness of robot-assisted gait training on improvements of functional gait parameters in children with cerebral palsy. *METHODS/DESIGN*: Children aged 6 to 18 years with bilateral spastic cerebral palsy who are able to walk at least 14 m with or without walking aids will be recruited in two pediatric therapy centers in Switzerland. Within a pragmatic cross-over design with randomized treatment sequences, they perform 5 weeks of robot-assisted gait training (three times per week with a maximum of 45 min walking time each) or a 5-week period of standard treatment,

which is individually customized to the needs of the child and usually consists of 1-2 sessions of physiotherapy per week and additional hippotherapy, circuit training as well as occupational therapy as necessary. Both interventions take place in an outpatient setting. The percentage score of the dimension E of the Gross Motor Function Measure-88 (GMFM-88) as primary outcome as well as the dimension D of the GMFM-88, 6-minute and 10-meter walking tests as secondary outcomes are assessed before and at the end of each intervention period. Additionally, a 5-week follow-up assessment is scheduled for the children who are assigned to the standard treatment first. Treatment effects, period effects as well as follow-up effects are analyzed with paired analyses and independent test statistics are used to assess carry-over effects. *DISCUSSION*: Although robot-assisted gait training has become an established treatment option to address gait impairments, evidence for its effectiveness is vague. This pragmatic trial will provide important information on its effects under clinical outpatient conditions. TRIAL *REGISTRATION*: ClinicalTrials.gov: NCT00887848 . Registered 23 April 2009.

Montross-Thomas, L. P., Meier, E. A., Reynolds-Norolahi, K., Raskin, E. E., Slater, D., Mills, P. J., MacElhern, L., and Kallenberg, G. Inpatients' Preferences, Beliefs, and Stated Willingness to Pay for Complementary and Alternative Medicine Treatments. J.Altern.Complement Med. 2017; 23(4):259-263; PM: 28112554

ABSTRACT: OBJECTIVES: Research demonstrates the benefits of complementary and alternative medicine (CAM) in myriad environments. Yet, the majority of CAM services are offered in outpatient settings. Incorporating CAM into hospital settings may lead to increased patient comfort, well-being, and overall satisfaction with hospital admissions. Few studies have examined CAM services among inpatients. Therefore, this study assessed inpatients' preferences and beliefs regarding CAM, as well as their stated willingness to pay for these services. *DESIGN*: Adult patients (n = 100), ranging in age from 19-95 years (M = 53 years; SD = 19.2 years), were recruited during their hospitalization in the University of California, San Diego, Healthcare System. The inpatients completed a brief individual interview to gather their perspectives on common CAM services, including acupuncture, aromatherapy, art therapy, guided imagery, healthy food, humor therapy, massage therapy, music therapy, pet therapy, Reiki, and stress management. Inpatients were asked which CAM therapies they perceived as being potentially the most helpful, their willingness to pay for those therapies, and their perceived beliefs regarding the use of those therapies. *RESULTS*: Inpatients most commonly perceived healthy food (85%), massage therapy (82%), and humor therapy (70%) to be the most helpful, and were most willing to pay for healthy food (71%), massage therapy (70%), and stress management (48%). Inpatients most commonly believed CAM treatments would provide relaxation (88%), increase well-being (86%), and increase their overall satisfaction with the hospitalization (85%). *CONCLUSIONS*: This study suggests that CAM services may be a beneficial addition to hospitals, as demonstrated by inpatients' interest and stated willingness to pay for these services. These findings may help organizational leaders when making choices regarding the development of CAM services within hospitals, particularly since a significant percentage of inpatients reported that CAM services would increase their overall satisfaction with the hospitalization. These results merit further attention given the need to increase cost savings while enhancing the overall patient experience in today's medical marketplace.

Mudge, S., Rewi, D., and Channon, A. Identifying an outcome measure to assess the impact of Mobility Dogs. Disabil.Rehabil.Assist.Technol. 2017; 12(1):73-83; PM: 26315326

ABSTRACT: PURPOSE: Mobility Dogs(R) trains dogs to work with people with physical disabilities to increase independence, confidence, self-esteem and participation. Mobility Dogs(R) seeks to critically evaluate and improve its services as it grows. This study aimed to identify and implement a standardised outcome measure into practice at Mobility Dogs(R). *METHOD*: Based on the Consolidated Framework for Implementation Research and guided by a steering group of key stakeholders, a three-phase approach was developed to identify and assess an outcome measure. The steering group highlighted the organisation's specific needs, selected participation as the assessment domain and identified core utility requirements of the measure. A comprehensive review of evidence was undertaken to identify and rank potential measures according to the specified needs. *RESULTS*: Of the seven participation outcome measures that met inclusion criteria, the three highest ranked measures were critically evaluated by the steering group to determine suitability against the organisation's needs. The Impact on Participation and Autonomy (IPA) was selected for implementation into practice at Mobility Dogs(R). *CONCLUSION*: Use of the IPA is an important first step for Mobility Dogs(R) to test the benefits of trained service dogs. This process could be replicated by other service dog organisations to identify outcome measures to assess their own services. Implications for Rehabilitation Service dogs (such as Mobility Dogs(R) in New Zealand) assist people living with physical impairments by performing tasks, however there is limited evidence on outcomes. The process for selecting an appropriate outcome measure for Mobility Dogs(R) involving partnership between Mobility Dogs(R) personnel and academics was an effective way to steer the project by determining important properties of the measure, before a search of the literature was undertaken. While the IPA was selected as the most appropriate outcome measure for use at Mobility Dogs(R), it was the process that is valuable to replicate if other organizations wish to select an outcome measure for use in their own practice.

Petersen, S., Houston, S., Qin, H., Tague, C., and Studley, J. The Utilization of Robotic Pets in Dementia Care. J.Alzheimers.Dis. 2017; 55(2):569-574; PM: 27716673

ABSTRACT: BACKGROUND: Behavioral problems may affect individuals with dementia, increasing the cost and burden of care. Pet therapy has been known to be emotionally beneficial for many years. Robotic pets have been shown to have similar positive effects without the negative aspects of traditional pets. Robotic pet therapy offers an alternative to traditional pet therapy. *OBJECTIVE*: The study rigorously assesses the effectiveness of the PARO robotic pet, an FDA approved biofeedback device, in treating dementia-related symptoms. *METHODS*: A randomized block design with repeated measurements guided the study. Before and after measures included reliable, valid tools such as: RAID, CSDD, GDS, pulse rate, pulse oximetry, and GSR. Participants interacted with the PARO robotic pet, and the control group received standard activity programs. Five urban secure dementia units comprised the setting. *RESULTS*: 61 patients, with 77% females, average 83.4 years in age, were randomized into control and treatment groups. Compared to the control group, RAID, CSDD, GSR, and pulse oximetry were increased in the treatment group, while pulse rate, pain medication, and psychoactive medication use were decreased. The changes in GSR, pulse oximetry, and pulse rate over time were plotted for both groups. The difference between groups was consistent throughout the 12-week study for pulse oximetry and pulse rate, while GSR had several weeks when changes were similar between groups. *CONCLUSIONS*: Treatment

with the PARO robot decreased stress and anxiety in the treatment group and resulted in reductions in the use of psychoactive medications and pain medications in elderly clients with dementia.

Rigby, B. R., Gloeckner, A. R., Sessums, S., Lanning, B. A., and Grandjean, P. W. Changes in Cardiorespiratory Responses and Kinematics With Hippotherapy in Youth With and Without Cerebral Palsy. Res.Q.Exerc.Sport. 2017; 88(1):26-35; PM: 28075704

ABSTRACT: PURPOSE: The purpose of this study was to characterize pelvic displacement and cardiorespiratory responses to simulated horseback riding and walking in youth with cerebral palsy and to compare responses to youth without cerebral palsy before and after 8 weeks of hippotherapy. *METHOD*: Eight youth with cerebral palsy (Mage = 10 +/- 4 years; Mheight = 137 +/- 24 cm; Mweight = 32 +/- 16 kg) and 8 youth without cerebral palsy (Mage = 11 +/- 2 years; Mheight = 149 +/- 14 cm; Mweight = 48 +/- 15 kg) underwent a hippotherapy intervention. Participants completed simulated horseback riding at an intensity approximating a fast walk (0.65 Hz) and walked on a treadmill (1 mph, 0% grade) before and after hippotherapy. Pelvic displacement along the anterior-posterior, vertical, and medial-lateral axes, heart rate, oxygen consumption, ventilation, and blood pressure were measured at rest and during steady-state exercise in both exercise modes. *RESULTS*: Kinematics and cardiorespiratory responses were similar between the 2 groups during simulated horseback riding ($p > .05$ for all) before the intervention. Significantly greater cardiorespiratory responses were observed in the youth with cerebral palsy compared with the group without cerebral palsy while walking before and after the intervention ($p < .05$, effect sizes 26% to 237% greater). Eight weeks of hippotherapy did not alter responses, but anecdotal improvements in gait, balance, posture, and range of motion were observed in those with cerebral palsy. *CONCLUSION*: These results contribute to our understanding regarding the efficacy of hippotherapy as an intervention to improve functional abilities in those with cerebral palsy.

Schoenfeld-Tacher, R. M. and Kogan, L. R. Professional Veterinary Programs' Perceptions and Experiences Pertaining to Emotional Support Animals and Service Animals, and Recommendations for Policy Development. J.Vet.Med.Educ. 2017; 44(1):166-178; PM: 27689948

ABSTRACT: Given the unique nature of programs in professional veterinary medicine (PVM), the increasing numbers of students requesting accommodations for emotional support animals (ESAs) in higher education settings is of growing interest to student affairs and administrative staff in PVM settings. Since the legislation pertaining to this type of support animal differs from the laws governing disability service animals, colleges and universities now need to develop new policies and guidelines. Representatives from a sample of 28 PVM programs completed a survey about the prevalence of student requests for ESAs and service animals. PVM associate deans for academic affairs also reported their perceptions of this issue and the challenges these requests might pose within veterinary teaching laboratories and patient treatment areas. Responses indicated that approximately one third of PVM programs have received requests for ESAs (32.1%) in the last 2 years, 17.9% have had requests for psychiatric service animals, and 17.9% for other types of service animals. Despite this, most associate deans reported not having or not being aware of university or college policies pertaining to these issues. Most associate deans are interested in learning more about this topic. This paper provides general recommendations for establishing university or PVM program policies.

Sollami, A., Gianferrari, E., Alfieri, M., Artioli, G., and Taffurelli, C. Pet therapy: an effective strategy to care for the elderly? An experimental study in a nursing home. Acta Biomed. 3-14-2017; 88(1 -S):25-31; PM: 28327492

ABSTRACT: BACKGROUND AND AIM: There has recently been a growing interest towards patients' affective and emotional needs, especially in relational therapies, which are considered vital as to increase the understanding of those needs and patients' well-being. In particular, we paid attention to those patients who are forced to spend the last phase of their existence in residential facilities, namely elderly people in nursing homes, who often feel marginalized, useless, depressed, unstimulated or unable to communicate. The aim of this study is to verify the effectiveness of pet therapy in improving well-being in the elderly living in a nursing home. *METHODS*: This is a longitudinal study with before and after intervention variables measurement in two groups of patients of a nursing home for elderly people. One group followed an AAI intervention (experimental group) the other one did not (control group). As to perform an assessment of well-being we measured the following dimensions in patients: anxiety (HAM-A), depression (GDS), apathy (AES), loneliness (UCLA), and quality of life (QUALID). Both groups filled the questionnaires as to measure the target variables (time 0). Once finished the scheduled meetings (time 1), all the participants, including the control group, filled the same questionnaires. *RESULTS*: In accordance with scientific evidence the results confirmed a significant reduction of the measured variables. Especially for the quality of life, which showed a greater reduction than the other. *CONCLUSIONS*: The implementation and success of the Pet Therapy could have a great emotional and social impact, bringing relief to patients and their family members, but also to health professionals.

Stergiou, A., Tzoufi, M., Ntzani, E., Varvarousis, D., Beris, A., and Ploumis, A. Therapeutic Effects of Horseback Riding Interventions: A Systematic Review and Meta-analysis. Am.J.Phys.Med.Rehabil. 3-1-2017; PM: 28252520

ABSTRACT: OBJECTIVE: Equine-assisted therapies, such as therapeutic riding and hippotherapy, are believed to have positive physical and emotional effects in individuals with neuromotor, developmental, and physical disabilities. The purpose of this review was to determine whether therapeutic riding and hippotherapy improve balance, motor function, gait, muscle symmetry, pelvic movement, psychosocial parameters, and the patients' overall quality of life. *DESIGN*: In this study, a literature search was conducted on MEDLINE, CINAHL, MBASE, SportDiscus, Cochrane Database of Systematic Reviews, Cochrane Controlled Trials Register, PEDro, DARE, Google Scholar, and Dissertation Abstracts. Only studies with a control/comparison group or self-controlled studies performing preintervention and postintervention assessment were included. Excluded were (1) studies not providing data on baseline score or end-point outcome, (2) single-subject studies, (3) studies providing only qualitative data, and (4) studies that used a mechanical horse. Sixteen trials were included. The methodologic quality of each study was evaluated using Downs and Black quality assessment tool. *RESULTS*: Most of the studies showed a trend toward a beneficial effect of therapeutic riding and hippotherapy on balance and gross motor function. The meta-analysis showed improvement in both the Berg Balance Scale and the Gross Motor Function Measure in therapeutic riding and hippotherapy programs. *CONCLUSION*: Programs such as therapeutic riding and hippotherapy are a viable intervention option for patients with balance, gait, and psychomotor disorders.

Wonsetler, E. C. and Bowden, M. G. A systematic review of mechanisms of gait speed change post-stroke. Part 1: spatiotemporal parameters and asymmetry ratios. Top.Stroke Rehabil. 2-21-2017; 1-12; PM: 28220715

ABSTRACT: BACKGROUND: In walking rehabilitation trials, self-selected walking speed (SSWS) has emerged as the dominant outcome measure to assess walking ability. However, this measure cannot differentiate between recovery of impaired movement and compensation strategies. Spatiotemporal variables and asymmetry ratios are frequently used to quantify gait deviations and are hypothesized markers of recovery. OBJECTIVES: The purpose of this review is to investigate spatiotemporal variables and asymmetry ratios as mechanistic recovery measures in physical therapy intervention studies post-stroke. *METHODS*: A systematic literature search was performed to identify physical therapy intervention studies with a statistically significant change in SSWS post intervention and concurrently collected spatiotemporal variables. Methodological quality was assessed using the Cochrane Collaboration's tool. Walking speed, spatiotemporal, and intervention data were extracted. *RESULTS*: 46 studies met the inclusion criteria, 41 of which reported raw spatiotemporal measures and 19 reported asymmetry ratio calculations. Study interventions included: aerobic training (n = 2), functional electrical stimulation (n = 5), hippotherapy (n = 2), motor dual task training (n = 2), multidimensional rehabilitation (n = 4), robotics (n = 4), sensory stimulation training (n = 8), strength/resistance training (n = 4), task specific locomotor rehabilitation (n = 9), and visually guided training (n = 6). *CONCLUSIONS*: Spatiotemporal variables help describe gait deviations, but scale to speed, so consequently, may not be an independent factor in describing functional recovery and gains. Therefore, these variables are limited in explaining mechanistic changes involved in improving gait speed. Use of asymmetry measures provides additional information regarding the coordinative requirements for gait and can potentially indicate recovery. Additional laboratory-based mechanistic measures may be required to truly understand how walking speed improves.

Yarborough, B. J., Owen-Smith, A. A., Stumbo, S. P., Yarborough, M. T., Perrin, N. A., and Green, C. A. An Observational Study of Service Dogs for Veterans With Posttraumatic Stress Disorder. Psychiatr.Serv. 3-15-2017; appips201500383; PM: 28292227

ABSTRACT: OBJECTIVES: This study examined needs related to posttraumatic stress disorder (PTSD), assistance by service dogs, and feasibility of data collection among veterans receiving service dogs. *METHODS*: Questionnaires assessed PTSD-related needs and services performed or expected to be performed by service dogs among 78 veterans who had or were on a wait list for a service dog (average age, 42; women, 31%). Analyses compared pre-post characteristics among 22 veterans who received a service dog as part of the study (91% follow-up; average follow-up=3.37+/-2.57 months). *RESULTS*: Veterans reported that the most important services performed were licking or nudging veterans to help them "stay present," preventing panic, and putting space between veterans and strangers. High follow-up rates and improvements in outcomes with moderate to large effect sizes among recipients of study-provided dogs suggest further study is warranted. *CONCLUSIONS*: Service dogs may be feasible supports for veterans with PTSD; randomized clinical trials are needed to assess effectiveness.

F. Maggot Debridement Therapy

Daeschlein, G., Napp, M., Assadian, O., von, Podewils S., Reese, K., Hinz, P., Matiasek, J., Spitzmueller, R., Humphreys, P., Junger, M., and Kramer, A. Viability of Lucilia sericata maggots after exposure to wound antiseptics. Int.Wound.J. 2017; 14(3):512-515; PM: 27396987

ABSTRACT: After debridement and before dressing a wound with maggots of calliphorid flies, one frequently performed step is the application of antiseptics to the prepared wound bed. However, the concomitant application of antiseptic agents during maggot therapy is regarded controversial as antiseptics may interfere with maggots' viability. In this experimental in vitro study, the viability of fly maggots was investigated after exposure to various antiseptics frequently used in wound care. Here, we show that Lucilia sericata fly maggots can survive up to an hour's exposure to wound antiseptics such as octenidine, povidone-iodine or polihexanide. Concomitant short-term application of wound antiseptics together with maggots on wound beds is tolerated by larvae and does not impair their viability.

Dauros, Singorenko P., Rosario, R., Windsor, J. A., Phillips, A. R., and Blenkiron, C. The transcriptional responses of cultured wound cells to the excretions and secretions of medicinal Lucilia sericata larvae. Wound.Repair Regen. 2017; 25(1):51-61; PM: 27868332

ABSTRACT: Maggots, through their excretions and secretions (ES), promote wound healing by removing necrotic tissue, counter bacterial infection, and activate wound associated cells. We investigated the effects of a physiological dose of maggot ES on four wound-associated cell types in vitro with Affymetrix gene expression arrays; keratinocytes, endothelial cells, fibroblasts, and monocytes. Keratinocytes showed the fewest ($n = 5$; $p < 0.05$, fold-change +/-2) and smallest fold-changes (up to 2.32x) in gene expression and conversely THP1 monocytes had the most ($n = 233$) and greatest magnitude (up to 44.3x). There were no genes that were altered in all four cell-lines. Gene pathway analysis identified an enrichment of immune response pathways in three of the treated cell-lines. Analyses by quantitative RT-PCR found many genes dynamically expressed in ES dose dependent manner during the three day treatments. Phenotype analyses, however, found no effects of ES on cell viability, proliferation, migration and angiogenesis. ES was 100x less potent at triggering IL-8 secretion than fibroblasts treated with purified bacterial lipopolysaccharide (LPS; in equivalent amounts to that found in ES; approximately 40 EU/ml). Furthermore, co-treatment with LPS and ES decreased the LPS-alone triggered IL-8 secretion by 13%. Although ES had no direct effect on wound cell phenotypes it did partially reduce the immune response to bacterial LPS exposure. These observations were consistent with the profile of transcriptional responses that were dominated by modulation of immune response genes. Maggot therapy may therefore improve wound healing through the secondary effects of these gene changes in the wound cells.

Masiero, F. S., Aquino, M. F., Nassu, M. P., Pereira, D. I., Leite, D. S., and Thyssen, P. J. First Record of Larval Secretions of Cochliomyia macellaria (Fabricius, 1775) (Diptera: Calliphoridae) Inhibiting the Growth of Staphylococcus aureus and Pseudomonas aeruginosa. Neotrop.Entomol. 2017; 46(1):125-129; PM: 27696133

ABSTRACT: Maggot debridement therapy (MDT) consists on the intentional and

controlled application of sterilized larvae of the order Diptera on necrotic skin lesions with the purpose of cleaning necrotic tissue and removing pathogenic bacteria. During MDT, a marked antimicrobial activity has been reported in literature specially associated with antibacterial substances from Lucilia sericata (Meigen); however, regarding Cochliomyia macellaria (Fabricius), little is known. This study aimed to evaluate in vitro inhibition of bacterial growth of Pseudomonas aeruginosa and Staphylococcus aureus in contact with excretions and secretions (ES) from C. macellaria larvae. Larval ES were extracted in sterile distilled water and divided in three groups: ES, containing 400 muL of autoclaved ES; ES+BAC, containing 400 muL of autoclaved ES+0.5-muL bacterial inoculum; and CONT-BAC, containing 400 muL of sterile distilled water +0.5 muL of bacterial inoculum. Aliquots of each experimental group were plated by spreading onto Petri dishes. Seedings were made at 0, 1, 2, 4, and 12 h after the extraction of ES. In ES+BAC groups, inhibition of S. aureus was verified between times 1 and 2 h and P. aeruginosa was inhibited between 0 and 4 h. There was no growth observed in any ES group. In the CONT-BAC groups, the number of colonies from time 4 h became countless for S. aureus and decreased for P. aeruginosa. As reported in the literature, we note here that ES have excellent bactericidal activity for both gram-positive and gram-negative bacteria, and this study shows for the first time the action of the bactericidal activity of exosecretions of C. macellaria against S. aureus and P. aeruginosa.

Mirabzadeh, A., Ladani, M. J., Imani, B., Rosen, S. A., and Sherman, R. A. Maggot therapy for wound care in Iran: a case series of the first 28 patients. J.Wound.Care. 3-2-2017; 26(3):137-143; PM: 28277993

ABSTRACT: OBJECTIVE: The need for improved wound care is receiving considerable attention in the Islamic Republic of Iran. Beginning in 2003, maggot therapy (MT) became part of Iran's effort to advance its wound care technology. The first cohort of patients treated with MT was analysed to evaluate the use of this treatment. *METHOD*: Patients treated with MT at three hospitals in Tehran were analysed retrospectively. Primary outcomes were time to wound debridement and time to wound healing. Factors potentially influencing primary outcomes were also recorded, including demographic factors (such as age, race, gender), wound characteristics, underlying medical illnesses, and treatment attitudes. *RESULTS*: We analysed 28 patients with 29 wounds. Most (55%) of the wounds were ischaemic, neuropathic or mixed-pathology foot ulcers in patients with diabetes. Half were considered unsalvageable. All were completely debrided and subsequently healed with MT, without amputation, grafts, or advanced interventions. Osteomyelitis was present in all cases before MT, but appeared to have been eradicated, without recurrence during at least three years' follow-up. The most common adverse events were malodour, with wound pain reported in two patients. All patients and therapists were pleased with their overall experience. *CONCLUSION*: Maggot therapy can provide advanced wound care even in resource-limited areas. Maggot therapy was very acceptable to the patients and their therapists.

Teh, C. H., Nazni, W. A., Nurulhusna, A. H., Norazah, A., and Lee, H. L. Determination of antibacterial activity and minimum inhibitory concentration of larval extract of fly via resazurin-based turbidometric assay. BMC.Microbiol. 2-16-2017; 17(1):36; PM: 28209130

ABSTRACT: BACKGROUND: Antimicrobial resistance is currently a major global issue. As the rate of emergence of antimicrobial resistance has superseded the rate of discovery and introduction of new effective drugs, the medical arsenal now is experiencing

shortage of effective drugs to combat diseases, particularly against diseases caused by the dreadful multidrug-resistant strains, such as the methicillin-resistant Staphylococcus aureus (MRSA). The ability of fly larvae to thrive in septic habitats has prompted us to determine the antibacterial activity and minimum inhibitory concentrations (MICs) of larval extract of flies, namely Lucilia cuprina, Sarcophaga peregrina and Musca domestica against 4 pathogenic bacteria [Staphylococcus aureus, methicillin-resistant S. aureus (MRSA), Pseudomonas aeruginosa and Escherichia coli] via a simple and sensitive antibacterial assay, resazurin-based turbidometric (TB) assay as well as to demonstrate the preliminary chemical profile of larval extracts using gas chromatography-mass spectrophotometry (GC-MS). *RESULTS*: The resazurin-based TB assay demonstrated that the L. cuprina larval extract was inhibitory against all tested bacteria, whilst the larval extract of S. peregrina and M. domestica were only inhibitory against the MRSA, with a MIC of 100 mg ml-1. Subsequent sub-culture of aliquots revealed that the larval extract of L. cuprina was bactericidal against MRSA whilst the larval extracts of S. peregrina and M. domestica were bacteriostatic against MRSA. The GC-MS analysis had quantitatively identified 20 organic compounds (fatty acids or their derivatives, aromatic acid esters, glycosides and phenol) from the larval extract of L. cuprina; and 5 fatty acid derivatives with known antimicrobial activities from S. peregrina and M. domestica. *CONCLUSION*: The resazurin-based turbidometric assay is a simple, reliable and feasible screening assay which evidently demonstrated the antibacterial activity of all fly larval extracts, primarily against the MRSA. The larval extract of L. cuprina exerted a broad spectrum antibacterial activity against all tested bacteria. The present study revealed probable development and use of novel and effective natural disinfectant(s) and antibacterial agent(s) from flies and efforts to screen more fly species for antibacterial activity using resazurin-based TB assay should be undertaken for initial screening for subsequent discovery and isolation of potential novel antimicrobial substances, particularly against the multi-drug resistant strains.

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G. Olfactory Detection and Diagnosis

Fisher, R. M., Barczak, R. J., varez Gaitan, J. P., Le-Minh, N., and Stuetz, R. M. Odorous volatile organic compound (VOC) emissions from ageing anaerobically stabilised biosolids. Water Sci.Technol. 2017; 75(7):1617-1624; PM: 28402302

ABSTRACT: Opportunities for the beneficial re-use of biosolids are limited by nuisance odour emissions. Volatile organic compounds (VOCs) from anaerobically stabilised biosolids were measured to identify compounds that could contribute to the overall odour character of nuisance emissions. Flux hood sampling and chemical analysis were used to identify VOCs emitted from biosolids as they were stored in ambient conditions. Compounds emitted varied as the biosolid cakes were stored for a period of 50 days. VOCs detected in the biosolids are likely to occur from catchment sources as well as abiotic and biotic generation in the wastewater processing and the biosolids as they are stored. Odour activity values (OAVs) were used to compare odorants. Trimethylamine was the only VOC detected that exceeded the sulfur compounds in terms of OAVs. Other compounds such as limonene, ethyl methyl benzene and acetic acid were detected at concentrations exceeding their olfactory detection limits, however at lower OAVs than sulfur compounds.

Fuermaier, A. B., Hupen, P., De Vries, S. M., Muller, M., Kok, F. M., Koerts, J., Heutink, J., Tucha, L., Gerlach, M., and Tucha, O. Perception in attention deficit hyperactivity disorder. Atten.Defic.Hyperact.Disord. 4-11-2017; PM: 28401487

ABSTRACT: A large body of research demonstrated that individuals with attention deficit hyperactivity disorder (ADHD) suffer from various neuropsychological deficits. In contrast, less is known and only divergent evidence exists on perceptual functions of individuals with ADHD. This is problematic as neuropsychological and perceptual functions are closely interrelated and are often difficult to disentangle in behavioral assessments. This study presents the conduct and results of a systematic literature review on perceptual functions in children and adults with ADHD. This review considers studies using psychophysical methods (objective measurements) and self- and informant reports (subjective measurements). Results indicate that individuals with ADHD have altered perceptual functions in various domains as compared to typically developing individuals. Increased perceptual functions in individuals with ADHD were found with regard to olfactory detection thresholds, whereas reduced perceptual functions were evident for aspects of visual and speech perception. Moreover, individuals with ADHD were found to experience discomfort to sensory stimuli at a lower level than typically developing individuals. Alterations of perceptual functions in individuals with ADHD were shown to be moderated by various factors, such as pharmacological treatment, cognitive functions, and symptom severity. We conclude by giving implications for daily life functioning and clinical practice.

Gros, J., Lavigne, V., Thibaud, F., Gammacurta, M., Moine, V., Dubourdieu, D., Darriet, P., and Marchal, A. Toward a Molecular Understanding of the Typicality of Chardonnay Wines: Identification of Powerful Aromatic Compounds Reminiscent of Hazelnut. J.Agric.Food Chem. 2-8-2017; 65(5):1058-1069; PM: 28064486

ABSTRACT: Chardonnay wines impart a unique complex aroma characterized by its buttery, yellow stone fruit, melon, bready, and woody notes. Among the terms used in

the sensory analysis of these wines, this study investigated hazelnut-like attributes. Multidimensional gas chromatography coupled to olfactometry identified five pyrroles reminiscent of hazelnut: 1-ethylpyrrole-2-carboxaldehyde, 1H-pyrrole, 2-acetyl-1H-pyrrole (first identification in wine), 1-methylpyrrole-2-carboxaldehyde, and 1H-pyrrole-2-carboxaldehyde. Quantitative analyses demonstrated their significantly higher abundance in Chardonnay wines. However, they proved irrelevant in sensory terms, given the low amounts measured in wine compared to their olfactory detection threshold. Nevertheless, the presence of methanethiol derivatives from these pyrroles was investigated in wine. 1-Methylpyrrole-2-methanethiol and 1-ethylpyrrole-2-methanethiol were identified and exhibited hazelnut-like aroma. These compounds, which have not been observed in natural products to date, are potent volatile compounds with detection thresholds of 0.7 and 1.4 ng/L, respectively, in model wine. These findings open up promising perspectives concerning the interpretation of the typical aromatic nuances of some Chardonnay wines.

Poitou, X., Thibon, C., and Darriet, P. 1,8-Cineole in French Red Wines: Evidence for a Contribution Related to Its Various Origins. J.Agric.Food Chem. 1-18-2017; 65(2):383-393; PM: 28060498

ABSTRACT: The aromatic descriptor "green", reflecting grape unripeness in French red wines, is frequently associated with the levels of 3-alkyl-2-methoxypyrazines, particularly 3-isobutyl-2-methoxypyrazine (IBMP), which has bell pepper nuances. Nevertheless, not all green aromatic expressions in red wines correlate with 3-alkyl-2-methoxypyrazine concentrations. This study considered sensory and chemical approaches using Cabernet Sauvignon wines obtained from grapes harvested at one-month intervals during the 2014 and 2015 vintages to investigate other volatile odoriferous compounds. Semipreparative HPLC fractionation of wine extracts revealed a fraction with specific green aromas in the early harvest wines. Its sensory impact was confirmed by omission and reconstitution tests. Then, multidimensional gas chromatography coupled with olfactometry and mass spectrometry (MDGC-O-MS/TOF) was used for molecular characterization of the aroma compounds associated with the green aromas. Surprisingly, eucalyptol (1,8-cineole), with menthol odor was highlighted and assayed at concentrations sometimes above its olfactory detection threshold in Cabernet Sauvignon and Fer Servadou wines. Sensory tests confirmed its impact at several concentrations detected in French red wines (up to 2.61 +/- 0.03 mug/L) on the menthol nuance and overall green perception, particularly via an additive effect with IBMP. Quantitation of 1,8-cineole in Cabernet Sauvignon and Merlot grapes during berry development in 2015 revealed its varietal origin with abundant concentrations in unripe berries and decrease during grape maturation. Moreover, the implication of an invasive plant (Artemisia verlotiorum) growing in certain vineyards was shown to be responsible for increased 1,8-cineole concentrations in some wines.

Sarrafchi, A. and Laska, M. Olfactory Sensitivity for the Mammalian Blood Odor Component Trans-4,5-epoxy-(E)-2-decenal in CD-1 Mice. Perception. 2017; 46(3-4):333-342; PM: 27251166

ABSTRACT: Using a conditioning paradigm and an automated olfactometer, we investigated the olfactory sensitivity of CD-1 mice for the mammalian blood odor component trans-4,5-epoxy-(E)-2-decenal. We found that two of the animals significantly discriminated concentrations down to 3.0 ppt (parts per trillion) from the solvent, and three animals even successfully detected dilutions as low as 0.3 ppt. Intraspecific

comparisons between the olfactory detection thresholds obtained here with those obtained in earlier studies with other odorants show that mice are extraordinarily sensitive to this blood odor component. Interspecific comparisons of olfactory detection thresholds show that human subjects are even more sensitive to trans-4,5-epoxy-(E)-2-decenal than the mice tested here. Both intra- and inter-specific comparisons suggest that neither neuroanatomical properties such as the size of the olfactory epithelium, the total number of olfactory receptor neurons, or the size of olfactory brain structures, nor genetic properties such as the number of functional olfactory receptor genes or the proportion of functional relative to the total number of olfactory receptor genes allow us to reliably predict a species' olfactory sensitivity. In contrast, the results support the notion that the behavioral relevance of an odorant rather than neuroanatomical or genetic properties may determine a species' olfactory sensitivity.



Blue Butterfly, Guido Daniele, used with permission from Guido Daniele

H. Phage Therapy

Abedon, S. T. Information Phage Therapy Research Should Report. Pharmaceuticals. (Basel). 4-30-2017; 10(2); PM: 28468287

ABSTRACT: Bacteriophages, or phages, are viruses which infect bacteria. A large subset of phages infect bactericidally and, consequently, for nearly one hundred years have been employed as antibacterial agents both within and outside of medicine. Clinically these applications are described as phage or bacteriophage therapy. Alternatively, and especially in the treatment of environments, this practice instead may be described as a phage-mediated biocontrol of bacteria. Though the history of phage therapy has involved substantial clinical experimentation, current standards along with drug regulations have placed a premium on preclinical approaches, i.e., animal experiments. As such, it is important for preclinical experiments not only to be held to high standards but also to be reported in a manner which improves translation to clinical utility. Here I address this latter issue, that of optimization of reporting of preclinical as well as clinical experiments. I do this by providing a list of pertinent information and data which, in my opinion, phage therapy experiments ought to present in publications, along with tips for best practices. The goal is to improve the ability of readers to gain relevant information from reports on phage therapy research, to allow other researchers greater potential to repeat or extend findings, to ease transitions from preclinical to clinical development, and otherwise simply to improve phage therapy experiments. Targeted are not just authors but also reviewers, other critical readers, writers of commentaries, and, perhaps, formulators of guidelines or policy. Though emphasizing therapy, many points are applicable to phage-mediated biocontrol of bacteria more generally.

Abouhmad, A., Dishisha, T., Amin, M. A., and Hatti-Kaul, R. Immobilization to Positively Charged Cellulose Nanocrystals Enhances the Antibacterial Activity and Stability of Hen Egg White and T4 Lysozyme. Biomacromolecules. 5-8-2017; 18(5):1600-1608; PM: 28350458

ABSTRACT: Antibacterial bionanostructures were produced from cellulose nanocrystals (CNC) with immobilized lysozyme from hen egg white (HEW) and T4 bacteriophage, respectively. The nanocrystals were prepared from microcrystalline cellulose by ammonium persulfate oxidation with a yield of 68% and having an average size of 250 nm and low polydispersity index. HEW lysozyme (HEWL) and T4 lysozyme (T4L) were immobilized to CNC by different mechanisms including adsorption and covalent coupling to carbodiimide-activated carboxylate groups and to glutaraldehyde-activated aminated CNC (Am-CNC), respectively. The effect of immobilization on the enzymatic activity (both lytic and hydrolytic) and antibacterial activity of the lysozymes was studied using different methods. Am-CNC-lysozyme conjugates retained the highest lytic activity, 86.3% and 78.3% for HEWL and T4L, respectively. They also showed enhanced bactericidal activity with high potency against Gram-positive as well as Gram-negative bacteria in a relatively shorter time as compared to the free enzymes and resulted in extensive cellular damage, as shown by transmission electron microscopy. The enhanced antibacterial activity was correlated with the increase in zeta potential of Am-CNC-lysozyme conjugates. The immobilized lysozyme preparations further exhibited enhanced storage stability at 4 and 22 degrees C.

Achigar, R., Magadan, A. H., Tremblay, D. M., Julia, Pianzzola M., and Moineau, S. Phage-host interactions in Streptococcus thermophilus: Genome analysis of phages isolated in Uruguay and ectopic spacer acquisition in CRISPR array. Sci.Rep. 3-6-2017; 7:43438; PM: 28262818

ABSTRACT: Three cos-type virulent Streptococcus thermophilus phages were isolated from failed mozzarella production in Uruguay. Genome analyses showed that these phages are similar to those isolated elsewhere around the world. The CRISPR1 and CRISPR3 arrays of the three S. thermophilus host strains from Uruguay were also characterized and similarities were noted with previously described model strains SMQ-301, LMD-9 and DGCC7710. Spontaneous bacteriophage-insensitive S. thermophilus mutants (BIMs) were obtained after challenging the phage-sensitive wild-type strain Uy02 with the phage 128 and their CRISPR content was analyzed. Analysis of 23 BIMs indicated that all of them had acquired at least one new spacer in their CRISPR1 array. While 14 BIMs had acquired spacer at the 5'-end of the array, 9 other BIMs acquired a spacer within the array. Comparison of the leader sequence in strains Uy02 and DGCC7710 showed a nucleotide deletion at position -1 in Uy02, which may be responsible for the observed ectopic spacer acquisition. Analysis of the spacer sequences upstream the newly acquired ectopic spacer indicated presence of a conserved adenine residue at position -2. This study indicates that natural strains of S. thermophilus can also acquire spacers within a CRISPR array.

Adabi, E., Saebi, F., Moradi Hasan-Abad, A., Teimoori-Toolabi, L., and Kardar, G. A. Evaluation of an Albumin-Binding Domain Protein Fused to Recombinant Human IL-2 and Its Effects on the Bioactivity and Serum Half-Life of the Cytokine. Iran Biomed.J. 2017; 21(2):77-83; PM: 27805072

ABSTRACT: BACKGROUND: Background: Cancer immunotherapy is a promising strategy for cancer treatment. In this strategy, the immune system is triggered to destroy cancer cells. IL-2 is an important factor in passive cancer immunotherapy that helps modulating some important immune functions. One of the IL-2 limitations is low serum half-life; therefore, repetitive high doses of the injections are required to maintain effective concentrations. High-dose IL-2 therapy results in severe side effects; thus, improvement of its serum half-life would provide therapeutic benefits. *METHODS*: We have investigated a strategy that is able to utilize an albumin-binding domain (ABD) from streptococcal protein G. In this strategy, the fusion protein ABD-rIL-2 binds to serum albumin, which results in improvement of the IL-2 serum half-life. PET26b+ plasmid was used as an expression vector, which encoded rIL-2 and ABD-rIL-2 both fused to pelB secretion signal under the control of the strong bacteriophage T7 promoter. The constructs were expressed in E. coli Rosetta (DE3) and secreted into the periplasm. *RESULTS*: The analysis of in vitro bioactivity proved that the fusion of ABD to rIL-2 does not interfere with its bioactivity. ABD-rIL-2 fusion protein indicated higher serum half-life compared to rIL-2, when it was tested in the BALB/c mice. *CONCLUSION*: The current study provides an alternative strategy to extend the half-life and improve pharmacokinetic properties of rIL-2 without reducing its bioactivity in vitro.

Adhikari, P. A., Cosby, D. E., Cox, N. A., Lee, J. H., and Kim, W. K. Effect of dietary bacteriophage supplementation on internal organs, fecal excretion, and ileal immune response in laying hens challenged by Salmonella Enteritidis. Poult.Sci. 4-26-2017; PM: 28453774

ABSTRACT: With the current researches on replacing antibiotics with different dietary interventions, bacteriophages (BP) are potential antimicrobial intervention because of their ability to affect specific bacteria. A study was conducted to evaluate the role of BP against Salmonella enterica serovar Enteritidis (SE) on SE internal organs colonization and ileum immune response in laying hens. Hens were challenged both orally and intracloacally with 108 cfu/mL cells of nalidixic acid resistant Salmonella Enteritidis (SENAR). Thirty-two Single Comb White Leghorns were randomly allocated to 4 dietary treatments: 1) unchallenged control (negative control; T1), 2) SENAR challenged control (positive control; T2), 3) SENAR challenged + 0.1% BP (T3), and 4) SENAR challenged + 0.2% BP (T4). The number of SENAR in the ceca was significantly reduced by 0.2% BP supplementation ($P < 0.05$) at 7 d post infection (dpi). The respective number of SENAR was reduced from 2.9 log cfu/gm in T2 and T3 to 2.0 log cfu/gm in T4. There was no significant effect of T3 on reduction of numbers of cecal SENAR. A significant reduction of SENAR was observed in the liver with gall bladder (LGB) from 0.75 in T2 to 0.18 log cfu/gm in T4. In the spleen, T4 significantly reduced ($P < 0.05$) SENAR to 0.56 log cfu/gm compared to T2 and T3 (0.94 log cfu/gm). There was no significant effect of T3 in reduction of prevalence of spleen SENAR. By supplementing 0.2% BP (T4), the SENAR in the ovary was reduced to 0 log cfu/gm. There was a significant reduction ($P < 0.05$) in fecal SENAR at 6 dpi by T4 (0.71 log cfu/gm) compared to the positive control (1.57 log cfu/gm). The expression of interferon (IFN)-Gamma, interleukin (IL)-6, and IL-10 was significantly increased in the ileum by SENAR challenge compared to the negative control. This study suggests that apart from commonly used prebiotics or probiotics, BP are pathogen-specific and can be used as one of the dietary strategies to reduce SE colonization and induce immune modulation in laying hens.

Adriaenssens, E. and Brister, J. R. How to Name and Classify Your Phage: An Informal Guide. Viruses. 4-3-2017; 9(4); PM: 28368359

ABSTRACT: With this informal guide, we try to assist both new and experienced phage researchers through two important stages that follow phage discovery; that is, naming and classification. Providing an appropriate name for a bacteriophage is not as trivial as it sounds, and the effects might be long-lasting in databases and in official taxon names. Phage classification is the responsibility of the Bacterial and Archaeal Viruses Subcommittee (BAVS) of the International Committee on the Taxonomy of Viruses (ICTV). While the BAVS aims at providing a holistic approach to phage taxonomy, for individual researchers who have isolated and sequenced a new phage, this can be a little overwhelming. We are now providing these researchers with an informal guide to phage naming and classification, taking a "bottom-up" approach from the phage isolate level.

Ahlgren, N. A., Ren, J., Lu, Y. Y., Fuhrman, J. A., and Sun, F. Alignment-free d_2^* oligonucleotide frequency dissimilarity measure improves prediction of hosts from metagenomically-derived viral sequences. Nucleic Acids Res. 1-9-2017; 45(1):39-53; PM: 27899557

ABSTRACT: Viruses and their host genomes often share similar oligonucleotide frequency (ONF) patterns, which can be used to predict the host of a given virus by finding the host with the greatest ONF similarity. We comprehensively compared 11 ONF metrics using several k-mer lengths for predicting host taxonomy from among approximately 32 000 prokaryotic genomes for 1427 virus isolate genomes whose true hosts are known. The

background-subtracting measure [Formula: see text] at k = 6 gave the highest host prediction accuracy (33%, genus level) with reasonable computational times. Requiring a maximum dissimilarity score for making predictions (thresholding) and taking the consensus of the 30 most similar hosts further improved accuracy. Using a previous dataset of 820 bacteriophage and 2699 bacterial genomes, [Formula: see text] host prediction accuracies with thresholding and consensus methods (genus-level: 64%) exceeded previous Euclidian distance ONF (32%) or homology-based (22-62%) methods. When applied to metagenomically-assembled marine SUP05 viruses and the human gut virus crAssphage, [Formula: see text]-based predictions overlapped (i.e. some same, some different) with the previously inferred hosts of these viruses. The extent of overlap improved when only using host genomes or metagenomic contigs from the same habitat or samples as the query viruses. The [Formula: see text] ONF method will greatly improve the characterization of novel, metagenomic viruses.

Aijaz, I. and Koudelka, G. B. Tetrahymena phagocytic vesicles as ecological micro-niches of phage transfer. FEMS Microbiol.Ecol. 4-1-2017; 93(4); PM: 28334205

ABSTRACT: The microbial communities in natural environments such as soil, pond water, or animal rumens are composed of a diverse mixture of bacteria and protozoa including ciliates or flagellates. In such microbiomes, a major source of bacterial mortality is grazing by phagocytic protists. Many protists are omnivorous heterotrophs, feeding on a range of different bacterial species. Due to this indiscriminate feeding, different bacterial species can assemble together in the same phagocytic vesicles where they can potentially exchange genetic material. Here we show that Tetrahymena thermophila imports and accumulates phage donor and recipient bacterial strains in its phagocytic vesicles and that under laboratory conditions the ingested bacteria remain viable for >/=2 h. Prophages in the ingested bacteria induce immediately after ingestion, and the released phages are concentrated in the phagocytic vesicles of the ciliate. These phages retain their ability to infect phage-susceptible bacterial strains. As a consequence of being confined within the phagosome, the frequency of lysogen formation in these vesicles increases 6-fold as compared with the bulk solution. Collectively, these observations suggest that T. thermophila aids in dissemination of bacteriophages by accumulating susceptible bacteria and phages in their phagocytic vesicles.

Aktas, G. B., Skouridou, V., and Masip, L. Nucleic acid sensing with enzyme-DNA binding protein conjugates cascade and simple DNA nanostructures. Anal.Bioanal.Chem. 2017; 409(14):3623-3632; PM: 28331958

ABSTRACT: A versatile and universal DNA sensing platform is presented based on enzyme-DNA binding protein tags conjugates and simple DNA nanostructures. Two enzyme conjugates were thus prepared, with horseradish peroxidase linked to the dimeric single-chain bacteriophage Cro repressor protein (HRP-scCro) and glucose oxidase linked to the dimeric headpiece domain of Escherichia coli LacI repressor protein (GOx-dHP), and used in conjunction with a hybrid ssDNA-dsDNA detection probe. This probe served as a simple DNA nanostructure allowing first for target recognition through its target-complementary single-stranded DNA (ssDNA) part and then for signal generation after conjugate binding on the double-stranded DNA (dsDNA) containing the specific binding sites for the dHP and scCro DNA binding proteins. The DNA binding proteins chosen in this work have different sequence specificity, high affinity, and lack of cross-reactivity. The proposed sensing system was validated for the detection of model target ssDNA from

high-risk human papillomavirus (HPV16) and the limits of detection of 45, 26, and 21 pM were achieved using the probes with scCro/dHP DNA binding sites ratio of 1:1, 2:1, and 1:2, respectively. The performance of the platform in terms of limit of detection was comparable to direct HRP systems using target-specific oligonucleotide-HRP conjugates. The ratio of the two enzymes can be easily manipulated by changing the number of binding sites on the detection probe, offering further optimization possibilities of the signal generation step. Moreover, since the signal is obtained in the absence of externally added hydrogen peroxide, the described platform is compatible with paper-based assays for molecular diagnostics applications. Finally, just by changing the ssDNA part of the detection probe, this versatile nucleic acid platform can be used for the detection of different ssDNA target sequences or in a multiplex detection configuration without the need to change any of the conjugates. Graphical abstract DNA sensing platform based on an immobilized ssDNA capture probe and a hybrid ssDNA-dsDNA detection probe that specifically hybridize with the ssDNA target. The hybrid ssDNA-dsDNA detection probe also provides the binding sites for the enzyme-DNA binding protein conjugates (HRP-scCro and GOx-dHP) that generate the colorimetric signal.

Al-Wrafy, F., Brzozowska, E., Gorska, S., and Gamian, A. Pathogenic factors of Pseudomonas aeruginosa - the role of biofilm in pathogenicity and as a target for phage therapy. Postepy Hig.Med.Dosw.(Online.). 2-14-2017; 71(0):78-91; PM: 28258668

ABSTRACT: Pseudomonas aeruginosa is an opportunistic pathogen that can cause several acute and chronic infections in humans, and it has become an important cause of nosocomial infections and antibiotic resistance. Biofilm represents an important virulence factor for these bacteria, plays a role in P. aeruginosa infections and avoidance of immune defence mechanisms, and has the ability to protect the bacteria from antibiotics. Alginate, Psl and Pel, three exopolysaccharides, are the main components in biofilm matrix, with many biological functions attributed to them, especially with respect to the protection of the bacterial cell from antibiotics and the immune system. Pseudomonas infections, biofilm formation and development of resistance to antibiotics all require better understanding to achieve the best results using alternative treatment with phage therapy. This review describes the P. aeruginosa pathogenicity and virulence factors with a special focus on the biofilm and its role in infection and resistance to antibiotics and summarizes phage therapy as an alternative approach in treatment of P. aeruginosa infections.

Alamian, S., Esmaelizad, M., Zahraei, T., Etemadi, A., Mohammadi, M., Afshar, D., and Ghaderi, S. A Novel PCR Assay for Detecting Brucella abortus and Brucella melitensis. Osong.Public Health Res.Perspect. 2017; 8(1):65-70; PM: 28443226

ABSTRACT: OBJECTIVES: Brucellosis is a major zoonotic disease that poses a significant public health threat worldwide. The classical bacteriological detection process used to identify Brucella spp. is difficult and time-consuming. This study aimed to develop a novel molecular assay for detecting brucellosis. *METHODS*: All complete sequences of chromosome 1 with 2.1-Mbp lengths were compared among all available Brucella sequences. A unique repeat sequence (URS) locus on chromosome 1 could differentiate Brucella abortus from Brucella melitensis. A primer set was designed to flank the unique locus. A total of 136 lymph nodes and blood samples were evaluated and classified by the URS-polymerase chain reaction (PCR) method in 2013-2014. *RESULTS*: Biochemical tests and bacteriophage typing as the golden standard indicated that all Brucella spp.

isolates were B. melitensis biovar 1 and B. abortus biovar 3. The PCR results were the same as the bacteriological method for detecting Brucella spp. The sensitivity and specificity of the URS-PCR method make it suitable for detecting B. abortus and B. melitensis. *CONCLUSION*: Quick detection of B. abortus and B. melitensis can provide the most effective strategies for control of these bacteria. The advantage of this method over other presented methods is that both B. abortus and B. melitensis are detectable in a single test tube. Furthermore, this method covered 100% of all B. melitensis and B. abortus biotypes. The development of this URS-PCR method is the first step toward the development of a novel kit for the molecular identification of B. abortus and B. melitensis.

Alexyuk, M. S., Turmagambetova, A. S., Alexyuk, P. G., Bogoyavlenskiy, A. P., and Berezin, V. E. Comparative study of viromes from freshwater samples of the Ile-Balkhash region of Kazakhstan captured through metagenomic analysis. Virusdisease. 2017; 28(1):18-25; PM: 28466051

ABSTRACT: Viruses are the most abundant biological entities on Earth and can be found in a variety of environments. A high prevalence of viruses in marine and freshwater systems was initially reported by Spencer in 1955, but the ecological significance of viruses is insufficiently known even until the present day. Viruses are known to play a key role in the biology of freshwater bacteria: controlling the bacterial abundance, composition of species, and acting as intermediaries in the transfer of genes between bacterial populations. In our study a variety of viromes of the Ile-Balkhash water basin were identified. It was found that the composition of viruses of the Ile-Balkhash region is made up not only of a wide variety of autochthonous viruses typical for phytoplankton hydro ecosystems, but also of representatives of allochthonous viruses-such families as Coronaviridae, Reoviridae and Herpesviridae-indicating anthropogenic pollution of the basin. The research designed to investigate the viral abundance, spread, infectious cycle, seasonal dynamics, composition of the viral community, and the influence of viruses on the bacteria, phytoplankton and recycling of nutrients, as well as the impact of environmental factors on the viral ecology in a variety of marine and freshwater systems is very relevant nowadays.

Ali, Q. and Wahl, L. M. Mathematical modelling of CRISPR-Cas system effects on biofilm formation. J.Biol.Dyn. 4-20-2017; 1-21; PM: 28426329

ABSTRACT: Clustered regularly interspaced short palindromic repeats (CRISPR), linked with CRISPR associated (Cas) genes, can confer adaptive immunity to bacteria, against bacteriophage infections. Thus from a therapeutic standpoint, CRISPR immunity increases biofilm resistance to phage therapy. Recently, however, CRISPR-Cas genes have been implicated in reducing biofilm formation in lysogenized cells. Thus CRISPR immunity can have complex effects on phage-host-lysogen interactions, particularly in a biofilm. In this contribution, we develop and analyse a series of dynamical systems to elucidate and disentangle these interactions. Two competition models are used to study the effects of lysogens (first model) and CRISPR-immune bacteria (second model) in the biofilm. In the third model, the effect of delivering lysogens to a CRISPR-immune biofilm is investigated. Using standard analyses of equilibria, stability and bifurcations, our models predict that lysogens may be able to displace CRISPR-immune bacteria in a biofilm, and thus suggest strategies to eliminate phage-resistant biofilms.

Alphonse, S. and Ghose, R. Cystoviral RNA-directed RNA polymerases: Regulation of RNA synthesis on multiple time and length scales. Virus Res. 1-16-2017; PM: 28104452

ABSTRACT: P2, an RNA-directed RNA polymerase (RdRP), is encoded on the largest of the three segments of the double-stranded RNA genome of cystoviruses. P2 performs the dual tasks of replication and transcription de novo on single-stranded RNA templates, and plays a critical role in the viral life-cycle. Work over the last few decades has yielded a wealth of biochemical and structural information on the functional regulation of P2, on its role in the spatiotemporal regulation of RNA synthesis and its variability across the Cystoviridae family. These range from atomic resolution snapshots of P2 trapped in functionally significant states, in complex with catalytic/structural metal ions, polynucleotide templates and substrate nucleoside triphosphates, to P2 in the context of viral capsids providing structural insight into the assembly of supramolecular complexes and regulatory interactions therein. They include in vitro biochemical studies using P2 purified to homogeneity and in vivo studies utilizing infectious core particles. Recent advances in experimental techniques have also allowed access to the temporal dimension and enabled the characterization of dynamics of P2 on the sub-nanosecond to millisecond timescale through measurements of nuclear spin relaxation in solution and single molecule studies of transcription from seconds to minutes. Below we summarize the most significant results that provide critical insight into the role of P2 in regulating RNA synthesis in cystoviruses.

Alves, E., Salman, A. M., Leoratti, F., Lopez-Camacho, C., Viveros-Sandoval, M. E., Lall, A., El-Turabi, A., Bachmann, M. F., Hill, A. V., Janse, C. J., Khan, S. M., and Reyes-Sandoval, A. Evaluation of Plasmodium vivax Cell-Traversal Protein for Ookinetes and Sporozoites as a Preerythrocytic P. vivax Vaccine. Clin.Vaccine Immunol. 2017; 24(4); PM: 28179403

ABSTRACT: Four different vaccine platforms, each targeting the human malaria parasite Plasmodium vivax cell-traversal protein for ookinetes and sporozoites (PvCelTOS), were generated and assessed for protective efficacy. These platforms consisted of a recombinant chimpanzee adenoviral vector 63 (ChAd63) expressing PvCelTOS (Ad), a recombinant modified vaccinia virus Ankara expressing PvCelTOS (MVA), PvCelTOS conjugated to bacteriophage Qbeta virus-like particles (VLPs), and a recombinant PvCelTOS protein expressed in eukaryotic HEK293T cells (protein). Inbred BALB/c mice and outbred CD-1 mice were immunized using the following prime-boost regimens: Ad-MVA, Ad-VLPs, and Ad-protein. Protective efficacy against sporozoite challenge was assessed after immunization using a novel chimeric rodent Plasmodium berghei parasite (Pb-PvCelTOS). This chimeric parasite expresses P. vivax CelTOS in place of the endogenous P. berghei CelTOS and produces fully infectious sporozoites. A single Ad immunization in BALB/c and CD-1 mice induced anti-PvCelTOS antibodies which were boosted efficiently using MVA, VLP, or protein immunization. PvCelTOS-specific gamma interferon- and tumor necrosis factor alpha-producing CD8+ T cells were induced at high frequencies by all prime-boost regimens in BALB/c mice but not in CD-1 mice; in CD-1 mice, they were only marginally increased after boosting with MVA. Despite the induction of anti-PvCelTOS antibodies and PvCelTOS-specific CD8+ T-cell responses, only low levels of protective efficacy against challenge with Pb-PvCelTOS sporozoites were obtained using any immunization strategy. In BALB/c mice, no immunization regimens provided significant protection against a Pb-PvCelTOS chimeric sporozoite challenge. In CD-1 mice, modest protective efficacy against challenge with chimeric P. berghei sporozoites expressing either PvCelTOS or P. falciparum CelTOS was observed using the Ad-protein vaccination regimen.

Amgarten, D., Martins, L. F., Lombardi, K. C., Antunes, L. P., de Souza, A. P. S., Nicastro, G. G., Kitajima, E. W., Quaggio, R. B., Upton, C., Setubal, J. C., and da Silva, A. M. Three novel Pseudomonas phages isolated from composting provide insights into the evolution and diversity of tailed phages. BMC.Genomics. 5-4-2017; 18(1):346; PM: 28472930

ABSTRACT: BACKGROUND: Among viruses, bacteriophages are a group of special interest due to their capacity of infecting bacteria that are important for biotechnology and human health. Composting is a microbial-driven process in which complex organic matter is converted into humus-like substances. In thermophilic composting, the degradation activity is carried out primarily by bacteria and little is known about the presence and role of bacteriophages in this process. *RESULTS*: Using Pseudomonas aeruginosa as host, we isolated three new phages from a composting operation at the Sao Paulo Zoo Park (Brazil). One of the isolated phages is similar to Pseudomonas phage Ab18 and belongs to the Siphoviridae YuA-like viral genus. The other two isolated phages are similar to each other and present genomes sharing low similarity with phage genomes in public databases; we therefore hypothesize that they belong to a new genus in the Podoviridae family. Detailed genomic descriptions and comparisons of the three phages are presented, as well as two new clusters of phage genomes in the Viral Orthologous Clusters database of large DNA viruses. We found sequences encoding homing endonucleases that disrupt a putative ribonucleotide reductase gene and an RNA polymerase subunit 2 gene in two of the phages. These findings provide insights about the evolution of two-subunits RNA polymerases and the possible role of homing endonucleases in this process. Infection tests on 30 different strains of bacteria reveal a narrow host range for the three phages, restricted to P. aeruginosa PA14 and three other P. aeruginosa clinical isolates. Biofilm dissolution assays suggest that these phages could be promising antimicrobial agents against P. aeruginosa PA14 infections. Analyses on composting metagenomic and metatranscriptomic data indicate association between abundance variations in both phage and host populations in the environment. *CONCLUSION*: The results about the newly discovered and described phages contribute to the understanding of tailed bacteriophage diversity, evolution, and role in the complex composting environment.

Anany, H., Chou, Y., Cucic, S., Derda, R., Evoy, S., and Griffiths, M. W. From Bits and Pieces to Whole Phage to Nanomachines: Pathogen Detection Using Bacteriophages. Annu.Rev.Food Sci.Technol. 2-28-2017; 8:305-329; PM: 28125341

ABSTRACT: The innate specificity of bacteriophages toward their hosts makes them excellent candidates for the development of detection assays. They can be used in many ways to detect pathogens, and each has its own advantages and disadvantages. Whole bacteriophages can carry reporter genes to alter the phenotype of the target. Bacteriophages can act as staining agents or the progeny of the infection process can be detected, which further increases the sensitivity of the detection assay. Compared with whole-phage particles, use of phage components as probes offers other advantages: for example, smaller probe size to enhance binding activity, phage structures that can be engineered for better affinity, as well as specificity, binding properties, and robustness. When no natural binding with the target exists, phages can be used as vehicles to identify new protein-ligand interactions necessary for diagnostics. This review comprehensively summarizes many uses of phages as detection tools and points the way toward how phage-based technologies may be improved.

Arthur, T. M., Kalchayanand, N., Agga, G. E., Wheeler, T. L., and Koohmaraie, M. Evaluation of Bacteriophage Application to Cattle in Lairage at Beef Processing Plants to Reduce Escherichia coli O157:H7 Prevalence on Hides and Carcasses. Foodborne.Pathog.Dis. 2017; 14(1):17-22; PM: 27870549

ABSTRACT: Escherichia coli O157:H7 is a major food safety concern for the beef industry. Several studies have provided evidence that cattle hides are the main source of beef carcass contamination during processing and that reductions in the E. coli O157:H7 load on the hides of cattle entering processing facilities will lead to reductions in carcass contamination. Bacteriophages have been proposed as a novel preharvest antimicrobial intervention to reduce the levels of E. coli O157:H7 on cattle hides. The objective of this study was to evaluate a commercialized phage application administered in the lairage area of commercial beef processing plants for the ability to reduce E. coli O157:H7 contamination of cattle hides and carcasses. Cattle lots either received phage spray treatment (n = 289) or did not (n = 301), as they entered the lairage environments in two separate experiments at two different commercial beef processing plants. Hide and carcass samples were collected and analyzed for E. coli O157:H7 prevalence and concentration. Cattle hides receiving phage treatment had an E. coli O157:H7 prevalence of 51.8%, whereas untreated hides had a prevalence of 57.6%. For carcass samples, the E. coli O157 prevalence in treated and untreated samples was 17.1% and 17.6%, respectively. The results obtained from these experiments demonstrated that the treatment of cattle hides with bacteriophages before processing did not produce a significant reduction of E. coli O157:H7 on cattle hides or beef carcasses during processing.

Ash, K. T., Drake, K. M., Gibbs, W. S., and Ely, B. Genomic Diversity of Type B3 Bacteriophages of Caulobacter crescentus. Curr.Microbiol. 4-10-2017; PM: 28393265

ABSTRACT: The genomes of the type B3 bacteriophages that infect Caulobacter crescentus are among the largest phage genomes thus far deposited into GenBank with sizes over 200 kb. In this study, we introduce six new bacteriophage genomes which were obtained from phage collected from various water systems in the southeastern United States and from tropical locations across the globe. A comparative analysis of the 12 available genomes revealed a "core genome" which accounts for roughly 1/3 of these bacteriophage genomes and is predominately localized to the head, tail, and lysis gene regions. Despite being isolated from geographically distinct locations, the genomes of these bacteriophages are highly conserved in both genome sequence and gene order. We also identified the insertions, deletions, translocations, and horizontal gene transfer events which are responsible for the genomic diversity of this group of bacteriophages and demonstrated that these changes are not consistent with the idea that modular reassortment of genomes occurs in this group of bacteriophages.

Assis, A. S., Otenio, M. H., Drumond, B. P., Fumian, T. M., Miagostovich, M. P., and da Rosa E Silva ML. Optimization of the skimmed-milk flocculation method for recovery of adenovirus from sludge. Sci.Total Environ. 4-1-2017; 583:163-168; PM: 28094048

ABSTRACT: Return of treated sludge to the environment poses concerns and has stimulated the development of studies on viral monitoring in this matrix, in order to assess its potential risks for public health. Human adenovirus (HAdV) has been identified as a

putative viral marker of faecal contamination due to its stability and resistance to the sewage treatment process. The aim of this study was to optimize the organic flocculation procedure in order to establish an appropriate methodology for HAdV recovery from sewage sludge samples. Four protocols (A-D) have been proposed, with changes in the initial sample dilution, in the stirring time and in the final concentration of skimmed-milk. A single sludge sample was obtained in Wastewater Treatment Plant (WWTP) and divided into aliquots. In each protocol, three aliquots were inoculated with HAdV and bacteriophage PP7 and a non-inoculated one was used as negative control. Viral load and recovery rate were determined by quantitative PCR. HAdV recovery rate varied between the protocols tested (p=0.016) and the best result was obtained through the protocol C. In order to confirm this result a field study with activated, thickened and digested sludge samples was carried out. Different types of sludge were obtained in two WWTPs and processed using protocol C. HAdV was detected in all samples, with a similar or higher viral load than those obtained with other concentration techniques already applied to sludge. Protocol C proved to be really efficient, with the advantage of showing low cost and practicability in routine laboratories.

az-Munoz, S. L. Viral coinfection is shaped by host ecology and virus-virus interactions across diverse microbial taxa and environments. Virus Evol. 2017; 3(1):vex011; PM: 28469939

ABSTRACT: Infection of more than one virus in a host, coinfection, is common across taxa and environments. Viral coinfection can enable genetic exchange, alter the dynamics of infections, and change the course of viral evolution. Yet, a systematic test of the factors explaining variation in viral coinfection across different taxa and environments awaits completion. Here I employ three microbial data sets of virus-host interactions covering cross-infectivity, culture coinfection, and single-cell coinfection (total: 6,564 microbial hosts, 13,103 viruses) to provide a broad, comprehensive picture of the ecological and biological factors shaping viral coinfection. I found evidence that ecology and virus-virus interactions are recurrent factors shaping coinfection patterns. Host ecology was a consistent and strong predictor of coinfection across all three data sets: cross-infectivity, culture coinfection, and single-cell coinfection. Host phylogeny or taxonomy was a less consistent predictor, being weak or absent in the cross-infectivity and single-cell coinfection models, yet it was the strongest predictor in the culture coinfection model. Virus-virus interactions strongly affected coinfection. In the largest test of superinfection exclusion to date, prophage sequences reduced culture coinfection by other prophages, with a weaker effect on extrachromosomal virus coinfection. At the single-cell level, prophage sequences eliminated coinfection. Virus-virus interactions also increased culture coinfection with ssDNA-dsDNA coinfections >2x more likely than ssDNA-only coinfections. The presence of CRISPR spacers was associated with a approximately 50% reduction in single-cell coinfection in a marine bacteria, despite the absence of exact spacer matches in any active infection. Collectively, these results suggest the environment bacteria inhabit and the interactions among surrounding viruses are two factors consistently shaping viral coinfection patterns. These findings highlight the role of virus-virus interactions in coinfection with implications for phage therapy, microbiome dynamics, and viral infection treatments.

Bedwell, G. J. and Prevelige, P. E., Jr. Targeted mutagenesis of the P22 portal protein reveals the mechanism of signal transmission during DNA packaging. Virology. 2017; 505:127-138; PM: 28242514

ABSTRACT: The portal vertex in dsDNA bacteriophage serves as the site for genome encapsidation and release. In several of these viruses, efficient termination of DNA packaging has been shown to be dependent on the density of packaged DNA. The portal protein has been implicated as being part of the sensor that regulates packaging termination through DNA-dependent conformational changes during packaging. The mechanism by which DNA induces these conformational changes remains unknown. In this study, we explore how point mutants in the portal core can result in changes in genome packaging density in P22. Mutations in the portal core that subtly alter the structure or dynamics of the protein result in an increase in the amount of DNA packaged. The magnitude of the change is amino acid and location specific. Our findings suggest a mechanism wherein compression of the portal core is an essential aspect of signal transmission during packaging.

Bernasconi, O. J., Dona, V., Tinguely, R., and Endimiani, A. In vitro activity of three commercial bacteriophage cocktails against multidrug-resistant Escherichia coli and Proteus spp. strains of human and non-human origin. J.Glob.Antimicrob.Resist. 2017; 8:179-185; PM: 28232228

ABSTRACT: OBJECTIVES: Bacteriophages may represent a therapeutic alternative to treat infections caused by multidrug-resistant (MDR) pathogens. However, studies analysing their activity against MDR Enterobacteriaceae are limited. *METHODS*: The in vitro lytic activity of three commercial bacteriophage cocktails (PYO, INTESTI and Septaphage) was evaluated against 70 Escherichia coli and 31 Proteus spp. of human and non-human origin. Isolates were characterised by phenotypic and genotypic methods and included 82 MDR strains [44 extended-spectrum-beta-lactamase (ESBL)-producers (18 CTX-M-15-like, including ST131/ST648 E. coli); 27 plasmid-mediated AmpC beta-lactamase (pAmpC)-producers (23 CMY-2-like, including ST131 E. coli); 3 ESBL+pAmpC-producers; and 8 carbapenemase-producers]. Phage susceptibility was determined by the spot test. *RESULTS*: E. coli susceptibility to PYO, INTESTI and Septaphage was 61%, 67% and 9%, whereas that of Proteus spp. was 29%, 39% and 19%, respectively. For the subgroup of ESBL-producing E. coli/Proteus spp., the following susceptibility rates were recorded: PYO, 57%; INTESTI, 59%; and Septaphage, 11%. With regard to pAmpC-producers, 59%, 70% and 11% were susceptible to PYO, INTESTI and Septaphage, respectively. Five of eight carbapenemase-producers and three of four colistin-resistant E. coli were susceptible to PYO and INTESTI. *CONCLUSIONS*: This is the first study analysing the activity of the above three cocktails against well-characterised MDR E. coli and Proteus spp. The overall narrow spectrum of activity observed could be related to the absence of specific bacteriophages targeting these contemporary MDR strains that are spreading in different settings. Therefore, bacteriophages targeting emerging MDR pathogens need to be isolated and integrated in such biopreparations.

Blanco, Fernandez, Barrios, M. E., Cammarata, R. V., Torres, C., Taboga, O. A., and Mbayed, V. A. Comparison of internal process control viruses for detection of food and waterborne viruses. Appl.Microbiol.Biotechnol. 2017; 101(10):4289-4298; PM: 28357543

ABSTRACT: Enteric viruses are pathogens associated with food- and waterborne outbreaks. The recovery of viruses from food or water samples is affected by the procedures applied to detect and concentrate them. The incorporation of an internal process control virus to the analyses allows monitoring the performance of the methodology. The aim of this study was to produce a recombinant adenovirus (rAdV)

and apply it together with bacteriophage PP7 as process controls. The rAdV carries a DNA construction in its genome to differentiate it from wild-type adenovirus by qPCR. The stability of both control viruses was evaluated at different pH conditions. The rAdV was stable at pH 3, 7, and 10 for 18 h. PP7 infectious particles were stable at pH 7 and showed a 2.14 log reduction at pH 10 and total decay at pH 3 after 18 h. Three virus concentration methods were evaluated: hollow-fiber tap water ultrafiltration, wastewater ultracentrifugation, and elution-PEG precipitation from lettuce. Total and infectious viruses were quantified and their recoveries were calculated. Virus recovery for rAdV and PP7 by ultrafiltration showed a wide range (2.10-84.42 and 13.54-84.62%, respectively), whereas that by ultracentrifugation was 5.05-13.71 and 6.98-13.27%, respectively. The performance of ultracentrifugation to concentrate norovirus and enteroviruses present in sewage was not significantly different to the recovery of control viruses. For detection of viruses from lettuce, genomic copies of PP7 were significantly more highly recovered than adenovirus (14.74-18.82 and 0.00-3.44%, respectively). The recovery of infectious virus particles was significantly affected during sewage ultracentrifugation and concentration from lettuce. The simultaneous use of virus controls with dissimilar characteristics and behaviors might resemble different enteric viruses.

Blasdel, B. G., Chevallereau, A., Monot, M., Lavigne, R., and Debarbieux, L. Comparative transcriptomics analyses reveal the conservation of an ancestral infectious strategy in two bacteriophage genera. ISME.J. 5-12-2017; PM: 28498372

ABSTRACT: Although the evolution of tailed bacteriophages has increasingly been better understood through comparisons of their DNA sequences, the functional consequences of this evolution on phage infectious strategies have remained unresolved. In this study, we comprehensively compared the transcriptional strategies of two related myoviruses, PAK_P3 and PAK_P4, infecting the same Pseudomonas aeruginosa host strain. Outside of the conservation of their structural clusters, their highly syntenic genomes display only limited DNA similarity. Despite this apparent divergence, we found that both viruses follow a similar infection scheme, relying on a temporal regulation of their gene expression, likely involving the use of antisense transcripts, as well as a rapid degradation of 90% of the host non-ribosomal mRNA, as previously reported for PAK_P3. However, the kinetics of the mRNA degradation is remarkably faster during PAK_P4 infection. Moreover, we found that each virus has evolved specific adaptations, as exemplified by the distinct patterns of their core genes expression as well as the specific manipulation of the expression of iron-related host genes by PAK_P4. This study enhances our understanding of the evolutionary process of virulent phages, which relies on adjusting globally conserved ancestral infection mechanisms.The ISME Journal advance online publication, 12 May 2017; doi:10.1038/ismej.2017.63.

Blesa, A., Baquedano, I., Quintans, N. G., Mata, C. P., Caston, J. R., and Berenguer, J. The transjugation machinery of Thermus thermophilus: Identification of TdtA, an ATPase involved in DNA donation. PLoS.Genet. 2017; 13(3):e1006669; PM: 28282376

ABSTRACT: In addition to natural competence, some Thermus thermophilus strains show a high rate of DNA transfer via direct cell-to-cell contact. The process is bidirectional and follows a two-step model where the donor cell actively pushes out DNA and the recipient cell employs the natural competence system to take up the DNA, in a hybrid transformation-dependent conjugation process (transjugation). While the DNA uptake machinery is well known as in other bacterial species that undergo transformation, the

pushing step of transjugation remains to be characterized. Here we have searched for hypothetical DNA translocases putatively involved in the pushing step of transjugation. Among candidates encoded by T. thermophilus HB27, the TdtA protein was found to be required for DNA pushing but not for DNA pulling during transjugation, without affecting other cellular processes. Purified TdtA shows ATPase activity and oligomerizes as hexamers with a central opening that can accommodate double-stranded DNA. The tdtA gene was found to belong to a mobile 14 kbp-long DNA element inserted within the 3' end of a tRNA gene, flanked by 47 bp direct repeats. The insertion also encoded a homolog of bacteriophage site-specific recombinases and actively self-excised from the chromosome at high frequency to form an apparently non-replicative circular form. The insertion also encoded a type II restriction endonuclease and a NurA-like nuclease, whose activities were required for efficient transjugation. All these data support that TdtA belongs to a new type of Integrative and Conjugative Element which promotes the generalized and efficient transfer of genetic traits that could facilitate its co-selection among bacterial populations.

Blower, T. R., Chai, R., Przybilski, R., Chindhy, S., Fang, X., Kidman, S. E., Tan, H., Luisi, B. F., Fineran, P. C., and Salmond, G. P. Evolution of Pectobacterium Bacteriophage PhiM1 To Escape Two Bifunctional Type III Toxin-Antitoxin and Abortive Infection Systems through Mutations in a Single Viral Gene. Appl.Environ.Microbiol. 4-15-2017; 83(8); PM: 28159786

ABSTRACT: Some bacteria, when infected by their viral parasites (bacteriophages), undergo a suicidal response that also terminates productive viral replication (abortive infection [Abi]). This response can be viewed as an altruistic act protecting the uninfected bacterial clonal population. Abortive infection can occur through the action of type III protein-RNA toxin-antitoxin (TA) systems, such as ToxINPa from the phytopathogen Pectobacterium atrosepticum Rare spontaneous mutants evolved in the generalized transducing phage PhiM1, which escaped ToxINPa-mediated abortive infection in P. atrosepticum PhiM1 is a member of the Podoviridae and a member of the "KMV-like" viruses, a subset of the T7 supergroup. Genomic sequencing of PhiM1 escape mutants revealed single-base changes which clustered in a single open reading frame. The "escape" gene product, M1-23, was highly toxic to the host bacterium when overexpressed, but mutations in M1-23 that enabled an escape phenotype caused M1-23 to be less toxic. M1-23 is encoded within the DNA metabolism modular section of the phage genome, and when it was overexpressed, it copurified with the host nucleotide excision repair protein UvrA. While the M1-23 protein interacted with UvrA in coimmunoprecipitation assays, a UvrA mutant strain still aborted PhiM1, suggesting that the interaction is not critical for the type III TA Abi activity. Additionally, PhiM1 escaped a heterologous type III TA system (TenpINPl) from Photorhabdus luminescens (reconstituted in P. atrosepticum) through mutations in the same protein, M1-23. The mechanistic action of M1-23 is currently unknown, but further analysis of this protein may provide insights into the mode of activation of both systems.IMPORTANCE Bacteriophages, the viral predators of bacteria, are the most abundant biological entities and are important factors in driving bacterial evolution. In order to survive infection by these viruses, bacteria have evolved numerous antiphage mechanisms. Many of the studies involved in understanding these interactions have led to the discovery of biotechnological and gene-editing tools, most notably restriction enzymes and more recently the clustered regularly interspaced short palindromic repeats (CRISPR)-Cas systems. Abortive infection is another such antiphage mechanism that warrants further investigation. It is unique in that activation of the system leads to the premature death of the infected cells. As bacteria infected with the virus are destined to die, undergoing precocious suicide

prevents the release of progeny phage and protects the rest of the bacterial population. This altruistic suicide can be caused by type III toxin-antitoxin systems, and understanding the activation mechanisms involved will provide deeper insight into the abortive infection process.

Bolduc, B., Jang, H. B., Doulcier, G., You, Z. Q., Roux, S., and Sullivan, M. B. vConTACT: an iVirus tool to classify double-stranded DNA viruses that infect Archaea and Bacteria. PeerJ. 2017; 5:e3243; PM: 28480138

ABSTRACT: Taxonomic classification of archaeal and bacterial viruses is challenging, yet also fundamental for developing a predictive understanding of microbial ecosystems. Recent identification of hundreds of thousands of new viral genomes and genome fragments, whose hosts remain unknown, requires a paradigm shift away from traditional classification approaches and towards the use of genomes for taxonomy. Here we revisited the use of genomes and their protein content as a means for developing a viral taxonomy for bacterial and archaeal viruses. A network-based analytic was evaluated and benchmarked against authority-accepted taxonomic assignments and found to be largely concordant. Exceptions were manually examined and found to represent areas of viral genome 'sequence space' that are under-sampled or prone to excessive genetic exchange. While both cases are poorly resolved by genome-based taxonomic approaches, the former will improve as viral sequence space is better sampled and the latter are uncommon. Finally, given the largely robust taxonomic capabilities of this approach, we sought to enable researchers to easily and systematically classify new viruses. Thus, we established a tool, vConTACT, as an app at iVirus, where it operates as a fast, highly scalable, user-friendly app within the free and powerful CyVerse cyberinfrastructure.

Bonanno, L., Delubac, B., Michel, V., and Auvray, F. Influence of Stress Factors Related to Cheese-Making Process and to STEC Detection Procedure on the Induction of Stx Phages from STEC O26:H11. Front Microbiol. 2017; 8:296; PM: 28316592

ABSTRACT: Shiga toxin-producing Escherichia coli (STEC) are responsible for human infections, ranging from mild watery diarrhea to hemorrhagic colitis (CH) that may be complicated by hemolytic uremic syndrome (HUS). The main STEC virulence factor is Shiga toxin encoded by the stx gene, located in the genome of a bacteriophage integrated into the bacterial chromosome. The serotype O26:H11 is the second HUS-causing serotype worldwide (after O157:H7), and the first found in dairy products such as raw-milk cheeses. A small number of HUS cases identified each year in France are caused by serotype O26:H11. Stx phage induction is known to result in STEC lysis and release of new Stx phages particles. This phenomenon could negatively impact STEC screening in foods based on stx gene detection by PCR. Here, we evaluated the influence of physicochemical parameters related to cheese-making process on the induction rate of Stx phages from STEC O26:H11, including H2O2, NaCl, lactic acid and temperature. In addition, selective agents from the analytical STEC enrichment and detection procedure (XP CEN ISO/TS 13136) were tested, including novobiocin, acrifavin, cefixim-tellurite, and bile salts. An impact of H2O2 and NaCl on Stx phage induction was observed. Production of Stx phages was also observed during a real cheese-making process. By contrast, no significant effect could be demonstrated for the chemical agents of the STEC detection procedure when tested separately, except for acriflavin and novobiocin which reduced Stx1 phage production in some cases. In conclusion,

these results suggest that the cheese-making process might trigger the production of Stx phages, potentially interfering with the analysis of STEC in food.

Boratynski, J. and Szermer-Olearnik, B. Endotoxin Removal from Escherichia coli Bacterial Lysate Using a Biphasic Liquid System. Methods Mol.Biol. 2017; 1600:107-112; PM: 28478561

ABSTRACT: Lipopolysaccharide (LPS, endotoxin, pyrogen) which is a component of the outer membrane of most Gram-negative bacteria is a troubling contaminant of crude bacteriophage suspension. Therefore, its removal is important for bacteriophage applications especially in preparations dedicated for use in therapy with bacterial infections treatment. The method presented here is used for extractive removal of endotoxins from bacteriophage preparations with a water immiscible solvent such as 1-octanol. During extraction most of the phage lytic activity is retained in the aqueous phase, while endotoxin accumulates in the organic solvent. The levels of endotoxin in the aqueous bacteriophage rich fraction are determine by Limulus Amebocyte Lysate or EndoLISA assay and are extremely low.

Borysowski, J., Miedzybrodzki, R., Wierzbicki, P., Klosowska, D., Korczak-Kowalska, G., Weber-Dabrowska, B., and Gorski, A. A3R Phage and Staphylococcus aureus Lysate Do Not Induce Neutrophil Degranulation. Viruses. 2-21-2017; 9(2)PM:28230780¶

ABSTRACT: The objective of this study was to evaluate the effects of A3R phage and Staphylococcus aureus lysate obtained after phage infection on neutrophil degranulation. The exocytosis of primary and secondary granules from neutrophils was investigated in vitro in whole blood specimens by flow cytometry based on the expression of specific markers of exocytosis (CD63 for primary granules and CD66b for secondary granules). We found that both A3R and S. aureus lysate had no significant effect on the exocytosis of primary and secondary granules. These data suggest that neither A3R virions nor any products of phage-induced lysis of S. aureus are likely to induce neutrophil degranulation in patients who are treated with phage preparations. Since neutrophil granules contain some potentially toxic proteins, our results provide an important argument for the safety of phage therapy. Moreover, these data indicate that the induction of neutrophil degranulation is not likely to contribute to antibacterial effects of phages.

Bosak, J., Mikalova, L., Cejkova, D., Smarda, J., and Smajs, D. Complete Genome Sequence of Bacteriophage SEN8, a Temperate Phage Isolated from Salmonella enterica subsp. salamae. Genome Announc. 5-11-2017; 5(19); PM: 28495765

ABSTRACT: A temperate phage, SEN8, having a broad activity against pathogenic Salmonella serovars, was isolated from Salmonella enterica subsp. salamae strain Sen8. The complete genome sequence of phage SEN8 was determined (35,203 bp) and showed relatedness to P2-like phages (Salmonella phages Fels-2 and RE-2010).

Brown, M. R., Johnson, S. A., Brorson, K. A., Lute, S. C., and Roush, D. J. A step-wise approach to define binding mechanisms of surrogate viral particles to multi-modal anion exchange resin in a single solute system. Biotechnol.Bioeng; 1-21-2017; PM: 28109126

ABSTRACT: Multi-modal anion exchange resins combine properties of both anion exchange and hydrophobic interaction chromatography for commercial protein polishing and may provide some viral clearance as well. From a regulatory viral clearance claim standpoint, it is unclear if multi-modal resins are truly orthogonal to either single-mode anion exchange or hydrophobic interaction columns. To answer this, a strategy of solute surface assays and High Throughput Screening of resin in concert with a scale-down model of large scale chromatography purification was employed to determine the predominant binding mechanisms of a panel of bacteriophage (i.e., PR772, PP7, and varphiX174) to multi-modal and single mode resins under various buffer conditions. The buffer conditions were restricted to buffer environments suggested by the manufacturer for the multi-modal resin. Each phage was examined for estimated net charge expression and relative hydrophobicity using chromatographic based methods. Overall, PP7 and PR772 bound to the multimodal resin via both anionic and hydrophobic moieties, while varphiX174 bound predominantly by the anionic moiety. Biotechnol. Bioeng. 2017;9999: 1-8. (c) 2017 Wiley Periodicals, Inc.

Brown, M. W., de la, Torre A., and Finkelstein, I. J. Inserting Extrahelical Structures into Long DNA Substrates for Single-Molecule Studies of DNA Mismatch Repair. Methods Enzymol. 2017; 582:221-238; PM: 28062036

ABSTRACT: The DNA mismatch repair (MMR) system corrects errors that occur during DNA replication. MMR needs the coordinated and highly dynamic assembly of repair enzymes at the site of the lesion. By visualizing transient intermediates of these assemblies, single-molecule approaches have shed critical insights into the mechanisms of MMR. These studies frequently require long (>20kb) DNA substrates with lesions and other extrahelical structures inserted at defined positions. DNA derived from bacteriophage lambda (lambda-DNA) is a high quality long (48.5kb) DNA substrate that is frequently used in single-molecule studies. Here we provide detailed protocols for site-specific incorporation of recombinant sequences and extrahelical structures into lambda-DNA. We also describe how to assemble DNA curtains, and how to collect and analyze single-molecule observations of lesion recognition by MMR proteins diffusing on these DNA curtains. These protocols will facilitate future single-molecule studies of DNA transcription, replication, and repair.

Brown, T. L., Thomas, T., Odgers, J., Petrovski, S., Spark, M. J., and Tucci, J. Bacteriophage formulated into a range of semisolid and solid dosage forms maintain lytic capacity against isolated cutaneous and opportunistic oral bacteria. J.Pharm.Pharmacol. 2017; 69(3):244-253; PM: 28033675

ABSTRACT: BACKGROUND: Resistance of bacteria to antimicrobial agents is of grave concern. Further research into the development of bacteriophage as therapeutic agents against bacterial infections may help alleviate this problem. *OBJECTIVES*: To formulate bacteriophage into a range of semisolid and solid dosage forms and investigate the capacity of these preparations to kill bacteria under laboratory conditions. *METHODS*: Bacteriophage suspensions were incorporated into dosage forms such as creams, ointments, pastes, pessaries and troches. These were applied to bacterial lawns in order to ascertain lytic capacity. Stability of these formulations containing phage was tested under various storage conditions. *KEY FINDINGS*: A range of creams and ointments were able to support phage lytic activity against

Propionibacterium acnes. Assessment of the stability of these formulations showed that storage at 4 degrees C in light-protected containers resulted in optimal phage viability after 90 days. Pessaries/suppositories and troches were able to support phage lytic activity against Rhodococcus equi. *CONCLUSIONS*: We report here the in-vitro testing of semisolid and solid formulations of bacteriophage lytic against a range of bacteria known to contribute to infections of the epithelia. This study provides a basis for the future formulation of diverse phage against a range of bacteria that infect epithelial tissues.

Browne, C. Global properties of nested network model with application to multi-epitope HIV/CTL dynamics. J.Math.Biol. 2-20-2017; PM: 28220205

ABSTRACT: Mathematical modeling and analysis can provide insight on the dynamics of ecosystems which maintain biodiversity in the face of competitive and prey-predator interactions. Of primary interests are the underlying structure and features which stabilize diverse ecological networks. Recently Korytowski and Smith (Theor Ecol 8(1):111-120, 2015) proved that a perfectly nested infection network, along with appropriate life history trade-offs, leads to coexistence and persistence of bacteria-phage communities in a chemostat model. In this article, we generalize their model in order to apply it to the within-host dynamics virus and immune response, in particular HIV and CTL (Cytotoxic T Lymphocyte) cells. Our model can describe sequential viral escape from dominant immune responses and rise in subdominant immune responses, consistent with observed patterns of HIV/CTL evolution. We find a Lyapunov function for the system which leads to rigorous characterization of persistent viral and immune variants, along with informing upon equilibria stability and global dynamics. Results are interpreted in the context of within-host HIV/CTL evolution and numerical simulations are provided.

Buttimer, C., Hendrix, H., Oliveira, H., Casey, A., Neve, H., McAuliffe, O., Ross, R. P., Hill, C., Noben, J. P., O'Mahony, J., Lavigne, R., and Coffey, A. Things Are Getting Hairy: Enterobacteria Bacteriophage vB_PcaM_CBB. Front Microbiol. 2017; 8:44; PM: 28174560

ABSTRACT: Enterobacteria phage vB_PcaM_CBB is a "jumbo" phage belonging to the family Myoviridae. It possesses highly atypical whisker-like structures along the length of its contractile tail. It has a broad host range with the capability of infecting species of the genera Erwinia, Pectobacterium, and Cronobacter. With a genome of 355,922 bp, excluding a predicted terminal repeat of 22,456 bp, phage CBB is the third largest phage sequenced to date. Its genome was predicted to encode 554 ORFs with 33 tRNAs. Based on prediction and proteome analysis of the virions, 29% of its predicted ORFs could be functionally assigned. Protein comparison shows that CBB shares between 33-38% of its proteins with Cronobacter phage GAP32, coliphages PBECO4 and 121Q as well as Klebsiella phage vB_KleM_Rak2. This work presents a detailed and comparative analysis of vB_PcaM_CBB of a highly atypical jumbo myoviridae phage, contributing to a better understanding of phage diversity and biology.

Cairns, J., Becks, L., Jalasvuori, M., and Hiltunen, T. Sublethal streptomycin concentrations and lytic bacteriophage together promote resistance evolution. Philos.Trans.R.Soc.Lond B Biol.Sci. 1-19-2017; 372(1712); PM: 27920385

ABSTRACT: Sub-minimum inhibiting concentrations (sub-MICs) of antibiotics frequently occur in natural environments owing to wide-spread antibiotic leakage by human

action. Even though the concentrations are very low, these sub-MICs have recently been shown to alter bacterial populations by selecting for antibiotic resistance and increasing the rate of adaptive evolution. However, studies are lacking on how these effects reverberate into key ecological interactions, such as bacteria-phage interactions. Previously, co-selection of bacteria by phages and antibiotic concentrations exceeding MICs has been hypothesized to decrease the rate of resistance evolution because of fitness costs associated with resistance mutations. By contrast, here we show that sub-MICs of the antibiotic streptomycin (Sm) increased the rate of phage resistance evolution, as well as causing extinction of the phage. Notably, Sm and the phage in combination also enhanced the evolution of Sm resistance compared with Sm alone. These observations demonstrate the potential of sub-MICs of antibiotics to impact key ecological interactions in microbial communities with evolutionary outcomes that can radically differ from those associated with high concentrations. Our findings also contribute to the understanding of ecological and evolutionary factors essential for the management of the antibiotic resistance problem.This article is part of the themed issue 'Human influences on evolution, and the ecological and societal consequences'.

Cairns, J., Frickel, J., Jalasvuori, M., Hiltunen, T., and Becks, L. Genomic evolution of bacterial populations under coselection by antibiotics and phage. Mol.Ecol. 2017; 26(7):1848-1859; PM: 27977892

ABSTRACT: Bacteria live in dynamic systems where selection pressures can alter rapidly, forcing adaptation to the prevailing conditions. In particular, bacteriophages and antibiotics of anthropogenic origin are major bacterial stressors in many environments. We previously observed that populations of the bacterium Pseudomonas fluorescens SBW25 exposed to the lytic bacteriophage SBW25Phi2 and a noninhibitive concentration of the antibiotic streptomycin (coselection) achieved higher levels of phage resistance compared to populations exposed to the phage alone. In addition, the phage became extinct under coselection while remaining present in the phage alone environment. Further, phenotypic tests indicated that these observations might be associated with increased mutation rate under coselection. In this study, we examined the genetic causes behind these phenotypes by whole-genome sequencing clones isolated from the end of the experiments. We were able to identify genetic factors likely responsible for streptomycin resistance, phage resistance and hypermutable (mutator) phenotypes. This constitutes genomic evidence in support of the observation that while the presence of phage did not affect antibiotic resistance, the presence of antibiotic affected phage resistance. We had previously hypothesized an association between mutators and elevated levels of phage resistance under coselection. However, our evidence regarding the mechanism was inconclusive, as although with phage mutators were only found under coselection, additional genomic evidence was lacking and phage resistance was also observed in nonmutators under coselection. More generally, our study provides novel insights into evolution between univariate and multivariate selection (here two stressors), as well as the potential role of hypermutability in natural communities.

Cardenas-Garcia, S. and Afonso, C. L. Reverse Genetics of Newcastle Disease Virus. Methods Mol.Biol. 2017; 1602:141-158; PM: 28508219

ABSTRACT: Reverse genetics allows for the generation of recombinant viruses or vectors used in functional studies, vaccine development, and gene therapy. This technique

enables genetic manipulation and cloning of viral genomes, gene mutation through site-directed mutagenesis, along with gene insertion or deletion, among other studies. An in vitro infection-based system including the highly attenuated vaccinia virus Ankara strain expressing the T7 RNA polymerase from bacteriophage T7, with co-transfection of three helper plasmids and a full-length cDNA plasmid, was successfully developed to rescue genetically modified Newcastle disease viruses in 1999. In this chapter, the materials and the methods involved in rescuing Newcastle disease virus (NDV) from cDNA, utilizing site-directed mutagenesis and gene replacement techniques, are described in detail.

Cater, K., Dandu, V. S., Bari, S. M., Lackey, K., Everett, G. F., and Hatoum-Aslan, A. A Novel Staphylococcus Podophage Encodes a Unique Lysin with Unusual Modular Design. mSphere. 2017; 2(2); PM: 28357414

ABSTRACT: Drug-resistant staphylococci, particularly Staphylococcus aureus and Staphylococcus epidermidis, are leading causes of hospital-acquired infections. Bacteriophages and their peptidoglycan hydrolytic enzymes (lysins) are currently being explored as alternatives to conventional antibiotics; however, only a limited diversity of staphylococcal phages and their lysins has yet been characterized. Here, we describe a novel staphylococcal phage and its lysins. Bacteriophage Andhra is the first reported S. epidermidis phage belonging to the family Podoviridae. Andhra possesses an 18,546-nucleotide genome with 20 open reading frames. BLASTp searches revealed that gene product 10 (gp10) and gp14 harbor putative catalytic domains with predicted peptidase and amidase activities, characteristic functions of phage lysins. We purified these proteins and show that both Andhra_gp10 and Andhra_gp14 inhibit growth and degrade cell walls of diverse staphylococci, with Andhra_gp10 exhibiting more robust activity against the panel of cell wall substrates tested. Site-directed mutagenesis of its predicted catalytic residues abrogated the activity of Andhra_gp10, consistent with the presence of a catalytic CHAP domain on its C terminus. The active site location combined with the absence of an SH3b cell wall binding domain distinguishes Andhra_gp10 from the majority of staphylococcal lysins characterized to date. Importantly, close homologs of Andhra_gp10 are present in related staphylococcal podophages, and we propose that these constitute a new class of phage-encoded lysins. Altogether, our results reveal insights into the biology of a rare family of staphylococcal phages while adding to the arsenal of antimicrobials with potential for therapeutic use. *IMPORTANCE*: The spread of antibiotic resistance among bacterial pathogens is inciting a global public health crisis. Drug-resistant Staphylococcus species, especially S. aureus and S. epidermidis, have emerged in both hospital and community settings, underscoring the urgent need for new strategies to combat staphylococcal infections. Bacterial viruses (phages) and the enzymes that they use to degrade bacterial cell walls (lysins) show promise as alternative antimicrobials; however, only a limited variety of staphylococcal phages and their lysins have yet been identified. Here, we report the discovery and characterization of a novel staphylococcal phage, Andhra. We show that Andhra encodes two lysins (Andhra_gp10 and Andhra_gp14) that inhibit growth and degrade the cell walls of diverse staphylococci, including S. aureus and S. epidermidis strains. Andhra and its unique lysins add to the arsenal of antimicrobials with potential for therapeutic use.

Chadha, P., Katare, O. P., and Chhibber, S. Liposome loaded phage cocktail: Enhanced therapeutic potential in resolving Klebsiella pneumoniae mediated burn wound infections. Burns. 5-11-2017; PM: 28502784

ABSTRACT: BACKGROUND: Klebsiella pneumoniae is one of the predominant pathogens in burn wound infections, and prevalence of multidrug resistant strains has further complicated the situation. An increased interest in phage therapy as a means of combating infection has been accruing in recent years. In order to overcome the drawbacks associated with phage therapy, the present study was conducted to evaluate the potential of liposomes as a delivery vehicle for phage in the treatment of burn wound infection. *METHODS*: Burn wound infection with Klebsiella pneumoniae B5055 was established in BALB/c mice. The therapeutic efficacy of free phage cocktail in comparison to liposome entrapped phage cocktail in resolving the course of burn wound infection in mice was evaluated. *RESULTS*: The results depicted that mice treated with liposomal entrapped phage cocktail showed higher reduction in bacterial load in blood and major organs. This was accompanied with faster resolution of the entire infection process as compared to non-liposomal free phage cocktail. The liposomes increased phage retention time in vivo thus potentiating efficacy. Liposomal phage preparation was able to protect all the test animals from death even when there was a delay of 24h in instituting the therapy. *CONCLUSION*: The results showed the potential of liposome entrapped phage cocktail for treating Klebsiella pneumoniae mediated infections. Thus, this strategy can serve as an effective approach for treating Klebsiella mediated burn wound infections in individuals who do not respond to conventional antibiotic therapy.

Champagne, C. P., Moineau, S., Lafleur, S., and Savard, T. The effect of bacteriophages on the acidification of a vegetable juice medium by microencapsulated Lactobacillus plantarum. Food Microbiol. 2017; 63:28-34; PM: 28040179

ABSTRACT: Starter cultures are increasingly being used for the production of sauerkraut, kimchi and other fermented vegetables. The goal of this study was to determine whether the microencapsulation of a bacterial culture can prevent phage infection during vegetable fermentation. Lactobacillus plantarum HER1325 was microencapsulated in alginate beads. Some beads were used without further processing, while others were freeze-dried prior to testing. Fresh beads (diameter of 2 mm) and dried cultures of the lactobacilli (particle size of 53-1000 mum) were added to a vegetable juice medium (VJM) at 1 x 107 CFU/mL. The virulent phage HER325 was added at an initial titer of 1 x 104 PFU/mL. In the absence of phages, the pH of the vegetable juice dropped to 4.2 after 40 h of fermentation at 19 degrees C. In the presence of phage HER325, acidification by both the non-microencapsulated and microencapsulated starter cultures stopped after 24 h. In all assays, the alginate particles dissolved during the 40 h of VJM fermentation. When 15 g/L of calcium chloride was added to the VJM, the alginate beads did not dissolve and significant phage protection was observed. The results suggest that phage-protected microencapsulated starter cultures can be used for vegetable fermentation if means are taken to prevent them from dissolving during acidification.

Chang, A. T., Tran, M., and Nikonowicz, E. P. Structure and Dynamics of the Tetra-A Loop and (A-A)-U Sequence Motif within the Coliphage GA Replicase RNA Operator. Biochemistry. 5-17-2017; PM: 28488852

ABSTRACT: The three-dimensional structure of a RNA hairpin containing the RNA operator binding site for bacteriophage GA coat protein is presented. The phage GA operator

contains the asymmetric (A-A)-U sequence motif and is capped by a four-adenine (tetra-A) loop. The uridine of the (A-A)-U motif preferentially pairs with the 5'-proximal cross-strand adenine, and the 3'-proximal adenine stacks into the helix. The tetra-A loop is well-ordered with adenine residues 2-4 forming a 3' stack. This loop conformation stands in contrast to the structure of the 5'-AUUA loop of the related phage MS2 operator in which residues 1 and 2 form a 5' stack. The context dependence of the (A-A)-U sequence motif conformation was examined using structures of 76 unique occurrences from the Protein Data Bank. The motif almost always has one adenine bulged and the other adenine adopting an A-U base pair. In the case in which the (A-A)-U motif is flanked by only one Watson-Crick base pair, the adenine adjacent to the flanking base pair tends to bulge; 80% of motifs with a 3' flanking pair have a 3' bulged adenine, and 84% of motifs with a 5' flanking pair have a 5' bulged adenine. The frequencies of 3'- and 5'-proximal adenines bulging are 33 and 67%, respectively, when the (A-A)-U motif is flanked by base pairs on both sides. Although a 3' flanking cytidine correlates (88%) with bulging of the 5'-proximal adenine, no strict dependence on flanking nucleotide identity was identified for the 5' side.

Chang, Y., Yoon, H., Kang, D. H., Chang, P. S., and Ryu, S. Endolysin LysSA97 is synergistic with carvacrol in controlling Staphylococcus aureus in foods. Int.J.Food Microbiol. 3-6-2017; 244:19-26; PM: 28063330

ABSTRACT: LysSA97 is an endolysin encoded by the bacteriophage SA97, the genome sequence of which has been recently revealed. LysSA97 has lytic activity against a variety of Staphylococcus strains that cause foodborne illness. In order to improve its potential as a biocontrol agent against Staphylococcus, various types of essential oil-derived active compounds were tested in combination with LysSA97; carvacrol exhibited significant synergistic effects when combined with LysSA97. The synergistic antimicrobial activity between endolysin and carvacrol in food products, including milk and beef, were investigated. While LysSA97 (376nM) and carvacrol (3.33mM) showed 0.8+/-0.2 and 1.0+/-0.0logCFU/mL reduction in Staphylococcus aureus cells, respectively; when applied alone in bacterial culture, the cocktail containing both at the same concentrations exhibited a bacterial decrease of 4.5+/-0.2logCFU/mL. The synergistic activity of carvacrol was also reproduced in combination with other endolysins, and their cooperative bactericidal effects were validated in ten additional S. aureus strains, including two methicillin-resistant S. aureus (MRSA), suggesting the wide application of carvacrol as a bactericidal agent coupled with endolysin. When LysSA97 and carvacrol were used in combination in foods, the synergistic activity appeared to be influenced by the total lipid content of foods, and bacteria in skim milk were more drastically inactivated than those in whole milk. Therefore, this is the first report demonstrating that endolysin and carvacrol act synergistically to inactivate S. aureus in food products.

Chang, Y. W., Rettberg, L. A., Ortega, D. R., and Jensen, G. J. In vivo structures of an intact type VI secretion system revealed by electron cryotomography. EMBO Rep. 5-9-2017; PM: 28487352

ABSTRACT: The type VI secretion system (T6SS) is a versatile molecular weapon used by many bacteria against eukaryotic hosts or prokaryotic competitors. It consists of a cytoplasmic bacteriophage tail-like structure anchored in the bacterial cell envelope via a cytoplasmic baseplate and a periplasmic membrane complex. Rapid contraction of the sheath in the bacteriophage tail-like structure propels an inner tube/spike complex

through the target cell envelope to deliver effectors. While structures of purified contracted sheath and purified membrane complex have been solved, because sheaths contract upon cell lysis and purification, no structure is available for the extended sheath. Structural information about the baseplate is also lacking. Here, we use electron cryotomography to directly visualize intact T6SS structures inside Myxococcus xanthus cells. Using sub-tomogram averaging, we resolve the structure of the extended sheath and membrane-associated components including the baseplate. Moreover, we identify novel extracellular bacteriophage tail fiber-like antennae. These results provide new structural insights into how the extended sheath prevents premature disassembly and how this sophisticated machine may recognize targets.

Chaudhary, K., Chattopadhyay, A., and Pratap, D. Anti-CRISPR proteins: Counterattack of phages on bacterial defense (CRISPR/Cas) system. J.Cell Physiol. 3-1-2017; PM: 28247934

ABSTRACT: Since the dawn of life there is a never ending strife between bacteria and phages. Both are perpetually changing their strategies to take over each other. CRISPR/Cas is the most widespread defense system used by bacteria against mobile genetic elements (MGEs) such as phages, cojugative palsmids, transoposons, and pathogenicity islands. This system utilizes small guide RNA molecules to protect against phages infection and invasion by MGEs. Phages circumvent to these antiviral barriers by point mutation in PAM (protospacer-adjacent motif) sequence, genome rearrangements and by using anti-CRISPR proteins.

Chaudhry, W. N., Concepcion-Acevedo, J., Park, T., Andleeb, S., Bull, J. J., and Levin, B. R. Synergy and Order Effects of Antibiotics and Phages in Killing Pseudomonas aeruginosa Biofilms. PLoS.One. 2017; 12(1):e0168615; PM: 28076361

ABSTRACT: In contrast to planktonic cells, bacteria imbedded biofilms are notoriously refractory to treatment by antibiotics or bacteriophage (phage) used alone. Given that the mechanisms of killing differ profoundly between drugs and phages, an obvious question is whether killing is improved by combining antibiotic and phage therapy. However, this question has only recently begun to be explored. Here, in vitro biofilm populations of Pseudomonas aeruginosa PA14 were treated singly and with combinations of two phages and bactericidal antibiotics of five classes. By themselves, phages and drugs commonly had only modest effects in killing the bacteria. However some phage-drug combinations reduced bacterial densities to well below that of the best single treatment; in some cases, bacterial densities were reduced even below the level expected if both agents killed independently of each other (synergy). Furthermore, there was a profound order effect in some cases: treatment with phages before drugs achieved maximum killing. Combined treatment was particularly effective in killing in Pseudomonas biofilms grown on layers of cultured epithelial cells. Phages were also capable of limiting the extent to which minority populations of bacteria resistant to the treating antibiotic ascend. The potential of combined antibiotic and phage treatment of biofilm infections is discussed as a realistic way to evaluate and establish the use of bacteriophage for the treatment of humans.

Chen, J., An, Y., Kumar, A., and Liu, Z. Improvement of chitinase Pachi with nematicidal activities by random mutagenesis. Int.J.Biol.Macromol. 2017; 96:171-176; PM: 27989482

ABSTRACT: Chitinase, an enzyme that can degrade the main compositions of insect intestine and cuticle, has been used in the bio-control field. Our previous work has reported the chitinase Pachi with nematicidal activity (Caenorhabditis elegans). In the present study, to improve the chitinolytic and nematicidal activities of Pachi, a random mutant library was constructed by error-prone PCR and screened by bacteriophage T7-based high-throughput screening system. One mutant, PachiN35D was obtained from about 10, 000 clones. The kinetics analysis revealed that PachiN35D exhibited a 63% decrease in Km value against chitosan, a 2.1-fold enhancement in kcat/Km value and a 1.2-fold increase in specific activity over the wild-type Pachi. Moreover, the mortality analysis against Caenorhabditis elegans showed that the 50% lethal concentration (LC50) of PachiN35D is 309.6+/-1.1mug/ml and a 20% increase in nematicidal activity over the wild-type Pachi (with a LC50 value of 387.3+/-31.7mug/ml). The structure modeling and superimposition indicated that the substitution N35D reduced the distance between substrate and substrate-binding site Asp141, finally resulting in an increase in substrate affinity, catalytic efficiency and specific activity. These results provide useful information for the study of structure-function relationship of Pachi and lay a foundation for its potential applications in agro-biotechnology.

Chertkov, O. V., Armeev, G. A., Uporov, I. V., Legotsky, S. A., Sykilinda, N. N., Shaytan, A. K., Klyachko, N. L., and Miroshnikov, K. A. Dual Active Site in the Endolytic Transglycosylase gp144 of Bacteriophage phiKZ. Acta Naturae. 2017; 9(1):81-87; PM: 28461978

ABSTRACT: Lytic transglycosylases are abundant peptidoglycan lysing enzymes that degrade the heteropolymers of bacterial cell walls in metabolic processes or in the course of a bacteriophage infection. The conventional catalytic mechanism of transglycosylases involves only the Glu or Asp residue. Endolysin gp144 of Pseudomonas aeruginosa bacteriophage phiKZ belongs to the family of Gram-negative transglycosylases with a modular composition and C-terminal location of the catalytic domain. Glu115 of gp144 performs the predicted role of a catalytic residue. However, replacement of this residue does not completely eliminate the activity of the mutant protein. Site-directed mutagenesis has revealed the participation of Tyr197 in the catalytic mechanism, as well as the presence of a second active site involving Glu178 and Tyr147. The existence of the dual active site was supported by computer modeling and monitoring of the molecular dynamics of the changes in the conformation and surface charge distribution as a consequence of point mutations.

Cherwa, J. E., Jr., Tyson, J., Bedwell, G. J., Brooke, D., Edwards, A. G., Dokland, T., Prevelige, P. E., and Fane, B. A. varphiX174 Procapsid Assembly: Effects of an Inhibitory External Scaffolding Protein and Resistant Coat Proteins In Vitro. J.Virol. 1-1-2017; 91(1); PM: 27795440

ABSTRACT: During varphiX174 morphogenesis, 240 copies of the external scaffolding protein D organize 12 pentameric assembly intermediates into procapsids, a reaction reconstituted in vitro In previous studies, varphiX174 strains resistant to exogenously expressed dominant lethal D genes were experimentally evolved. Resistance was achieved by the stepwise acquisition of coat protein mutations. Once resistance was established, a stimulatory D protein mutation that greatly increased strain fitness arose. In this study, in vitro biophysical and biochemical methods were utilized to elucidate the mechanistic details and evolutionary trade-offs created by the resistance mutations. The

kinetics of procapsid formation was analyzed in vitro using wild-type, inhibitory, and experimentally evolved coat and scaffolding proteins. Our data suggest that viral fitness is correlated with in vitro assembly kinetics and demonstrate that in vivo experimental evolution can be analyzed within an in vitro biophysical context. IMPORTANCE: Experimental evolution is an extremely valuable tool. Comparisons between ancestral and evolved genotypes suggest hypotheses regarding adaptive mechanisms. However, it is not always possible to rigorously test these hypotheses in vivo We applied in vitro biophysical and biochemical methods to elucidate the mechanistic details that allowed an experimentally evolved virus to become resistant to an antiviral protein and then evolve a productive use for that protein. Moreover, our results indicate that the respective roles of scaffolding and coat proteins may have been redistributed during the evolution of a two-scaffolding-protein system. In one-scaffolding-protein virus assembly systems, coat proteins promiscuously interact to form heterogeneous aberrant structures in the absence of scaffolding proteins. Thus, the scaffolding protein controls fidelity. During varphiX174 assembly, the external scaffolding protein acts like a coat protein, self-associating into large aberrant spherical structures in the absence of coat protein, whereas the coat protein appears to control fidelity.

Chung, C. H., Walter, M. H., Yang, L., Chen, S. G., Winston, V., and Thomas, M. A. Predicting genome terminus sequences of Bacillus cereus-group bacteriophage using next generation sequencing data. BMC.Genomics. 5-4-2017; 18(1):350; PM: 28472946

ABSTRACT: BACKGROUND: Most tailed bacteriophages (phages) feature linear dsDNA genomes. Characterizing novel phages requires an understanding of complete genome sequences, including the definition of genome physical ends. *RESULT*: We sequenced 48 Bacillus cereus phage isolates and analyzed Next-generation sequencing (NGS) data to resolve the genome configuration of these novel phages. Most assembled contigs featured reads that mapped to both contig ends and formed circularized contigs. Independent assemblies of 31 nearly identical I48-like Bacillus phage isolates allowed us to observe that the assembly programs tended to produce random cleavage on circularized contigs. However, currently available assemblers were not capable of reporting the underlying phage genome configuration from sequence data. To identify the genome configuration of sequenced phage in silico, a terminus prediction method was developed by means of 'neighboring coverage ratios' and 'read edge frequencies' from read alignment files. Termini were confirmed by primer walking and supported by phylogenetic inference of large DNA terminase protein sequences. *CONCLUSIONS*: The Terminus package using phage NGS data along with the contig circularity could efficiently identify the proximal positions of phage genome terminus. Complete phage genome sequences allow a proposed characterization of the potential packaging mechanisms and more precise genome annotation.

Cisek, A. A., Dabrowska, I., Gregorczyk, K. P., and Wyzewski, Z. Phage Therapy in Bacterial Infections Treatment: One Hundred Years After the Discovery of Bacteriophages. Curr.Microbiol. 2017; 74(2):277-283; PM: 27896482

ABSTRACT: The therapeutic use of bacteriophages has seen a renewal of interest blossom in the last few years. This reversion is due to increased difficulties in the treatment of antibiotic-resistant strains of bacteria. Bacterial resistance to antibiotics, a serious problem in contemporary medicine, does not implicate resistance to phage lysis mechanisms. Lytic bacteriophages are able to kill antibiotic-resistant bacteria at the end

of the phage infection cycle. Thus, the development of phage therapy is potentially a way to improve the treatment of bacterial infections. However, there are antibacterial phage therapy difficulties specified by broadening the knowledge of the phage nature and influence on the host. It has been shown during experiments that both innate and adaptive immunity are involved in the clearance of phages from the body. Immunological reactions against phages are related to the route of administration and may vary depending on the type of bacterial viruses. For that reason, it is very important to test the immunological response of every single phage, particularly if intravenous therapy is being considered. The lack of these data in previous years was one of the reasons for phage therapy abandonment despite its century-long study. Promising results of recent research led us to look forward to a phage therapy that can be applied on a larger scale and subsequently put it into practice.

Colavecchio, A., Jeukens, J., Freschi, L., Edmond Rheault, J. G., Kukavica-Ibrulj, I., Levesque, R., and Goodridge, L. AnCo3, a New Member of the Emerging Family of Phage-Like Plasmids. Genome Announc. 5-11-2017; 5(19);PM: 28495760

ABSTRACT: A phage-like plasmid isolated from a clinical isolate of Salmonella enterica serovar Derby has strong nucleotide sequence identity to the phage-like plasmids pSTM_phi isolated from Salmonella enterica serovar Typhimurium L495, AnCo1 and AnCo2 from Escherichia coli 243 and Escherichia coli 244, and the virulent Salmonella-specific SSU5 bacteriophage.

Colavecchio, A., Jeukens, J., Freschi, L., Edmond Rheault, J. G., Kukavica-Ibrulj, I., Levesque, R. C., LeJeune, J., and Goodridge, L. Complete Genome Sequences of Two Phage-Like Plasmids Carrying the CTX-M-15 Extended-Spectrum beta-Lactamase Gene. Genome Announc. 5-11-2017; 5(19); PM: 28495759

ABSTRACT: Two similar phage-like plasmids carrying CTX-M-15 resistance cassettes were identified from two environmental Escherichia coli isolates. They demonstrate strong nucleotide sequence identity to the phage-like plasmid pECOH89 and Salmonella bacteriophage SSU5.

Colom, J., Cano-Sarabia, M., Otero, J., rinez-Soriano, J., Cortes, P., Maspoch, D., and Llagostera, M. Microencapsulation with alginate/CaCO3: A strategy for improved phage therapy. Sci.Rep. 1-25-2017; 7:41441; PM: 28120922

ABSTRACT: Bacteriophages are promising therapeutic agents that can be applied to different stages of the commercial food chain. In this sense, bacteriophages can be orally administered to farm animals to protect them against intestinal pathogens. However, the low pH of the stomach, the activities of bile and intestinal tract enzymes limit the efficacy of the phages. This study demonstrates the utility of an alginate/CaCO3 encapsulation method suitable for bacteriophages with different morphologies and to yield encapsulation efficacies of ~100%. For the first time, a cocktail of three alginate/CaCO3-encapsulated bacteriophages was administered as oral therapy to commercial broilers infected with Salmonella under farm-like conditions. Encapsulation protects the bacteriophages against their destruction by the gastric juice. Phage release from capsules incubated in simulated intestinal fluid was also demonstrated, whereas encapsulation ensured sufficient intestinal retention of the phages. Moreover, the small

size of the capsules (125-150 mum) enables their use in oral therapy and other applications in phage therapy. This study evidenced that a cocktail of the three alginate/CaCO3-encapsulated bacteriophages had a greater and more durable efficacy than a cocktail of the corresponding non-encapsulated phages in as therapy in broilers against Salmonella, one of the most common foodborne pathogen.

Costa, V., Righelli, D., Russo, F., De, Berardinis P., Angelini, C., and D'Apice, L. Distinct Antigen Delivery Systems Induce Dendritic Cells' Divergent Transcriptional Response: New Insights from a Comparative and Reproducible Computational Analysis. Int.J.Mol.Sci. 2-25-2017; 18(3); PM: 28245601

ABSTRACT: Vaccination is the most successful and cost-effective method to prevent infectious diseases. However, many vaccine antigens have poor in vivo immunogenic potential and need adjuvants to enhance immune response. The application of systems biology to immunity and vaccinology has yielded crucial insights about how vaccines and adjuvants work. We have previously characterized two safe and powerful delivery systems derived from non-pathogenic prokaryotic organisms: E2 and fd filamentous bacteriophage systems. They elicit an in vivo immune response inducing CD8+ T-cell responses, even in absence of adjuvants or stimuli for dendritic cells' maturation. Nonetheless, a systematic and comparative analysis of the complex gene expression network underlying such activation is missing. Therefore, we compared the transcriptomes of ex vivo isolated bone marrow-derived dendritic cells exposed to these antigen delivery systems. Significant differences emerged, especially for genes involved in innate immunity, co-stimulation, and cytokine production. Results indicate that E2 drives polarization toward the Th2 phenotype, mainly mediated by Irf4, Ccl17, and Ccr4 over-expression. Conversely, fd-scalphaDEC-205 triggers Th1 T cells' polarization through the induction of Il12b, Il12rb, Il6, and other molecules involved in its signal transduction. The data analysis was performed using RNASeqGUI, hence, addressing the increasing need of transparency and reproducibility of computational analysis.

Costantini, A., Doria, F., Saiz, J. C., and Garcia-Moruno, E. Phage-host interactions analysis of newly characterized Oenococcus oeni bacteriophages: Implications for malolactic fermentation in wine. Int.J.Food Microbiol. 4-4-2017; 246:12-19; PM: 28189899

ABSTRACT: Nowadays, only few phages infecting Oenococcus oeni, the principal lactic acid bacteria (LAB) species responsible for malolactic fermentation (MLF) in wine, have been characterized. In the present study, to better understanding the factors affecting the lytic activity of Oenococcus phages, fifteen O. oeni bacteriophages have been studied in detail, both with molecular and microbiological methods. No correlations were found between genome sizes, type of integrase genes, or morphology and the lytic activity of the 15 tested phages. Interestingly, though phage attack in a wine at the end of alcoholic fermentation seems not to be a problem, it can indeed represent a risk factor for MLF when the alcohol content is low, feature that may be a key point for choosing the appropriate time for malolactic starter inoculation. Additionally, it was observed that some phages genomes bear 2 or 3 types of integrase genes, which point to horizontal gene transfer between O. oeni bacteriophages.

Criscuolo, E., Spadini, S., Lamanna, J., Ferro, M., and Burioni, R. Bacteriophages and Their Immunological Applications against Infectious Threats. J.Immunol.Res. 2017; 2017:3780697; PM: 28484722

ABSTRACT: Bacteriophage therapy dates back almost a century, but the discovery of antibiotics led to a rapid decline in the interests and investments within this field of research. Recently, the novel threat of multidrug-resistant bacteria highlighted the alarming drop in research and development of new antibiotics: 16 molecules were discovered during 1983-87, 10 new therapeutics during the nineties, and only 5 between 2003 and 2007. Phages are therefore being reconsidered as alternative therapeutics. Phage display technique has proved to be extremely promising for the identification of effective antibodies directed against pathogens, as well as for vaccine development. At the same time, conventional phage therapy uses lytic bacteriophages for treatment of infections and recent clinical trials have shown great potential. Moreover, several other approaches have been developed in vitro and in vivo using phage-derived proteins as antibacterial agents. Finally, their use has also been widely considered for public health surveillance, as biosensor phages can be used to detect food and water contaminations and prevent bacterial epidemics. These novel approaches strongly promote the idea that phages and their proteins can be exploited as an effective weapon in the near future, especially in a world which is on the brink of a "postantibiotic era.".

Cuba, Samaniego C., Giordano, G., Blanchini, F., and Franco, E. Stability analysis of an artificial biomolecular oscillator with non-cooperative regulatory interactions. J.Biol.Dyn. 2017; 11(1):102-120; PM: 27830588

ABSTRACT: Oscillators are essential to fuel autonomous behaviours in molecular systems. Artificial oscillators built with programmable biological molecules such as DNA and RNA are generally easy to build and tune, and can serve as timers for biological computation and regulation. We describe a new artificial nucleic acid biochemical reaction network, and we demonstrate its capacity to exhibit oscillatory solutions. This network can be built in vitro using nucleic acids and three bacteriophage enzymes, and has the potential to be implemented in cells. Numerical simulations suggest that oscillations occur in a realistic range of reaction rates and concentrations.

Cui, L. and Shearwin, K. E. Clonetegration Using OSIP Plasmids: One-Step DNA Assembly and Site-Specific Genomic Integration in Bacteria. Methods Mol.Biol. 2017; 1472:139-155; PM: 27671938

ABSTRACT: Clonetegration is a method for site-specific insertion of DNA into prokaryotic chromosomes, based on bacteriophage integrases. The method combines DNA cloning/assembly and chromosomal integration into a single step, providing a simple and rapid strategy for inserting DNA sequences into bacterial chromosomes.

Cui, Z., Guo, X., Dong, K., Zhang, Y., Li, Q., Zhu, Y., Zeng, L., Tang, R., and Li, L. Safety assessment of Staphylococcus phages of the family Myoviridae based on complete genome sequences. Sci.Rep. 1-24-2017; 7:41259; PM: 28117392

ABSTRACT: Staphylococcus phages of the Myoviridae family have a wide host range and potential applications in phage therapy. In this report, safety assessments of these phages were conducted based on their complete genome sequences. The complete

genomes of Staphylococcus phages of the Myoviridae family were analyzed, and the Open Reading Frame (ORFs) were compared with a pool of virulence and antibiotic resistance genes using the BLAST algorithm. In addition, the lifestyle of the phages (virulent or temperate) was also confirmed using PHACTS. The results showed that all phages were lytic and did not contain resistance or virulence genes based on bioinformatic analyses, excluding the possibility that they could be vectors for the dissemination of these undesirable genes. These findings suggest that the phages are safe at the genome level. The SceD-like transglycosylase, which is a biomarker for vancomycin-intermediate strains, was widely distributed in the phage genomes. Approximately 70% of the ORFs encoded in the phage genomes have unknown functions; therefore, their roles in the antibiotic resistance and virulence of Staphylococcus aureus are still unknown and require consideration before use in phage therapy.

Cui, Z., Feng, T., Gu, F., Li, Q., Dong, K., Zhang, Y., Zhu, Y., Han, L., Qin, J., and Guo, X. Characterization and complete genome of the virulent Myoviridae phage JD007 active against a variety of Staphylococcus aureus isolates from different hospitals in Shanghai, China. Virol.J. 2-8-2017; 14(1):26;PM: 28179010

ABSTRACT: BACKGROUND: The implementation of phage therapy is re-emerging with the increase in widespread antibiotic-resistant bacteria. *METHODS*: Staphylococcus phage JD007 was characterized and its complete genome sequence analysed. RESULTS: Staphylococcus phage JD007 was classified as belonging to the Myoviridae family based on its morphology, as observed by transmission electron microscopy. Its lytic activity was stable between pH 5-11 and below 42 degrees C; moreover, an absorbance curve showed that nearly 90% of the viral particles had adsorbed to its host after a 20 min co-incubation. The complete genome size is 141,836 bp, making JD007 one of the largest Staphylococcus phages of Myoviridae. No identifiable resistance or virulence genes were found in the JD007 genome. JD007 was able to lyse 95% of S. aureus isolates, including the prevalent ST239-MRSA and ST59-MRSA strains isolated from different hospitals in Shanghai, China, and inhibition assays showed that JD007 could inhibit S. aureus growth at a multiplicity of infection of 0.1. *CONCLUSIONS*: The results suggested that Staphylococcus phage JD007 can potentially be used in phage therapy or for the detection of S. aureus.

Dai, X., Li, Z., Lai, M., Shu, S., Du, Y., Zhou, Z. H., and Sun, R. In situ structures of the genome and genome-delivery apparatus in a single-stranded RNA virus. Nature. 1-5-2017; 541(7635):112-116; PM: 27992877

ABSTRACT: Packaging of the genome into a protein capsid and its subsequent delivery into a host cell are two fundamental processes in the life cycle of a virus. Unlike double-stranded DNA viruses, which pump their genome into a preformed capsid, single-stranded RNA (ssRNA) viruses, such as bacteriophage MS2, co-assemble their capsid with the genome; however, the structural basis of this co-assembly is poorly understood. MS2 infects Escherichia coli via the host 'sex pilus' (F-pilus); it was the first fully sequenced organism and is a model system for studies of translational gene regulation, RNA-protein interactions, and RNA virus assembly. Its positive-sense ssRNA genome of 3,569 bases is enclosed in a capsid with one maturation protein monomer and 89 coat protein dimers arranged in a T = 3 icosahedral lattice. The maturation protein is responsible for attaching the virus to an F-pilus and delivering the viral genome into the host during infection, but

how the genome is organized and delivered is not known. Here we describe the MS2 structure at 3.6 A resolution, determined by electron-counting cryo-electron microscopy (cryoEM) and asymmetric reconstruction. We traced approximately 80% of the backbone of the viral genome, built atomic models for 16 RNA stem-loops, and identified three conserved motifs of RNA-coat protein interactions among 15 of these stem-loops with diverse sequences. The stem-loop at the 3' end of the genome interacts extensively with the maturation protein, which, with just a six-helix bundle and a six-stranded beta-sheet, forms a genome-delivery apparatus and joins 89 coat protein dimers to form a capsid. This atomic description of genome-capsid interactions in a spherical ssRNA virus provides insight into genome delivery via the host sex pilus and mechanisms underlying ssRNA-capsid co-assembly, and inspires speculation about the links between nucleoprotein complexes and the origins of viruses.

Darch, S. E., Kragh, K. N., Abbott, E. A., Bjarnsholt, T., Bull, J. J., and Whiteley, M. Phage Inhibit Pathogen Dissemination by Targeting Bacterial Migrants in a Chronic Infection Model. MBio. 4-4-2017; 8(2); PM:28377527

ABSTRACT: The microbial communities inhabiting chronic infections are often composed of spatially organized micrometer-sized, highly dense aggregates. It has recently been hypothesized that aggregates are responsible for the high tolerance of chronic infections to host immune functions and antimicrobial therapies. Little is currently known regarding the mechanisms controlling aggregate formation and antimicrobial tolerance primarily because of the lack of robust, biologically relevant experimental systems that promote natural aggregate formation. Here, we developed an in vitro model based on chronic Pseudomonas aeruginosa infection of the cystic fibrosis (CF) lung. This model utilizes a synthetic sputum medium that readily promotes the formation of P. aeruginosa aggregates with sizes similar to those observed in human CF lung tissue. Using high-resolution imaging, we exploited this model to elucidate the life history of P. aeruginosa and the mechanisms that this bacterium utilizes to tolerate antimicrobials, specifically, bacteriophage. In the early stages of growth in synthetic sputum, planktonic cells form aggregates that increase in size over time by expansion. In later growth, migrant cells disperse from aggregates and colonize new areas, seeding new aggregates. When added simultaneously with phage, P. aeruginosa was readily killed and aggregates were unable to form. When added after initial aggregate formation, phage were unable to eliminate all of the aggregates because of exopolysaccharide production; however, seeding of new aggregates by dispersed migrants was inhibited. We propose a model in which aggregates provide a mechanism that allows P. aeruginosa to tolerate phage therapy during chronic infection without the need for genetic mutation.IMPORTANCE Bacteria in chronic infections often reside in communities composed of micrometer-sized, highly dense aggregates. A primary challenge for studying aggregates has been the lack of laboratory systems that promote natural aggregate formation in relevant environments. Here, we developed a growth medium that mimics chronic lung infection and promotes natural aggregate formation by the bacterium Pseudomonas aeruginosa High-resolution, single-cell microscopy allowed us to characterize P. aeruginosa's life history-seeding, aggregate formation, and dispersal-in this medium. Our results reveal that this bacterium readily forms aggregates that release migrants to colonize new areas. We also show that aggregates allow P. aeruginosa to tolerate therapeutic bacteriophage addition, although this treatment limits P. aeruginosa dissemination by targeting migrants.

Davies, E. V., James, C. E., Brockhurst, M. A., and Winstanley, C. Evolutionary diversification of Pseudomonas aeruginosa in an artificial sputum model. BMC.Microbiol. 1-5-2017; 17(1):3; PM: 28056789

ABSTRACT: BACKGROUND: During chronic lung infections of cystic fibrosis patients Pseudomonas aeruginosa populations undergo extensive evolutionary diversification. However, the selective drivers of this evolutionary process are poorly understood. To test the effects of temperate phages on diversification in P. aeruginosa biofilms we experimentally evolved populations of P. aeruginosa for approximately 240 generations in artificial sputum medium with or without a community of three temperate phages. *RESULTS*: Analysis of end-point populations using a suite of phenotypic tests revealed extensive phenotypic diversification within populations, but no significant differences between the populations evolved with or without phages. The most common phenotypic variant observed was loss of all three types of motility (swimming, swarming and twitching) and resistance to all three phages. Despite the absence of selective pressure, some members of the population evolved antibiotic resistance. The frequency of antibiotic resistant isolates varied according to population and the antibiotic tested. However, resistance to ceftazidime and tazobactam-piperacillin was observed more frequently than resistance to other antibiotics, and was associated with higher prevelence of isolates exhibiting a hypermutable phenotype and increased beta-lactamase production. *CONCLUSIONS*: We observed considerable within-population phenotypic diversity in P. aeruginosa populations evolving in the artificial sputum medium biofilm model. Replicate populations evolved both in the presence and absence of phages converged upon similar sets of phenotypes. The evolved phenotypes, including antimicrobial resistance, were similar to those observed amongst clinical isolates from cystic fibrosis infections.

de, Leeuw M., Baron, M., Brenner, A., and Kushmaro, A. Genome Analysis of a Novel Broad Host Range Proteobacteria Phage Isolated from a Bioreactor Treating Industrial Wastewater. Genes (Basel). 1-18-2017; 8(1); PM: 28106814

ABSTRACT: Bacteriophages are viruses that infect bacteria, and consequently they have a major impact on the development of a microbial population. In this study, the genome of a novel broad host range bacteriophage, Aquamicrobium phage P14, isolated from a wastewater treatment plant, was analyzed. The Aquamicrobium phage P14 was found to infect members of different Proteobacteria classes (Alphaproteobacteria and Betaproteobacteria). This phage contains a 40,551 bp long genome and 60% of its genes had blastx hits. Furthermore, the bacteriophage was found to share more than 50% of its genes with several podoviruses and has the same gene order as other polyvalent bacteriophages. The results obtained in this study led to the conclusion that indeed general features of the genome of the Aquamicrobium phage P14 are shared with other broad host range bacteriophages, however further analysis of the genome is needed in order to identify the specific mechanisms which enable the bacteriophage to infect both Alphaproteobacteria and Betaproteobacteria.

Delgado, A., Arco, R., Ibarra-Molero, B., and Sanchez-Ruiz, J. M. Using Resurrected Ancestral Proviral Proteins to Engineer Virus Resistance. Cell Rep. 5-9-2017; 19(6):1247-1256; PM: 28494872

ABSTRACT: Proviral factors are host proteins hijacked by viruses for processes essential for

virus propagation such as cellular entry and replication. Pathogens and their hosts co-evolve. It follows that replacing a proviral factor with a functional ancestral form of the same protein could prevent viral propagation without fatally compromising organismal fitness. Here, we provide proof of concept of this notion. Thioredoxins serve as general oxidoreductases in all known cells. We report that several laboratory resurrections of Precambrian thioredoxins display substantial levels of functionality within Escherichia coli. Unlike E. coli thioredoxin, however, these ancestral thioredoxins are not efficiently recruited by the bacteriophage T7 for its replisome and therefore prevent phage propagation in E. coli. These results suggest an approach to the engineering of virus resistance. Diseases caused by viruses may have a devastating effect in agriculture. We discuss how the suggested approach could be applied to the engineering of plant virus resistance.

Dendooven, T., Van den, Bossche A., Hendrix, H., Ceyssens, P. J., Voet, M., Bandyra, K. J., De, Maeyer M., Aertsen, A., Noben, J. P., Hardwick, S. W., Luisi, B. F., and Lavigne, R. Viral interference of the bacterial RNA metabolism machinery. RNA.Biol. 1-2-2017; 14(1):6-10; PM: 27834591

ABSTRACT: In a recent publication, we reported a unique interaction between a protein encoded by the giant myovirus phiKZ and the Pseudomonas aeruginosa RNA degradosome. Crystallography, site-directed mutagenesis and interactomics approaches revealed this 'degradosome interacting protein' or Dip, to adopt an 'open-claw' dimeric structure that presents acidic patches on its outer surface which hijack 2 conserved RNA binding sites on the scaffold domain of the RNase E component of the RNA degradosome. This interaction prevents substrate RNAs from being bound and degraded by the RNA degradosome during the virus infection cycle. In this commentary, we provide a perspective into the biological role of Dip, its structural analysis and its mysterious evolutionary origin, and we suggest some therapeutic and biotechnological applications of this distinctive viral protein.

Denyes, J. M., Dunne, M., Steiner, S., Mittelviefhaus, M., Weiss, A., Schmidt, H., Klumpp, J., and Loessner, M. J. Modified bacteriophage S16 long tail fiber proteins for rapid and specific immobilization and detection of Salmonella cells. Appl.Environ.Microbiol. 4-14-2017; PM: 28411223

ABSTRACT: Bacteriophage-based assays and biosensors rival traditional antibody-based immunoassays for detection of low-level Salmonella contaminations. In this study, we harnessed the binding specificity of the long tail fiber (LTF) from bacteriophage S16 as an affinity molecule for immobilization, enrichment, and detection of Salmonella We demonstrate that paramagnetic beads (MBs) coated with recombinant gp37-gp38 LTF complexes (LTF-MBs) are highly effective tools for rapid affinity magnetic separation and enrichment of Salmonella Within 45 minutes, the LTF-MBs consistently captured over 95% of Salmonella Typhimurium cells from suspensions containing 10-105 CFU.ml-1, and yielded equivalent recovery rates (93 +/- 5%, n = 10) for other tested Salmonella spp. LTF-MBs also captured Salmonella from various food sample pre-enrichments, allowing detection of initial contaminations of 1-10 CFU per 25 g/ml. While plating of bead-captured cells allowed ultrasensitive, but time-consuming detection, the integration of LTF-based enrichment in a sandwich assay with horseradish peroxidase-conjugated LTF (HRP-LTF) as a detection probe produced a rapid and and easy-to-use Salmonella detection assay. The novel Enzyme-linked LTF Assay (ELLTA) uses HRP-LTF to label bead-

captured Salmonella for subsequent identification by HRP-catalyzed conversion of chromogenic 3,3' ,5,5' -Tetramethylbenzidine substrate. Color development was proportional to Salmonella concentrations between 102-107 CFU.ml-1, as determined by spectrophotometric quantification. The ELLTA assay takes 2 h to complete and detected as few as 102 CFU.ml-1 of S. Typhimurium cells. It positively identified 21 different Salmonella strains, with no cross-reactivity for other bacteria. In conclusion, the phage-based ELLTA represents a rapid, sensitive, and specific diagnostic assay, which appears superior to other currently available tests.Importance The incidence of foodborne diseases has increased over the years resulting in major global public health issues. Conventional methods for pathogen detection can be laborious, expensive, and require lengthy pre-enrichment steps. Rapid enrichment-based diagnostic assays, such as immunomagnetic separation, can reduce detection times while also remaining sensitive and specific. A critical component in these tests is implementing affinity molecules that retain the ability to specifically capturing target pathogens over a wide-range of in situ applications. The protein complex that forms the distal tip of the bacteriophage S16 long tail fiber is here shown to represent a highly sensitive affinity molecule for the specific enrichment and detection of Salmonella Phage-encoded long tail fibers have huge potential for development as novel affinity molecules, for robust and specific diagnostics of a vast spectrum of bacteria.

Descamps, E. C., Meunier, D., Brutesco, C., Preveral, S., Franche, N., Bazin, I., Miclot, B., Larosa, P., Escoffier, C., Fantino, J. R., Garcia, D., Ansaldi, M., Rodrigue, A., Pignol, D., Cholat, P., and Ginet, N. Semi-autonomous inline water analyzer: design of a common light detector for bacterial, phage, and immunological biosensors. Environ.Sci.Pollut.Res.Int. 2017; 24(1):66-72; PM: 27838908

ABSTRACT: The use of biosensors as sensitive and rapid alert systems is a promising perspective to monitor accidental or intentional environmental pollution, but their implementation in the field is limited by the lack of adapted inline water monitoring devices. We describe here the design and initial qualification of an analyzer prototype able to accommodate three types of biosensors based on entirely different methodologies (immunological, whole-cell, and bacteriophage biosensors), but whose responses rely on the emission of light. We developed a custom light detector and a reaction chamber compatible with the specificities of the three systems and resulting in statutory detection limits. The water analyzer prototype resulting from the COMBITOX project can be situated at level 4 on the Technology Readiness Level (TRL) scale and this technical advance paves the way to the use of biosensors on-site.

Diard, M., Bakkeren, E., Cornuault, J. K., Moor, K., Hausmann, A., Sellin, M. E., Loverdo, C., Aertsen, A., Ackermann, M., De, Paepe M., Slack, E., and Hardt, W. D. Inflammation boosts bacteriophage transfer between Salmonella spp. Science. 3-17-2017; 355(6330):1211-1215; PM: 28302859

ABSTRACT: Bacteriophage transfer (lysogenic conversion) promotes bacterial virulence evolution. There is limited understanding of the factors that determine lysogenic conversion dynamics within infected hosts. A murine Salmonella Typhimurium (STm) diarrhea model was used to study the transfer of SopEPhi, a prophage from STm SL1344, to STm ATCC14028S. Gut inflammation and enteric disease triggered >55% lysogenic conversion of ATCC14028S within 3 days. Without inflammation, SopEPhi transfer was

reduced by up to 105-fold. This was because inflammation (e.g., reactive oxygen species, reactive nitrogen species, hypochlorite) triggers the bacterial SOS response, boosts expression of the phage antirepressor Tum, and thereby promotes free phage production and subsequent transfer. Mucosal vaccination prevented a dense intestinal STm population from inducing inflammation and consequently abolished SopEPhi transfer. Vaccination may be a general strategy for blocking pathogen evolution that requires disease-driven transfer of temperate bacteriophages.

Dieterle, M. E., Spinelli, S., Sadovskaya, I., Piuri, M., and Cambillau, C. Evolved distal tail carbohydrate binding modules of Lactobacillus phage J-1: a novel type of anti-receptor widespread among lactic acid bacteria phages. Mol.Microbiol. 2017; 104(4):608-620; PM: 28196397

ABSTRACT: Bacteriophage replication requires specific host-recognition. Some siphophages harbour a large complex, the baseplate, at the tip of their non-contractile tail. This baseplate holds receptor binding proteins (RBPs) that can recognize the host cell-wall polysaccharide (CWPS) and specifically attach the phage to its host. While most phages possess a dedicated RBP, the phage J-1 that infects Lactobacillus casei seemed to lack one. It has been shown that the phage J-1 distal tail protein (Dit) plays a role in host recognition and that its sequence comprises two inserted modules compared with 'classical' Dits. The first insertion is similar to carbohydrate-binding modules (CBMs), whereas the second insertion remains undocumented. Here, we determined the structure of the second insertion and found it also similar to several CBMs. Expressed insertion CBM2, but not CBM1, binds to L. casei cells and neutralize phage attachment to the bacterial cell wall and the isolated and purified CWPS of L. casei BL23 prevents CBM2 attachment to the host. Electron microscopy single particle reconstruction of the J-1 virion baseplate revealed that CBM2 is projected at the periphery of Dit to optimally bind the CWPS receptor. Taken together, these results identify J-1 evolved Dit as the phage RBP.

Dilly, S. J., Clark, A. J., Marsh, A., Mitchell, D. A., Cain, R., Fishwick, C. W., and Taylor, P. C. A chemical genomics approach to drug reprofiling in oncology: Antipsychotic drug risperidone as a potential adenocarcinoma treatment. Cancer Lett. 5-1-2017; 393:16-21; PM: 28188816

ABSTRACT: Drug reprofiling is emerging as an effective paradigm for discovery of cancer treatments. Herein, an antipsychotic drug is immobilised using the Magic Tag(R) chemical genomics tool and screened against a T7 bacteriophage displayed library of polypeptides from Drosophila melanogaster, as a whole genome model, to uncover an interaction with a section of 17-beta-HSD10, a proposed prostate cancer target. A computational study and enzyme inhibition assay with full length human 17-beta-HSD10 identifies risperidone as a drug reprofiling candidate. When formulated with rumenic acid, risperidone slows proliferation of PC3 prostate cancer cells in vitro and retards PC3 prostate cancer tumour growth in vivo in xenografts in mice, presenting an opportunity to reprofile risperidone as a cancer treatment.

Djacem, K., Tavares, P., and Oliveira, L. Bacteriophage SPP1 pac Cleavage: A Precise Cut without Sequence Specificity Requirement. J.Mol.Biol. 5-5-2017; 429(9):1381-1395; PM: 28082080

ABSTRACT: In many tailed bacteriophages, DNA packaging is initiated by recognition and cleavage of a specific sequence pac by the small (TerS) and large (TerL) terminase subunits. It was previously shown that the SPP1 pac region has two sequences where TerS binds (pacR and pacL), flanking the segment where TerL cleaves the SPP1 DNA (pacC). However, the pac-specific sequences required to achieve this endonucleolytic cut were not established. Their characterization is essential to understand the underlying mechanism. We show that the pacR sequence localized within 35bp downstream of the pac cut can be extensively degenerated, including its c1 and c2 repeats, and that only a disruption of a 5-bp polyadenine tract impairs the pac cleavage. This result together with deletion analysis of pacL shows that the specific DNA sequences required for targeting the terminase for pac cleavage are considerably shorter than the large region bound by TerS. Furthermore, extensive degeneration of the 6-bp target sequence within pacC where pac cleavage occurs reveals that TerL maintains, remarkably, its precise position of cleavage. Studies with SPP1-related phages show the conservation of the cut position, irrespective of the sequence variation in pacC and in pacR or the changes in pacL-pacC distance. Mechanistically, our data are compatible with a model in which TerS interactions with part of the pacL sequence and a poly-A tract in pacR are sufficient to orient very accurately the TerL nuclease to a defined pacC position. They also demonstrate that the resulting precise cut at pacC is independent of the targeted DNA sequence.

Doore, S. M., Schweers, N. J., and Fane, B. A. Elevating fitness after a horizontal gene exchange in bacteriophage phiX174. Virology. 1-15-2017; 501:25-34; PM: 27855283

ABSTRACT: In an earlier study, protein-based barriers to horizontal gene transfer were investigated by placing the bacteriophage G4 G gene, encoding the major spike protein, into the phiX174 genome. The foreign G protein promoted off-pathway assembly reactions, resulting in a lethal phenotype. After three targeted genetic selections, one of two foreign spike proteins was productively integrated into the phiX174 system: the complete G4 or a recombinant G4/phiX174 protein (94% G4:6% phiX174). However, strain fitness was very low. In this study, the chimeras were characterized and experimentally evolved. Inefficient assembly was the primary contributor to low fitness: accordingly, mutations affecting assembly restored fitness. The spike protein preference of the ancestral and evolved strains was determined in competition experiments between the foreign and phiX174G proteins. Before adaptation, both G proteins were incorporated into virions; afterwards, the foreign proteins were strongly preferred. Thus, a previously inhibitory protein became the preferred substrate during assembly.

Dorosky, R. J., Yu, J. M., Pierson, L. S., III, and Pierson, E. A. Pseudomonas chlororaphis produces two distinct R-tailocins that contribute to bacterial competition in biofilms and on roots. Appl.Environ.Microbiol. 5-19-2017; PM: 28526791

ABSTRACT: R-type tailocins are high molecular weight bacteriocins that resemble bacteriophage tails and are encoded within the genomes of many Pseudomonas species. In this study, analysis of the P. chlororaphis 30-84 R-tailocin gene cluster revealed that it encodes the structural components to produce two R-tailocins of different ancestral origin. Two distinct R-tailocin populations differing in length were observed in UV induced lysates of P. chlororaphis 30-84 via transmission electron microscopy. Mutants defective in the production of one or both R-tailocins demonstrated that the killing

spectrum of each tailocin is limited to Pseudomonas species. The spectrum of pseudomonads killed by the two R-tailocins differed, although a few Pseudomonas species were either killed by or insusceptible to both tailocins. Tailocin release was disrupted by deletion of the holin gene within the tailocin gene cluster, demonstrating that the lysis cassette is required for the release of both R-tailocins. The loss of functional tailocin production reduced the ability of P. chlororaphis 30-84 to compete with an R-tailocin sensitive strain within biofilms and rhizosphere communities. Our study demonstrates that Pseudomonas species can produce more than one functional R-tailocin particle sharing the same lysis cassette, but differing in their killing spectrum. This study provides evidence for the role of R-tailocins as determinants of bacterial competition among plant-associated Pseudomonas in biofilms and the rhizosphere. *IMPORTANCE*: Recent studies have identified R-tailocin gene clusters potentially encoding more than one R-tailocin within the genomes of plant-associated Pseudomonas, but have not demonstrated that more than one particle is produced or the ecological significance of the production of multiple R-tailocins. This study demonstrates for the first time that Pseudomonas strains can produce two distinct R-tailocins with different killing spectra, both of which contribute to bacterial competition between rhizosphere-associated bacteria. These results provide new insight into the previously uncharacterized role of R-tailocin production by plant-associated Pseudomonas species in bacterial population dynamics within surface attached biofilms and on roots.

Doss, J., Culbertson, K., Hahn, D., Camacho, J., and Barekzi, N. A Review of Phage Therapy against Bacterial Pathogens of Aquatic and Terrestrial Organisms. Viruses. 3-18-2017; 9(3); PM: 28335451

ABSTRACT: Since the discovery of bacteriophage in the early 1900s, there have been numerous attempts to exploit their innate ability to kill bacteria. The purpose of this report is to review current findings and new developments in phage therapy with an emphasis on bacterial diseases of marine organisms, humans, and plants. The body of evidence includes data from studies investigating bacteriophage in marine and land environments as modern antimicrobial agents against harmful bacteria. The goal of this paper is to present an overview of the topic of phage therapy, the use of phage-derived protein therapy, and the hosts that bacteriophage are currently being used against, with an emphasis on the uses of bacteriophage against marine, human, animal and plant pathogens.

Drilling, A. J., Ooi, M. L., Miljkovic, D., James, C., Speck, P., Vreugde, S., Clark, J., and Wormald, P. J. Long-Term Safety of Topical Bacteriophage Application to the Frontal Sinus Region. Front Cell Infect.Microbiol. 2017; 7:49; PM: 28286740

ABSTRACT: Background: Staphylococcus aureus biofilms contribute negatively to a number of chronic conditions, including chronic rhinosinusitis (CRS). With the inherent tolerance of biofilm-bound bacteria to antibiotics and the global problem of bacterial antibiotic resistance, the need to develop novel therapeutics is paramount. Phage therapy has previously shown promise in treating sinonasal S. aureus biofilms. *Methods*: This study investigates the long term (20 days) safety of topical sinonasal flushes with bacteriophage suspensions. The bacteriophage cocktail NOV012 against S. aureus selected for this work contains two highly characterized and different phages, P68 and K710. Host range was assessed against S. aureus strains isolated from CRS patients using

agar spot tests. NOV012 was applied topically to the frontal sinus region of sheep, twice daily for 20 days. General sheep wellbeing, mucosal structural changes and inflammatory load were assessed to determine safety of NOV012 application. *Results*: NOV012 could lyse 52/61 (85%) of a panel of locally derived CRS clinical isolates. Application of NOV012 to the frontal sinuses of sheep for 20 days was found to be safe, with no observed inflammatory infiltration or tissue damage within the sinus mucosa. *Conclusion*: NOV012 cocktail appears safe to apply for extended periods to sheep sinuses and it could infect and lyse a wide range of S. aureus CRS clinical isolates. This indicates that phage therapy has strong potential as a treatment for chronic bacterial rhinosinusitis.

Dubert, J., Barja, J. L., and Romalde, J. L. New Insights into Pathogenic Vibrios Affecting Bivalves in Hatcheries: Present and Future Prospects. Front Microbiol. 2017; 8:762; PM: 28515714

ABSTRACT: Hatcheries constitute nowadays the only viable solution to support the husbandry of bivalve molluscs due to the depletion and/or overexploitation of their natural beds. Hatchery activities include the broodstock conditioning and spawning, rearing larvae and spat, and the production of microalgae to feed all stages of the production cycle. However, outbreaks of disease continue to be the main bottleneck for successful larval and spat production, most of them caused by different representatives of the genus Vibrio. Therefore, attention must be paid on preventive and management measures that allow the control of such undesirable bacterial populations. The present review provides an updated picture of the recently characterized Vibrio species associated with disease of bivalve molluscs during early stages of development, including the controversial taxonomic affiliation of some of them and relevant advances in the knowledge of their virulence determinants. The problematic use of antibiotics, as well as its eco-friendly alternatives are also critically discussed.

Duenas, F., Rivera, D., Toledo, V., Tardone, R., Herve-Claude, L. P., Hamilton-West, C., and Switt, A. I. Short communication: Characterization of Salmonella phages from dairy calves on farms with history of diarrhea. J.Dairy Sci. 2017; 100(3):2196-2200; PM: 28041722

ABSTRACT: Salmonella enterica can cause disease and mortality in calves. This pathogen is also a zoonosis that can be transmitted by animal contact or by food. The prevalence of Salmonella in dairy farms has been reported to range from 0 to 64%, and, due to the diversity of Salmonella serovars that can be circulating, Salmonella is an important concern for dairy production. Bacteriophages that infect Salmonella have been documented to be abundant and widely distributed in the dairy environment. The current study investigated the diversity of Salmonella serovars and Salmonella phages in 8 dairy farms with a history of diarrhea in southern Chile. A total of 160 samples from sick calves, healthy calves, and the environment were analyzed for Salmonella and phage. Isolated phages were characterized and classified by their host range using a panel of 26 Salmonella isolates representing 23 serovars. Host ranges were classified according to lysis profiles (LP) and their spatial distribution was mapped. Salmonella-infecting phages were identified, but none of the 160 samples were positive for Salmonella. A total of 45 phage isolates were obtained from sick calves (11), healthy calves (16), or the environment (18). According to their host range, 19 LP were identified, with LP1 being the most common on all 8 farms; LP1 represents phages that only lyse serogroup D Salmonella. The identification of Salmonella phages but not Salmonella in the same samples could suggest that these phages are controlling Salmonella in these farms.

Dufour, N. and Debarbieux, L. [Phage therapy: a realistic weapon against multidrug resistant bacteria]. Med.Sci.(Paris). 2017; 33(4):410-416; PM: 28497737

ABSTRACT: The continuous increase in antibiotic resistance among bacteria in infectious diseases associated with the lack of new antibiotics able to circumvent them are urging physicians, researchers and politicians to look for others options for treatments. Among those, phage therapy (use of natural viruses that infect bacteria, called bacteriophages) is one of the most promising approaches. In this review, we first focus on the problematic raised by multidrug resistant bacteria before addressing the main biological characteristics of bacteriophages, as well as the credibility and the relevance of phage therapy. We then introduce human applications, their potentials and limits.

Dufour, N., Delattre, R., Ricard, J. D., and Debarbieux, L. The Lysis of Pathogenic Escherichia coli by Bacteriophages Releases Less Endotoxin Than by beta-Lactams. Clin.Infect.Dis. 6-1-2017; 64(11):1582-1588; PM: 28329379

ABSTRACT: *Background*: Other than numerous experimental data assessing phage therapy efficacy, questions regarding safety of this approach are not sufficiently addressed. In particular, as phages can kill bacterial cells within <10 minutes, the associated endotoxin release (ER) in severe infections caused by gram-negative bacteria could be a matter of concern. *Methods*: Two therapeutic virulent phages and 4 reference antibiotics were studied in vitro for their ability to kill 2 pathogenic strains of Escherichia coli and generate an ER. The early interaction (first 3 hours) between these actors was assessed over time by studying the instantaneous cell viability, the colony-forming unit count, the concentration of free endotoxin released, and the cell morphology under light microscope. *Results*: While beta-lactams have a relatively slow effect, both tested phages, as well as amikacin, were able to rapidly abolish the bacterial growth. Even when considering the fastest phage (cell lysis in 9 minutes), the concentrations of phage-induced ER never reached the highest values, which were recorded with antibiotic treatments. Cumulative concentrations of endotoxin over time in phage-treated conditions were lower than those observed with beta-lactams and close to those observed with amikacin. Whereas beta-lactams were responsible for strong cell morphology changes (spheroplast with imipenem, filamentous cells with cefoxitin and ceftriaxone), amikacin and phages did not modify cell shape but produced intracellular inclusion bodies. *Conclusions*: This work provides important and comforting data regarding the safety of phage therapy. Therapeutically relevant phages, with their low endotoxin release profile and fast bactericidal effect, are not inferior to beta-lactams.

Duncan, A. B., Dusi, E., Jacob, F., Ramsayer, J., Hochberg, M. E., and Kaltz, O. Hot spots become cold spots: coevolution in variable temperature environments. J.Evol.Biol. 2017; 30(1):55-65; PM: 27711983

ABSTRACT: Antagonistic coevolution between hosts and parasites is a key process in the genesis and maintenance of biological diversity. Whereas coevolutionary dynamics show distinct patterns under favourable environmental conditions, the effects of more realistic, variable conditions are largely unknown. We investigated the impact of a fluctuating environment on antagonistic coevolution in experimental microcosms of Pseudomonas fluorescens SBW25 and lytic phage SBWPhi2. High-frequency temperature

fluctuations caused no deviations from typical coevolutionary arms race dynamics. However, coevolution was stalled during periods of high temperature under intermediate- and low-frequency fluctuations, generating temporary coevolutionary cold spots. Temperature variation affected population density, providing evidence that eco-evolutionary feedbacks act through variable bacteria-phage encounter rates. Our study shows that environmental fluctuations can drive antagonistic species interactions into and out of coevolutionary cold and hot spots. Whether coevolution persists or stalls depends on the frequency of change and the environmental optima of both interacting players.

Dunkin, N., Weng, S., Schwab, K. J., McQuarrie, J., Bell, K., and Jacangelo, J. G. Comparative Inactivation of Murine Norovirus and MS2 Bacteriophage by Peracetic Acid and Monochloramine in Municipal Secondary Wastewater Effluent. Environ.Sci.Technol. 3-7-2017; 51(5):2972-2981; PM: 28165216

ABSTRACT: Chlorination has long been used for disinfection of municipal wastewater (MWW) effluent while the use peracetic acid (PAA) has been proposed more recently in the United States. Previous work has demonstrated the bactericidal effectiveness of PAA and monochloramine in wastewater, but limited information is available for viruses, especially ones of mammalian origin (e.g., norovirus). Therefore, a comparative assessment was performed of the virucidal efficacy of PAA and monochloramine against murine norovirus (MNV) and MS2 bacteriophage in secondary effluent MWW and phosphate buffer (PB). A suite of inactivation kinetic models was fit to the viral inactivation data. Predicted concentration-time (CT) values for 1-log10 MS2 reduction by PAA and monochloramine in MWW were 1254 and 1228 mg-min/L, respectively. The 1-, 2-, and 3-log10 model predicted CT values for MNV viral reduction in MWW were 32, 47, and 69 mg-min/L for PAA and 6, 13, and 28 mg-min/L for monochloramine, respectively. Wastewater treatment plant disinfection practices informed by MS2 inactivation data will likely be protective for public health but may overestimate CT values for reduction of MNV. Additionally, equivalent CT values in PB resulted in greater viral reduction which indicate that viral inactivation data in laboratory grade water may not be generalizable to MWW applications.

Easwaran, M., Dananjaya, S. H. S., Park, S. C., Lee, J., Shin, H. J., and De, Zoysa M. Characterization of bacteriophage pAh-1 and its protective effects on experimental infection of Aeromonas hydrophila in Zebrafish (Danio rerio). J.Fish.Dis. 2017; 40(6):841-846; PM: 27454188

No Abstract Available.

Ehgartner, D., Sagmeister, P., Langemann, T., Meitz, A., Lubitz, W., and Herwig, C. A novel method to recover inclusion body protein from recombinant E. coli fed-batch processes based on phage PhiX174-derived lysis protein E. Appl.Microbiol.Biotechnol. 4-20-2017; PM: 28429059

ABSTRACT: Production of recombinant proteins as inclusion bodies is an important strategy in the production of technical enzymes and biopharmaceutical products. So far, protein from inclusion bodies has been recovered from the cell factory through mechanical or chemical disruption methods, requiring additional cost-intensive unit

operations. We describe a novel method that is using a bacteriophage-derived lysis protein to directly recover inclusion body protein from Escherichia coli from high cell density fermentation process: The recombinant inclusion body product is expressed by using a mixed feed fed-batch process which allows expression tuning via adjusting the specific uptake rate of the inducing substrate. Then, bacteriophage PhiX174-derived lysis protein E is expressed to induce cell lysis. Inclusion bodies in empty cell envelopes are harvested via centrifugation of the fermentation broth. A subsequent solubilization step reveals the recombinant protein. The process was investigated by analyzing the impact of fermentation conditions on protein E-mediated cell lysis as well as cell lysis kinetics. Optimal cell lysis efficiencies of 99% were obtained with inclusion body titers of >2.0 g/l at specific growth rates higher 0.12 h-1 and inducer uptake rates below 0.125 g/(g x h). Protein E-mediated cell disruption showed a first-order kinetics with a kinetic constant of -0.8 +/- 0.3 h-1. This alternative inclusion body protein isolation technique was compared to the one via high-pressure homogenization. SDS gel analysis showed 10% less protein impurities when cells had been disrupted via high-pressure homogenization, than when empty cell envelopes including inclusion bodies were investigated. Within this contribution, an innovative technology, tuning recombinant protein production and substituting cost-intensive mechanical cell disruption, is presented. We anticipate that the presented method will simplify and reduce the production costs of inclusion body processes to produce technical enzymes and biopharmaceutical products.

ElSawy, K. M. The impact of viral RNA on the association free energies of capsid protein assembly: bacteriophage MS2 as a case study. J.Mol.Model. 2017; 23(2):47; PM: 28154984

ABSTRACT: A large number of single-stranded RNA viruses assemble their capsid and their genomic material simultaneously. The RNA viral genome plays multiple roles in this process that are currently only partly understood. In this work, we investigated the thermodynamic basis of the role of viral RNA on the assembly of capsid proteins. The viral capsid of bacteriophage MS2 was considered as a case study. The MS2 virus capsid is composed of 60 AB and 30 CC protein dimers. We investigated the effect of RNA stem loop (the translational repressor TR) binding to the capsid dimers on the dimer-dimer relative association free energies. We found that TR binding results in destabilization of AB self-association compared with AB and CC association. This indicates that the association of the AB and CC dimers is the most likely assembly pathway for the MS2 virus, which explains the experimental observation of alternating patterns of AB and CC dimers in dominant assembly intermediates of the MS2 virus. The presence of viral RNA, therefore, dramatically channels virus assembly to a limited number of pathways, thereby enhancing the efficiency of virus self-assembly process. Interestingly, Thr59Ser and Thr45Ala mutations of the dimers, in the absence of RNA stem loops, lead to stabilization of AB self-association compared with the AB and CC associations, thereby channelling virus assembly towards a fivefold (AB)5 pentamer intermediate, providing a testable hypothesis of our thermodynamic arguments.

Emmoth, E., Rovira, J., Rajkovic, A., Corcuera, E., Wilches, Perez D., Dergel, I., Ottoson, J. R., and Widen, F. Inactivation of Viruses and Bacteriophages as Models for Swine Hepatitis E Virus in Food Matrices. Food Environ.Virol. 2017; 9(1):20-34; PM: 27783334

ABSTRACT: Hepatitis E virus has been recognised as a food-borne virus hazard in pork products, due to its zoonotic properties. This risk can be reduced by adequate treatment

of the food to inactivate food-borne viruses. We used a spectrum of viruses and bacteriophages to evaluate the effect of three food treatments: high pressure processing (HPP), lactic acid (LA) and intense light pulse (ILP) treatments. On swine liver at 400 MPa for 10 min, HPP gave log10 reductions of >/=4.2, >/=5.0 and 3.4 for feline calicivirus (FCV) 2280, FCV wildtype (wt) and murine norovirus 1 (MNV 1), respectively. Escherichia coli coliphage varphiX174 displayed a lower reduction of 1.1, while Escherichia coli coliphage MS2 was unaffected. For ham at 600 MPa, the corresponding reductions were 4.1, 4.4, 2.9, 1.7 and 1.3 log10. LA treatment at 2.2 M gave log10 reductions in the viral spectrum of 0.29-2.1 for swine liver and 0.87-3.1 for ham, with varphiX174 and MNV 1, respectively, as the most stable microorganisms. The ILP treatment gave log10 reductions of 1.6-2.8 for swine liver, 0.97-2.2 for ham and 1.3-2.3 for sausage, at 15-60 J cm-2, with MS2 as the most stable microorganism. The HPP treatment gave significantly ($p < 0.05$) greater virus reduction on swine liver than ham for the viruses at equivalent pressure/time combinations. For ILP treatment, reductions on swine liver were significantly ($p < 0.05$) greater than on ham for all microorganisms. The results presented here could be used in assessments of different strategies to protect consumers against virus contamination and in advice to food producers. Conservative model indicators for the pathogenic viruses could be suggested.

Endersen, L., Buttimer, C., Nevin, E., Coffey, A., Neve, H., Oliveira, H., Lavigne, R., and O'Mahony, J. Investigating the biocontrol and anti-biofilm potential of a three phage cocktail against Cronobacter sakazakii in different brands of infant formula. Int.J.Food Microbiol. 4-21-2017; 253:1-11; PM: 28460269

ABSTRACT: In recent years, the microbiological safety of powdered infant formula has gained increasing attention due to the identification of contaminating C. sakazakii and its epidemiological link with life-threatening neonatal infections. Current intervention strategies have fallen short of ensuring the production of infant formula that is free from C. sakazakii. In this study, we describe the isolation and characterisation of three bacteriophages (phages) and their application as a phage cocktail to inhibit the growth of C. sakazakii in different brands of infant formula, while also assessing the phages ability to prevent biofilm formation. All three phages, isolated from slurry, possess a relatively broad host range, verified by their ability to infect across genera and species. When all three phages were combined and used as part of a phage cocktail, 73% coverage was obtained across all Cronobacter strains tested. Optimum thermo-tolerance and pH stability were determined between 4 degrees C-37 degrees C, and pH6-8, respectively, well within the normal range of application of infant formula. Genome sequencing and analysis revealed all the phages to be free from lysogenic properties, a trait which renders each favourable for phage therapy applications. As such, the combined-phage preparation (3x108pfu/mL) was found to possess a strong bactericidal effect on C. sakazakii/C. sakazakii LUX cells (</=104cfu/mL), resulting in a significant reduction in cell numbers, to below the limit of detection (<10cfu/mL). This was observed following a 20h challenge in different brands of infant formula, where samples in the absence of the phage cocktail reached concentrations of ~109cfu/mL. The phage cocktail also demonstrated promise in preventing the establishment of biofilm, as biofilm formation could not be detected for up to 48h post treatment. These results highlight the potential application of this phage preparation for biocontrol of C. sakazakii contamination in reconstituted infant formula and also as a preventative agent against biofilm formation.

Fan, N., Qi, R., and Yang, M. Isolation and characterization of a virulent bacteriophage infecting Acinetobacter johnsonii from activated sludge. Res.Microbiol. 2-14-2017; PM: 28213104

ABSTRACT: A double-stranded DNA phage named AJO1, infecting Acinetobacter johnsonii, which plays an important role in wastewater treatment, was isolated from activated sludge in a full-scale municipal wastewater treatment plant. Based on morphological taxonomy, AJO1, with an icosahedral head 55 +/- 2 nm in diameter and a non-contractile tail 8 +/- 2 nm in length, was classified as a member of the Podoviridae family. Bacterial infection characteristics were as follows: no polyvalent infectivity, optimal multiplicity of infection of 10-2; eclipse and burst size of 30 min and 51.2 PFU-infected cells-1, respectively. It showed considerable infectivity under a neutral pH condition (pH 6.0-9.0) and relatively high temperature (55 degrees C). Whole-genome sequencing of AJO1 revealed a linearly permuted DNA (41 437 bp) carrying 54 putative open reading frames and 4 repeats. This is the first report of isolation of an A. johnsonii phage, whose bacteriophage distribution and population dynamics are not well known. The results of this study could contribute to subsequent research on the interaction between bacteriophages and their hosts during wastewater treatment. In addition, AJO1 may become a candidate for potential therapy against A. johnsonii infection in clinical applications, since this species is an opportunistic pathogen.

Fang, P. Y., Gomez Ramos, L. M., Holguin, S. Y., Hsiao, C., Bowman, J. C., Yang, H. W., and Williams, L. D. Functional RNAs: combined assembly and packaging in VLPs. Nucleic Acids Res. 4-7-2017; 45(6):3519-3527; PM: 27903913

ABSTRACT: We describe here a one pot RNA production, packaging and delivery system based on bacteriophage Qbeta. We demonstrate a method for production of a novel RNAi scaffold, packaged within Qbeta virus-like particles (VLPs). The RNAi scaffold is a general utility chimera that contains a functional RNA duplex with paired silencing and carrier sequences stabilized by a miR-30 stem-loop. The Qbeta hairpin on the 5 end confers affinity for the Qbeta coat protein (CP). Silencing sequences can include mature miRNAs and siRNAs, and can target essentially any desired mRNA. The VLP-RNAi assembles upon co-expression of CP and the RNAi scaffold in E. coli. The annealing of the scaffold to form functional RNAs is intramolecular and is therefore robust and concentration independent. We demonstrate dose- and time-dependent inhibition of GFP expression in human cells with VLP-RNAi. In addition, we target the 3UTR of oncogenic Ras mRNA and suppress Pan-Ras expression, which attenuates cell proliferation and promotes mortality of brain tumor cells. This combination of RNAi scaffold design with Qbeta VLP packaging is demonstrated to be target-specific and efficient.

Farley, M. M., Tu, J., Kearns, D. B., Molineux, I. J., and Liu, J. Ultrastructural analysis of bacteriophage Phi29 during infection of Bacillus subtilis. J.Struct.Biol. 2017; 197(2):163-171; PM: 27480510

ABSTRACT: Recent advances in cryo-electron tomography (cryo-ET) have allowed direct visualization of the initial interactions between bacteriophages and their hosts. Previous studies focused on phage infection in Gram-negative bacteria but it is of particular interest how phages penetrate the thick, highly cross-linked Gram-positive cell wall. Here we detail structural intermediates of phage Phi29 during infection of Bacillus subtilis. Use of a minicell-producing strain facilitated in situ tomographic reconstructions of infecting

phage particles. Phi29 initially contacts the cell wall at an angle through a subset of the twelve appendages, which are attached to the collar at the head proximal portion of the tail knob. The appendages are flexible and switch between extended and downward conformations during this stage of reversible adsorption; appendages enzymatically hydrolyze wall teichoic acids to bring the phage closer to the cell. A cell wall-degrading enzyme at the distal tip of the tail knob locally digests peptidoglycan, facilitating penetration of the tail further into the cell wall, and the phage particle reorients so that the tail becomes perpendicular to the cell surface. All twelve appendages attain the same "down" conformation during this stage of adsorption. Once the tail has become totally embedded in the cell wall, the tip can fuse with the cytoplasmic membrane. The membrane bulges out, presumably to facilitate genome ejection into the cytoplasm, and the deformation remains after complete ejection. This study provides the first visualization of the structural changes occurring in a phage particle during adsorption and genome transfer into a Gram-positive bacterium.

Fauconnier, A. Regulating phage therapy: The biological master file concept could help to overcome regulatory challenge of personalized medicines. EMBO Rep. 2017; 18(2):198-200; PM: 28082313

No Abstract Available.

Fernandes, S. and Sao-Jose, C. Probing the function of the two holin-like proteins of bacteriophage SPP1. Virology. 2017; 500:184-189; PM: 27825035

ABSTRACT: Double-stranded DNA bacteriophages employ holin and endolysin functions to lyse host bacteria after virus multiplication. Holins oligomerize in the cytoplasmic membrane and trigger to form holes that cause cell death. For most systems these holes are also required for endolysin release to the cell wall, where it cleaves the peptidoglycan network. Orfs 25 and 26 of Bacillus subtilis phage SPP1 were predicted to encode the endolysin and holin functions, respectively. However, the product of the upstream orf 24.1 exhibits also holin features. We show that production of gp24.1 or gp26 in B. subtilis causes no major impact on cell growth, despite their ability to insert in the cytoplasmic membrane. Instant growth cessation and cell death is observed only upon co-production of the two holin-like proteins. Surprisingly, a constitutive promoter was identified within orf 24.1, which we propose to correspond to the previously described SPP1 early promoter PE5.

Fernandez, L., Gonzalez, S., Campelo, A. B., Martinez, B., Rodriguez, A., and Garcia, P. Low-level predation by lytic phage phiIPLA-RODI promotes biofilm formation and triggers the stringent response in Staphylococcus aureus. Sci.Rep. 1-19-2017; 7:40965; PM: 28102347

ABSTRACT: An important lesson from the war on pathogenic bacteria has been the need to understand the physiological responses and evolution of natural microbial communities. Bacterial populations in the environment are generally forming biofilms subject to some level of phage predation. These multicellular communities are notoriously resistant to antimicrobials and, consequently, very difficult to eradicate. This has sparked the search for new therapeutic alternatives, including phage therapy. This study demonstrates that S. aureus biofilms formed in the presence of a non-lethal dose of phage phiIPLA-RODI exhibit a unique physiological state that could potentially benefit both the host and the predator. Thus, biofilms formed under phage pressure are thicker

and have a greater DNA content. Also, the virus-infected biofilm displayed major transcriptional differences compared to an untreated control. Significantly, RNA-seq data revealed activation of the stringent response, which could slow down the advance of the bacteriophage within the biofilm. The end result would be an equilibrium that would help bacterial cells to withstand environmental challenges, while maintaining a reservoir of sensitive bacterial cells available to the phage upon reactivation of the dormant carrier population.

Fink, G. and Aylett, C. H. S. Tubulin-Like Proteins in Prokaryotic DNA Positioning. Subcell.Biochem. 2017; 84:323-356; PM: 28500531

ABSTRACT: A family of tubulin-related proteins (TubZs) has been identified in prokaryotes as being important for the inheritance of virulence plasmids of several pathogenic Bacilli and also being implicated in the lysogenic life cycle of several bacteriophages. Cell biological studies and reconstitution experiments revealed that TubZs function as prokaryotic cytomotive filaments, providing one-dimensional motive forces. Plasmid-borne TubZ filaments most likely transport plasmid centromeric complexes by depolymerisation, pulling on the plasmid DNA, in vitro. In contrast, phage-borne TubZ (PhuZ) pushes bacteriophage particles (virions) to mid cell by filament growth. Structural studies by both crystallography and electron cryo-microscopy of multiple proteins, both from the plasmid partitioning sub-group and the bacteriophage virion centring group of TubZ homologues, allow a detailed consideration of the structural phylogeny of the group as a whole, while complete structures of both crystallographic protofilaments at high resolution and fully polymerised filaments at intermediate resolution by cryo-EM have revealed details of the polymerisation behaviour of both TubZ sub-groups.

Fogg, P. C., Haley, J. A., Stark, W. M., and Smith, M. C. Genome Integration and Excision by a New Streptomyces Bacteriophage, varphiJoe. Appl.Environ.Microbiol. 3-1-2017; 83(5); PM: 28003200

ABSTRACT: Bacteriophages are the source of many valuable tools for molecular biology and genetic manipulation. In Streptomyces, most DNA cloning vectors are based on serine integrase site-specific DNA recombination systems derived from phage. Because of their efficiency and simplicity, serine integrases are also used for diverse synthetic biology applications. Here, we present the genome of a new Streptomyces phage, varphiJoe, and investigate the conditions for integration and excision of the varphiJoe genome. varphiJoe belongs to the largest Streptomyces phage cluster (R4-like) and encodes a serine integrase. The attB site from Streptomyces venezuelae was used efficiently by an integrating plasmid, pCMF92, constructed using the varphiJoe int-attP locus. The attB site for varphiJoe integrase was occupied in several Streptomyces genomes, including that of S. coelicolor, by a mobile element that varies in gene content and size between host species. Serine integrases require a phage-encoded recombination directionality factor (RDF) to activate the excision reaction. The varphiJoe RDF was identified, and its function was confirmed in vivo Both the integrase and RDF were active in in vitro recombination assays. The varphiJoe site-specific recombination system is likely to be an important addition to the synthetic biology and genome engineering toolbox.IMPORTANCEStreptomyces spp. are prolific producers of secondary metabolites, including many clinically useful antibiotics. Bacteriophage-derived integrases are important tools for genetic engineering, as they enable integration of heterologous DNA into the Streptomyces chromosome with ease and high efficiency.

Recently, researchers have been applying phage integrases for a variety of applications in synthetic biology, including rapid assembly of novel combinations of genes, biosensors, and biocomputing. An important requirement for optimal experimental design and predictability when using integrases, however, is the need for multiple enzymes with different specificities for their integration sites. In order to provide a broad platform of integrases, we identified and validated the integrase from a newly isolated Streptomyces phage, varphiJoe. varphiJoe integrase is active in vitro and in vivo The specific recognition site for integration is present in a wide range of different actinobacteria, including Streptomyces venezuelae, an emerging model bacterium in Streptomyces research.

Fongaro, G., Garcia-Gonzalez, M. C., Hernandez, M., Kunz, A., Barardi, C. R., and Rodriguez-Lazaro, D. Different Behavior of Enteric Bacteria and Viruses in Clay and Sandy Soils after Biofertilization with Swine Digestate. Front Microbiol. 2017; 8:74; PM: 28197137

ABSTRACT: Enteric pathogens from biofertilizer can accumulate in the soil, subsequently contaminating water and crops. We evaluated the survival, percolation and leaching of model enteric pathogens in clay and sandy soils after biofertilization with swine digestate: PhiX-174, mengovirus (vMC0), Salmonella enterica Typhimurium and Escherichia coli O157:H7 were used as biomarkers. The survival of vMC0 and PhiX-174 in clay soil was significantly lower than in sandy soil (iT90 values of 10.520 +/- 0.600 vs. 21.270 +/- 1.100 and 12.040 +/- 0.010 vs. 43.470 +/- 1.300, respectively) and PhiX-174 showed faster percolation and leaching in sandy soil than clay soil (iT90 values of 0.46 and 2.43, respectively). S. enterica Typhimurium was percolated and inactivated more slowly than E. coli O157:H7 (iT90 values of 9.340 +/- 0.200 vs. 6.620 +/- 0.500 and 11.900 +/- 0.900 vs. 10.750 +/- 0.900 in clay and sandy soils, respectively), such that E. coli O157:H7 was transferred more quickly to the deeper layers of both soils evaluated (percolation). Our findings suggest that E. coli O157:H7 may serve as a useful microbial biomarker of depth contamination and leaching in clay and sandy soil and that bacteriophage could be used as an indicator of enteric pathogen persistence. Our study contributes to development of predictive models for enteric pathogen behavior in soils, and for potential water and food contamination associated with biofertilization, useful for risk management and mitigation in swine digestate recycling.

Frietze, K. M., Pascale, J. M., Moreno, B., Chackerian, B., and Peabody, D. S. Pathogen-specific deep sequence-coupled biopanning: A method for surveying human antibody responses. PLoS.One. 2017; 12(2):e0171511; PM: 28152075

ABSTRACT: Identifying the targets of antibody responses during infection is important for designing vaccines, developing diagnostic and prognostic tools, and understanding pathogenesis. We developed a novel deep sequence-coupled biopanning approach capable of identifying the protein epitopes of antibodies present in human polyclonal serum. Here, we report the adaptation of this approach for the identification of pathogen-specific epitopes recognized by antibodies elicited during acute infection. As a proof-of-principle, we applied this approach to assessing antibodies to Dengue virus (DENV). Using a panel of sera from patients with acute secondary DENV infection, we panned a DENV antigen fragment library displayed on the surface of bacteriophage MS2 virus-like particles and characterized the population of affinity-selected peptide epitopes by deep sequence analysis. Although there was considerable variation in the responses of individuals, we found several epitopes within the Envelope glycoprotein and

Non-Structural Protein 1 that were commonly enriched. This report establishes a novel approach for characterizing pathogen-specific antibody responses in human sera, and has future utility in identifying novel diagnostic and vaccine targets.

Fuller, J. R. and Rice, P. A. Target DNA bending by the Mu transpososome promotes careful transposition and prevents its reversal. Elife. 2-13-2017; 6; PM: 28177285

ABSTRACT: The transposition of bacteriophage Mu serves as a model system for understanding DDE transposases and integrases. All available structures of these enzymes at the end of the transposition reaction, including Mu, exhibit significant bends in the transposition target site DNA. Here we use Mu to investigate the ramifications of target DNA bending on the transposition reaction. Enhancing the flexibility of the target DNA or prebending it increases its affinity for transpososomes by over an order of magnitude and increases the overall reaction rate. This and FRET confirm that flexibility is interrogated early during the interaction between the transposase and a potential target site, which may be how other DNA binding proteins can steer selection of advantageous target sites. We also find that the conformation of the target DNA after strand transfer is involved in preventing accidental catalysis of the reverse reaction, as conditions that destabilize this conformation also trigger reversal.

Gan, W., Gu, Y., Han, J., Li, C. X., Sun, J., and Liu, P. Chitosan-Modified Filter Paper for Nucleic Acid Extraction and "in Situ PCR" on a Thermoplastic Microchip. Anal.Chem. 3-21-2017; 89(6):3568-3575; PM: 28230980

ABSTRACT: Plastic microfluidic devices with embedded chitosan-modified Fusion 5 filter paper (unmodified one purchased from GE Healthcare) have been successfully developed for DNA extraction and concentration, utilizing two different mechanisms for DNA capture: the physical entanglement of long-chain DNA molecules with the fiber matrix of the filter paper and the electrostatic adsorption of DNA to the chitosan-modified filter fibers. This new method not only provided a high DNA extraction efficiency at a pH of 5 by synergistically combining these two capture mechanisms together, but also resisted the elution of DNA from filters at a pH > 8 due to the entanglement of DNA with fibers. As a result, PCR buffers can be directly loaded into the extraction chamber for "in situ PCR", in which the captured DNA were used for downstream analysis without any loss. We demonstrated that the capture efficiencies of a 3-mm-diameter filter disc in a microchip were 98% and 95% for K562 human genomic DNA and bacteriophage lambda-DNA, respectively. The washes with DI water, PCR mixture, and TE buffer cannot elute the captured DNA. In addition, the filter disc can enrich 62% of lambda-DNA from a diluted sample (0.05 ng/muL), providing a concentration factor more than 30-fold. Finally, a microdevice with a simple two-chamber structure was developed for on-chip cell lysis, DNA extraction, and 15-plex short tandem repeat amplification from blood. This DNA extraction coupled with "in situ PCR" has great potential to be utilized in fully integrated microsystems for rapid, near-patient nucleic acid testing.

Garrido-Cardenas, J. A., Garcia-Maroto, F., varez-Bermejo, J. A., and Manzano-Agugliaro, F. DNA Sequencing Sensors: An Overview. Sensors.(Basel). 3-14-2017; 17(3); PM: 28335417

ABSTRACT: The first sequencing of a complete genome was published forty years ago by the double Nobel Prize in Chemistry winner Frederick Sanger. That corresponded to the

small sized genome of a bacteriophage, but since then there have been many complex organisms whose DNA have been sequenced. This was possible thanks to continuous advances in the fields of biochemistry and molecular genetics, but also in other areas such as nanotechnology and computing. Nowadays, sequencing sensors based on genetic material have little to do with those used by Sanger. The emergence of mass sequencing sensors, or new generation sequencing (NGS) meant a quantitative leap both in the volume of genetic material that was able to be sequenced in each trial, as well as in the time per run and its cost. One can envisage that incoming technologies, already known as fourth generation sequencing, will continue to cheapen the trials by increasing DNA reading lengths in each run. All of this would be impossible without sensors and detection systems becoming smaller and more precise. This article provides a comprehensive overview on sensors for DNA sequencing developed within the last 40 years.

Gasper, R., Schwach, J., Hartmann, J., Holtkamp, A., Wiethaus, J., Riedel, N., Hofmann, E., and Frankenberg-Dinkel, N. Distinct Features of Cyanophage-encoded T-type Phycobiliprotein Lyase PhiCpeT: THE ROLE OF AUXILIARY METABOLIC GENES. J.Biol.Chem. 2-24-2017; 292(8):3089-3098; PM: 28073912

ABSTRACT: Auxiliary metabolic genes (AMG) are commonly found in the genomes of phages that infect cyanobacteria and increase the fitness of the cyanophage. AMGs are often homologs of host genes, and also typically related to photosynthesis. For example, the PhicpeT gene in the cyanophage P-HM1 encodes a putative phycobiliprotein lyase related to cyanobacterial T-type lyases, which facilitate attachment of linear tetrapyrrole chromophores to Cys-155 of phycobiliprotein beta-subunits, suggesting that PhiCpeT may also help assemble light-harvesting phycobiliproteins during infection. To investigate this possibility, we structurally and biochemically characterized recombinant PhiCpeT. The solved crystal structure of PhiCpeT at 1.8-A resolution revealed that the protein adopts a similar fold as the cyanobacterial T-type lyase CpcT from Nostoc sp. PCC7120 but overall is more compact and smaller. PhiCpeT specifically binds phycoerythrobilin (PEB) in vitro leading to a tight complex that can also be formed in Escherichia coli when it is co-expressed with genes encoding PEB biosynthesis (i.e. ho1 and pebS). The formed PhiCpeT.PEB complex was very stable as the chromophore was not lost during chromatography and displayed a strong red fluorescence with a fluorescence quantum yield of PhiF = 0.3. This complex was not directly able to transfer PEB to the host phycobiliprotein beta-subunit. However, it could assist the host lyase CpeS in its function by providing a pool of readily available PEB, a feature that might be important for fast phycobiliprotein assembly during phage infection.

Gebhart, D., Williams, S. R., and Scholl, D. Bacteriophage SP6 encodes a second tailspike protein that recognizes Salmonella enterica serogroups C2 and C3. Virology. 2017; 507:263-266; PM: 28285722

ABSTRACT: SP6 is a salmonella phage closely related to coliphage K1-5. K1-5 is notable in that it encodes two polysaccharide-degrading tailspike proteins, an endosialidase that allows it to infect E. coli K1, and a lyase that enables it to infect K5 strains. SP6 is similar to K1-5 except that it encodes a P22-like endorhamnosidase tailspike, gp46, allowing it to infect group B Salmonella. We show here that SP6 can also infect Salmonella serogroups C2 and C3 and that a mutation in a putative second tailspike, gp47, eliminates this

specificity. Gene 47 was fused to the coding region of the N-terminal portion of the Pseudomonas aeruginosa R2 pyocin tail fiber and expressed in trans such that the fusion protein becomes incorporated into pyocin particles. These pyocins, termed AvR2-SP47, killed serogroups C2 and C3Salmonella. We conclude that SP6 encodes two tail proteins providing it a broad host range among Salmonella enterica.

Gencay, Y. E., Birk, T., Sorensen, M. C., and Brondsted, L. Methods for Isolation, Purification, and Propagation of Bacteriophages of Campylobacter jejuni. Methods Mol.Biol. 2017; 1512:19-28; PM: 27885595

ABSTRACT: Here, we describe the methods for isolation, purification, and propagation of Campylobacter jejuni bacteriophages from samples expected to contain high number of phages such as chicken feces. The overall steps are (1) liberation of phages from the sample material; (2) observation of plaque-forming units on C. jejuni lawns using a spot assay; (3) isolation of single plaques; (4) consecutive purification procedures; and (5) propagation of purified phages from a plate lysate to prepare master stocks.

Geue, L., Menge, C., Eichhorn, I., Semmler, T., Wieler, L. H., Pickard, D., Berens, C., and Barth, S. A. Evidence for Contemporary Switching of the O-Antigen Gene Cluster between Shiga Toxin-Producing Escherichia coli Strains Colonizing Cattle. Front Microbiol. 2017; 8:424; PM: 28377748

ABSTRACT: Shiga toxin-producing Escherichia coli (STEC) comprise a group of zoonotic enteric pathogens with ruminants, especially cattle, as the main reservoir. O-antigens are instrumental for host colonization and bacterial niche adaptation. They are highly immunogenic and, therefore, targeted by the adaptive immune system. The O-antigen is one of the most diverse bacterial cell constituents and variation not only exists between different bacterial species, but also between individual isolates/strains within a single species. We recently identified STEC persistently infecting cattle and belonging to the different serotypes O156:H25 (n = 21) and O182:H25 (n = 15) that were of the MLST sequence types ST300 or ST688. These STs differ by a single nucleotide in purA only. Fitness-, virulence-associated genome regions, and CRISPR/CAS (clustered regularly interspaced short palindromic repeats/CRISPR associated sequence) arrays of these STEC O156:H25 and O182:H25 isolates were highly similar, and identical genomic integration sites for the stx converting bacteriophages and the core LEE, identical Shiga toxin converting bacteriophage genes for stx1a, identical complete LEE loci, and identical sets of chemotaxis and flagellar genes were identified. In contrast to this genomic similarity, the nucleotide sequences of the O-antigen gene cluster (O-AGC) regions between galF and gnd and very few flanking genes differed fundamentally and were specific for the respective serotype. Sporadic aEPEC O156:H8 isolates (n = 5) were isolated in temporal and spatial proximity. While the O-AGC and the corresponding 5' and 3' flanking regions of these aEPEC isolates were identical to the respective region in the STEC O156:H25 isolates, the core genome, the virulence associated genome regions and the CRISPR/CAS elements differed profoundly. Our cumulative epidemiological and molecular data suggests a recent switch of the O-AGC between isolates with O156:H8 strains having served as DNA donors. Such O-antigen switches can affect the evaluation of a strain's pathogenic and virulence potential, suggesting that NGS methods might lead to a more reliable risk assessment.

Ghugare, G. S., Nair, A., Nimkande, V., Sarode, P., Rangari, P., and Khairnar, K. Membrane filtration immobilization technique-a simple and novel method for primary isolation and enrichment of bacteriophages. J.Appl.Microbiol. 2017; 122(2):531-539; PM: 27862682

ABSTRACT: AIM: To develop a method for the isolation and enrichment of bacteriophages selectively against specific bacteria coupled with a membrane filtration technique. *METHODS AND RESULTS*: Rapid isolation and concentration of host-specific bacteriophages was achieved by exposure of the sample suspected to contain bacteriophages to a specific host immobilized on a 0.45 mum membrane in a membrane filtration unit. The principle behind this method is the exploitation of host-specific interaction of bacteriophages with their host and maximizing this interaction using a classic membrane filtration method. This provides a chance for each bacteriophage in the sample to interact with the specific host on the membrane filter fitted with a vacuum pump. Specific bacteriophages of the host are retained on the membrane along with its host cells due to the effect of adsorption and these adsorbed bacteriophages (along with their hosts) on the filter disc are then amplified and enriched in regular nutritive broth tryptose soya broth by incubation. With the help of the plaque assay method, host-specific phages of various bacterial species were isolated, segregated and enriched. *CONCLUSIONS*: The phage concentration method coupled with membrane filtration immobilization of host bacteria was able to isolate and enrich the host-specific bacteriophages by several fold using a lower quantity of an environmental water sample, or other phage suspensions. Enrichment of phages from single plaques was also achieved. *SIGNIFICANCE AND IMPACT OF THE STUDY*: The isolation and detection of host-specific bacteriophages from a low density bacteriophage water sample in a single step by the use of a simple and basic microbiological technique can be achieved. Enrichment of phages from low phage titre suspensions is also achieved very effectively.

Ghusinga, K. R., Dennehy, J. J., and Singh, A. First-passage time approach to controlling noise in the timing of intracellular events. Proc.Natl.Acad.Sci.U.S.A. 1-24-2017; 114(4):693-698; PM: 28069947

ABSTRACT: In the noisy cellular environment, gene products are subject to inherent random fluctuations in copy numbers over time. How cells ensure precision in the timing of key intracellular events despite such stochasticity is an intriguing fundamental problem. We formulate event timing as a first-passage time problem, where an event is triggered when the level of a protein crosses a critical threshold for the first time. Analytical calculations are performed for the first-passage time distribution in stochastic models of gene expression. Derivation of these formulas motivates an interesting question: Is there an optimal feedback strategy to regulate the synthesis of a protein to ensure that an event will occur at a precise time, while minimizing deviations or noise about the mean? Counterintuitively, results show that for a stable long-lived protein, the optimal strategy is to express the protein at a constant rate without any feedback regulation, and any form of feedback (positive, negative, or any combination of them) will always amplify noise in event timing. In contrast, a positive feedback mechanism provides the highest precision in timing for an unstable protein. These theoretical results explain recent experimental observations of single-cell lysis times in bacteriophage [Formula: see text] Here, lysis of an infected bacterial cell is orchestrated by the expression and accumulation of a stable [Formula: see text] protein up to a threshold, and precision in timing is achieved via feedforward rather than feedback control. Our

results have broad implications for diverse cellular processes that rely on precise temporal triggering of events.

Gilmer, D. B., Schmitz, J. E., Thandar, M., Euler, C. W., and Fischetti, V. A. The Phage Lysin PlySs2 Decolonizes Streptococcus suis from Murine Intranasal Mucosa. PLoS.One. 2017; 12(1):e0169180; PM: 28046082

ABSTRACT: Streptococcus suis infects pigs worldwide and may be zoonotically transmitted to humans with a mortality rate of up to 20%. S. suis has been shown to develop in vitro resistance to the two leading drugs of choice, penicillin and gentamicin. Because of this, we have pursued an alternative therapy to treat these pathogens using bacteriophage lysins. The bacteriophage lysin PlySs2 is derived from an S. suis phage and displays potent lytic activity against most strains of that species including serotypes 2 and 9. At 64 mug/ml, PlySs2 reduced multiple serotypes of S. suis by 5 to 6-logs within 1 hour in vitro and exhibited a minimum inhibitory concentration (MIC) of 32 mug/ml for a S. suis serotype 2 strain and 64 mug/ml for a serotype 9 strain. Using a single 0.1-mg dose, the colonizing S. suis serotype 9 strain was reduced from the murine intranasal mucosa by >4 logs; a 0.1-mg dose of gentamicin reduced S. suis by <3-logs. A combination of 0.05 mg PlySs2 + 0.05 mg gentamicin reduced S. suis by >5-logs. While resistance to gentamicin was induced after systematically increasing levels of gentamicin in an S. suis culture, the same protocol resulted in no observable resistance to PlySs2. Thus, PlySs2 has both broad and high killing activity against multiple serotypes and strains of S. suis, making it a possible tool in the control and prevention of S. suis infections in pigs and humans.

Girlich, D., Bonnin, R. A., Bogaerts, P., De Laveleye, M., Huang, D. T., Dortet, L., Glaser, P., Glupczynski, Y., and Naas, T. Chromosomal Amplification of the blaOXA-58 Carbapenemase Gene in a Proteus mirabilis Clinical Isolate. Antimicrob.Agents Chemother. 2017; 61(2); PM: 27855079

ABSTRACT: Horizontal gene transfer may occur between distantly related bacteria, thus leading to genetic plasticity and in some cases to acquisition of novel resistance traits. Proteus mirabilis is an enterobacterial species responsible for human infections that may express various acquired beta-lactam resistance genes, including different classes of carbapenemase genes. Here we report a Proteus mirabilis clinical isolate (strain 1091) displaying resistance to penicillin, including temocillin, together with reduced susceptibility to carbapenems and susceptibility to expanded-spectrum cephalosporins. Using biochemical tests, significant carbapenem hydrolysis was detected in P. mirabilis 1091. Since PCR failed to detect acquired carbapenemase genes commonly found in Enterobacteriaceae, we used a whole-genome sequencing approach that revealed the presence of blaOXA-58 class D carbapenemase gene, so far identified only in Acinetobacter species. This gene was located on a 3.1-kb element coharboring a blaAmpC-like gene. Remarkably, these two genes were bracketed by putative XerC-XerD binding sites and inserted at a XerC-XerD site located between the terminase-like small- and large-subunit genes of a bacteriophage. Increased expression of the two bla genes resulted from a 6-time tandem amplification of the element as revealed by Southern blotting. This is the first isolation of a clinical P. mirabilis strain producing OXA-58, a class D carbapenemase, and the first description of a XerC-XerD-dependent insertion of antibiotic resistance genes within a bacteriophage. This study revealed a new role for the XerC-XerD recombinase in bacteriophage biology.

Gong, C. and Jiang, X. Application of bacteriophages to reduce Salmonella attachment and biofilms on hard surfaces. Poult.Sci. 2-23-2017; PM: 28339743

ABSTRACT: This study evaluated the effectiveness of bacteriophage treatment for reducing Salmonella attachment and biofilms on hard surfaces. Bacteriophages (n = 6) were selected for bacteriophage treatment based on host ranges against Salmonella isolates (n = 10) obtained from rendering plants. The effectiveness of bacteriophage treatment (104-108 PFU/mL) was initially evaluated against strong Salmonella biofilm formers in 96-well microplate. Then, the bacteriophage treatment (109 PFU/mL) was applied for 7 d to reduce Salmonella attached to the stainless steel surfaces under laboratory and greenhouse conditions. The inhibition of biofilm formation and reduction of pre-formed biofilm in 96-well microplate with bacteriophage treatment reached up to 90 and 66%, respectively. Under laboratory conditions, bacteriophage treatment reduced up to 2.9 and 3.0 log CFU/cm2 of attachment and slightly formed biofilm of selected top 10 Salmonella strains and an avirulent Salmonella Typhimurium strain 8243, respectively, as compared with reductions of 3.4, 1.4, and 3.0 log CFU/cm2 of S. Typhimurium strain 8243 in summer, fall/winter, and spring seasons under greenhouse conditions, respectively. Clearly, bacteriophages were effective on reducing Salmonella attachment and biofilms formed on hard surfaces under both laboratory and greenhouse conditions. The use of bacteriophages on hard surfaces may have merits in reducing the likelihood of finished rendered products being recontaminated with Salmonella in rendering plants.

Gonzales-Gustavson, E., Cardenas-Youngs, Y., Calvo, M., da Silva, M. F., Hundesa, A., Amoros, I., Moreno, Y., Moreno-Mesonero, L., Rosell, R., Ganges, L., Araujo, R., and Girones, R. Characterization of the efficiency and uncertainty of skimmed milk flocculation for the simultaneous concentration and quantification of water-borne viruses, bacteria and protozoa. J.Microbiol.Methods. 2017; 134:46-53 PM: 28093213

ABSTRACT: In this study, the use of skimmed milk flocculation (SMF) to simultaneously concentrate viruses, bacteria and protozoa was evaluated. We selected strains of faecal indicator bacteria and pathogens, such as Escherichia coli and Helicobacter pylori. The viruses selected were adenovirus (HAdV 35), rotavirus (RoV SA-11), the bacteriophage MS2 and bovine viral diarrhoea virus (BVDV). The protozoa tested were Acanthamoeba, Giardia and Cryptosporidium. The mean recoveries with q(RT)PCR were 66% (HAdV 35), 24% (MS2), 28% (RoV SA-11), 15% (BVDV), 60% (E. coli), 30% (H. pylori) and 21% (Acanthamoeba castellanii). When testing the infectivity, the mean recoveries were 59% (HAdV 35), 12% (MS2), 26% (RoV SA-11) and 0.7% (BVDV). The protozoa Giardia lamblia and Cryptosporidium parvum were studied by immunofluorescence with recoveries of 18% and 13%, respectively. Although q(RT)PCR consistently showed higher quantification values (as expected), q(RT)PCR and the infectivity assays showed similar recoveries for HAdV 35 and RoV SA-11. Additionally, we investigated modelling the variability and uncertainty of the recovery with this method to extrapolate the quantification obtained by q(RT)PCR and estimate the real concentration. The 95% prediction intervals of the real concentration of the microorganisms inoculated were calculated using a general non-parametric bootstrap procedure adapted in our context to estimate the technical error of the measurements. SMF shows recoveries with a low variability that permits the use of a mathematical approximation to predict the concentration of the pathogen and indicator with acceptable low intervals. The values

of uncertainty may be used for a quantitative microbial risk analysis or diagnostic purposes.

Gonzalez, S., Fernandez, L., Campelo, A. B., Gutierrez, D., Martinez, B., Rodriguez, A., and Garcia, P. The Behavior of Staphylococcus aureus Dual-Species Biofilms Treated with Bacteriophage phiIPLA-RODI Depends on the Accompanying Microorganism. Appl.Environ.Microbiol. 2-1-2017; 83(3); PM: 27836851

ABSTRACT: The use of bacteriophages as antimicrobials against pathogenic bacteria offers a promising alternative to traditional antibiotics and disinfectants. Significantly, phages may help to remove biofilms, which are notoriously resistant to commonly used eradication methods. However, the successful development of novel antibiofilm strategies must take into account that real-life biofilms usually consist of mixed-species populations. Within this context, this study aimed to explore the effectiveness of bacteriophage-based sanitation procedures for removing polymicrobial biofilms from food industry surfaces. We treated dual-species biofilms formed by the food pathogenic bacterium Staphylococcus aureus in combination with Lactobacillus plantarum, Enterococcus faecium, or Lactobacillus pentosus with the staphylococcal phage phiIPLA-RODI. Our results suggest that the impact of bacteriophage treatment on S. aureus mixed-species biofilms varies depending on the accompanying species and the infection conditions. For instance, short treatments (4 h) with a phage suspension under nutrient-limiting conditions reduced the number of S. aureus cells in 5-h biofilms by approximately 1 log unit without releasing the nonsusceptible species. In contrast, longer infection periods (18 h) with no nutrient limitation increased the killing of S. aureus cells by the phage (decrease of up to 2.9 log units). However, in some cases, these conditions promoted the growth of the accompanying species. For example, the L. plantarum cell count in the treated sample was up to 2.3 log units higher than that in the untreated control. Furthermore, phage propagation inside dual-species biofilms also depended greatly on the accompanying species, with the highest rate detected in biofilms formed by S. aureus-L. pentosus Scanning electron microscopy (SEM) and confocal laser scanning microscopy (CLSM) also showed changes in the three-dimensional structures of the mixed-species biofilms after phage treatment. Altogether, the results presented here highlight the need to study the impact of phage therapy on microbial communities that reflect a more realistic setting. IMPORTANCE: Biofilms represent a major source of contamination in industrial and hospital settings. Therefore, developing efficient strategies to combat bacterial biofilms is of the utmost importance from medical and economic perspectives. Bacteriophages have shown potential as novel antibiofilm agents, but further research is still required to fully understand the interactions between phages and biofilm-embedded bacteria. The results presented in this study contribute to achieving a better understanding of such interactions in a more realistic context, considering that most biofilms in the environment consist of mixed-species populations.

Goren, M., Yosef, I., and Qimron, U. Sensitizing pathogens to antibiotics using the CRISPR-Cas system. Drug Resist.Updat. 2017; 30:1-6; PM: 28363331

ABSTRACT: The extensive use of antibiotics over the last century has resulted in a significant artificial selection pressure for antibiotic-resistant pathogens to evolve. Various strategies to fight these pathogens have been introduced including new antibiotics, naturally-derived enzymes/peptides that specifically target pathogens and bacteriophages that lyse these pathogens. A new tool has recently been introduced in the fight against drug-resistant pathogens-the prokaryotic defense mechanism-clustered

regularly interspaced short palindromic repeats-CRISPR associated (CRISPR-Cas) system. The CRISPR-Cas system acts as a nuclease that can be guided to cleave any target DNA, allowing sophisticated, yet feasible, manipulations of pathogens. Here, we review pioneering studies that use the CRISPR-Cas system to specifically edit bacterial populations, eliminate their resistance genes and combine these two strategies in order to produce an artificial selection pressure for antibiotic-sensitive pathogens. We suggest that intelligent design of this system, along with efficient delivery tools into pathogens, may significantly reduce the threat of antibiotic-resistant pathogens.

Goz, E., Mioduser, O., Diament, A., and Tuller, T. Evidence of translation efficiency adaptation of the coding regions of the bacteriophage lambda. DNA Res. 2-28-2017; PM: 28338832

ABSTRACT: Deciphering the way gene expression regulatory aspects are encoded in viral genomes is a challenging mission with ramifications related to all biomedical disciplines. Here, we aimed to understand how the evolution shapes the bacteriophage lambda genes by performing a high resolution analysis of ribosomal profiling data and gene expression related synonymous/silent information encoded in bacteriophage coding regions. We demonstrated evidence of selection for distinct compositions of synonymous codons in early and late viral genes related to the adaptation of translation efficiency to different bacteriophage developmental stages. Specifically, we showed that evolution of viral coding regions is driven, among others, by selection for codons with higher decoding rates; during the initial/progressive stages of infection the decoding rates in early/late genes were found to be superior to those in late/early genes, respectively. Moreover, we argued that selection for translation efficiency could be partially explained by adaptation to Escherichia coli tRNA pool and the fact that it can change during the bacteriophage life cycle.An analysis of additional aspects related to the expression of viral genes, such as mRNA folding and more complex/longer regulatory signals in the coding regions, is also reported. The reported conclusions are likely to be relevant also to additional viruses.

Grant, A., Parveen, S., Schwarz, J., Hashem, F., and Vimini, B. Reduction of Salmonella in ground chicken using a bacteriophage. Poult.Sci. 3-23-2017; PM: 28371846

ABSTRACT: This study's goal was to ascertain the effectiveness of a commercially available Salmonella bacteriophage during ground chicken production focusing on: water source, different Salmonella serovars, and time. Salmonella-free boneless, skinless chicken meat was inoculated with 4.0 Log CFU/cm2 of either a cocktail of 3 Salmonella isolates derived from ground chicken (GC) or a cocktail of 3 Salmonella strains not isolated from ground chicken (non-GC). Bacteriophages were spread onto the chicken using sterile tap or filtered water for 30 min or 8 h. Salmonella was recovered using standard plating method. Greater Salmonella reduction was observed when the bacteriophage was diluted in sterile tap water than in sterile filtered water: 0.39 Log CFU/cm2 and 0.23 Log CFU/cm2 reduction after 30 min, respectively ($P < 0.05$). The non-GC isolates showed reductions of 0.71 Log CFU/cm2 and 0.90 Log CFU/cm2 after 30 min and 8 h, respectively ($P < 0.05$). The GC isolates were less sensitive to the bacteriophage: 0.39 Log CFU/cm2 and 0.67 Log CFU/cm2 reductions after 30 min and 8 h, respectively ($P < 0.05$). In conclusion, bacteriophage reduction was dependent on water used to dilute the bacteriophage, Salmonella's susceptibility to the bacteriophage, and treatment time.

Guo, M., Feng, C., Ren, J., Zhuang, X., Zhang, Y., Zhu, Y., Dong, K., He, P., Guo, X., and Qin, J. A Novel Antimicrobial Endolysin, LysPA26, against Pseudomonas aeruginosa. Front Microbiol. 2017; 8:293; PM: 28289407

ABSTRACT: The global increase in multidrug resistant (MDR) bacteria has led to phage therapy being refocused upon. A novel endolysin, LysPA26, containing a lysozyme-like domain, was screened against Pseudomonas aeruginosa in this study. It had activity against MDR P. aeruginosa without pretreatment with an outer-membrane permeabilizer. LysPA26 could kill up to 4 log units P. aeruginosa in 30 min. In addition, temperature and pH effect assays revealed that LysPA26 had good stability over a broad range of pH and temperatures. Moreover, LysPA26 could kill other Gram-negative bacteria, such as Klebsiella pneumonia, Acinetobacter baumannii and Escherichia coli, but not Gram-positive bacteria. Furthermore, LysPA26 could eliminate P. aeruginosa in biofilm formation. Our current results show that LysPA26 is a new and promising antimicrobial agent for the combat of Gram-negative pathogens.

Gupta, J. C., Hada, R. S., Sahai, P., and Talwar, G. P. Development of a novel recombinant LHRH fusion protein for therapy of androgen and estrogen dependent cancers. Protein Expr.Purif. 4-12-2017; 134:132-138; PM: 28410993

ABSTRACT: LHRH based vaccines are promising candidates for therapy of androgen and estrogen dependent cancers. We report in this communication development of a novel recombinant protein vaccine candidate against LHRH. A synthetic gene was designed in which the codon sequence in the LHRH decapeptide was modified by substituting the codon for 6-glycine with that of l-leucine. Further the LHRH(6leu) gene was linked to heat-labile enterotoxin of E. coli (LTB) as carrier. This LHRH(6leu)-LTB gene was cloned into a prokaryotic expression vector under the control of inducible and strong bacteriophage T7 promoter to over-express LHRH(leu) fused to LTB as recombinant protein in E. coli. Recombinant LHRH(leu)-LTB protein of approximately 14 kDa size, was purified from inclusion bodies using in-situ refolding on the column and Ni-NTA based immobilized affinity chromatography. Western blot confirmed the immunoreactivity of purified LHRH(leu)-LTB fusion protein with anti-LHRH monoclonal antibody. The vaccine protein was further characterized by mass spectroscopy, circular dichroism and fluorescence spectroscopy. This communication reports a recombinant LHRH fusion protein with potential for blocking of sex hormones production for eventual therapy of sex hormones dependent neoplasms.

Gurney, J., Aldakak, L., Betts, A., Gougat-Barbera, C., Poisot, T., Kaltz, O., and Hochberg, M. E. Network structure and local adaptation in co-evolving bacteria-phage interactions. Mol.Ecol. 2017; 26(7):1764-1777; PM: 28092408

ABSTRACT: Numerous theoretical and experimental studies have investigated antagonistic co-evolution between parasites and their hosts. Although experimental tests of theory from a range of biological systems are largely concordant regarding the influence of several driving processes, we know little as to how mechanisms acting at the smallest scales (individual molecular and phenotypic changes) may result in the emergence of structures at larger scales, such as co-evolutionary dynamics and local adaptation. We capitalized on methods commonly employed in community ecology to quantify how the structure of community interaction matrices, so-called bipartite

networks, reflected observed co-evolutionary dynamics, and how phages from these communities may or may not have adapted locally to their bacterial hosts. We found a consistent nested network structure for two phage types, one previously demonstrated to exhibit arms race co-evolutionary dynamics and the other fluctuating co-evolutionary dynamics. Both phages increased their host ranges through evolutionary time, but we found no evidence for a trade-off with impact on bacteria. Finally, only bacteria from the arms race phage showed local adaptation, and we provide preliminary evidence that these bacteria underwent (sometimes different) molecular changes in the wzy gene associated with the LPS receptor, while bacteria co-evolving with the fluctuating selection phage did not show local adaptation and had partial deletions of the pilF gene associated with type IV pili. We conclude that the structure of phage-bacteria interaction networks is not necessarily specific to co-evolutionary dynamics, and discuss hypotheses for why only one of the two phages was, nevertheless, locally adapted.

Hannigan, G. D., Zheng, Q., Meisel, J. S., Minot, S. S., Bushman, F. D., and Grice, E. A. Evolutionary and functional implications of hypervariable loci within the skin virome. PeerJ. 2017; 5:e2959; PM: 28194314

ABSTRACT: Localized genomic variability is crucial for the ongoing conflicts between infectious microbes and their hosts. An understanding of evolutionary and adaptive patterns associated with genomic variability will help guide development of vaccines and antimicrobial agents. While most analyses of the human microbiome have focused on taxonomic classification and gene annotation, we investigated genomic variation of skin-associated viral communities. We evaluated patterns of viral genomic variation across 16 healthy human volunteers. Human papillomavirus (HPV) and Staphylococcus phages contained 106 and 465 regions of diversification, or hypervariable loci, respectively. Propionibacterium phage genomes were minimally divergent and contained no hypervariable loci. Genes containing hypervariable loci were involved in functions including host tropism and immune evasion. HPV and Staphylococcus phage hypervariable loci were associated with purifying selection. Amino acid substitution patterns were virus dependent, as were predictions of their phenotypic effects. We identified diversity generating retroelements as one likely mechanism driving hypervariability. We validated these findings in an independently collected skin metagenomic sequence dataset, suggesting that these features of skin virome genomic variability are widespread. Our results highlight the genomic variation landscape of the skin virome and provide a foundation for better understanding community viral evolution and the functional implications of genomic diversification of skin viruses.

Harrison, E., Hall, J. P. J., Paterson, S., Spiers, A. J., and Brockhurst, M. A. Conflicting selection alters the trajectory of molecular evolution in a tripartite bacteria-plasmid-phage interaction. Mol.Ecol. 2017; 26(10):2757-2764 PM: 28247474

ABSTRACT: Bacteria engage in a complex network of ecological interactions, which includes mobile genetic elements (MGEs) such as phages and plasmids. These elements play a key role in microbial communities as vectors of horizontal gene transfer but can also be important sources of selection for their bacterial hosts. In natural communities, bacteria are likely to encounter multiple MGEs simultaneously and conflicting selection among MGEs could alter the bacterial evolutionary response to each MGE. Here, we test the effect of interactions with multiple MGEs on bacterial molecular evolution in the tripartite interaction between the bacterium, Pseudomonas fluorescens, the lytic bacteriophage, SBW25phi2, and conjugative plasmid, pQBR103, using genome

sequencing of experimentally evolved bacteria. We show that individually, both plasmids and phages impose selection leading to bacterial evolutionary responses that are distinct from bacterial populations evolving without MGEs, but that together, plasmids and phages impose conflicting selection on bacteria, constraining the evolutionary responses observed in pairwise interactions. Our findings highlight the likely difficulties of predicting evolutionary responses to multiple selective pressures from the observed evolutionary responses to each selective pressure alone. Understanding evolution in complex microbial communities comprising many species and MGEs will require that we go beyond studies of pairwise interactions.

Hathaway, H., Ajuebor, J., Stephens, L., Coffey, A., Potter, U., Sutton, J. M., and Jenkins, A. T. Thermally triggered release of the bacteriophage endolysin CHAPK and the bacteriocin lysostaphin for the control of methicillin resistant Staphylococcus aureus (MRSA). J.Control Release. 1-10-2017; 245:108-115; PM: 27908758

ABSTRACT: Staphylococcus aureus infections of the skin and soft tissue pose a major concern to public health, largely owing to the steadily increasing prevalence of drug resistant isolates. As an alternative mode of treatment both bacteriophage endolysins and bacteriocins have been shown to possess antimicrobial efficacy against multiple species of bacteria including otherwise drug resistant strains. Despite this, the administration and exposure of such antimicrobials should be restricted until required in order to discourage the continued evolution of bacterial resistance, whilst maintaining the activity and stability of such proteinaceous structures. Utilising the increase in skin temperature during infection, the truncated bacteriophage endolysin CHAPK and the staphylococcal bacteriocin lysostaphin have been co-administered in a thermally triggered manner from Poly(N-isopropylacrylamide) (PNIPAM) nanoparticles. The thermoresponsive nature of the PNIPAM polymer has been employed in order to achieve the controlled expulsion of a synergistic enzybiotic cocktail consisting of CHAPK and lysostaphin. The point at which this occurs is modifiable, in this case corresponding to the threshold temperature associated with an infected wound. Consequently, bacterial lysis was observed at 37 degrees C, whilst growth was maintained at the uninfected skin temperature of 32 degrees C.

He, Y., Wang, M., Fan, E., Ouyang, H., Yue, H., Su, X., Liao, G., Wang, L., Lu, S., and Fu, Z. Highly Specific Bacteriophage-Affinity Strategy for Rapid Separation and Sensitive Detection of Viable Pseudomonas aeruginosa. Anal.Chem. 2-7-2017; 89(3):1916-1921; PM: 28208306

ABSTRACT: A virulent bacteriophage highly specific to Pseudomonas aeruginosa (P. aeruginosa) was isolated from hospital sewage using a lambda bacteriophage isolation protocol. The bacteriophage, named as PAP1, was used to functionalize tosyl-activated magnetic beads to establish a bacteriophage-affinity strategy for separation and detection of viable P. aeruginosa. Recognition of the target bacteria by tail fibers and baseplate of the bacteriophage led to capture of P. aeruginosa onto the magnetic beads. After a replication cycle of about 100 min, the progenies lysed the target bacteria and released the intracellular adenosine triphosphate. Subsequently, firefly luciferase-adenosine triphosphate bioluminescence system was used to quantitate the amount of P. aeruginosa. This bacteriophage-affinity strategy for viable P. aeruginosa detection showed a linear range of 6.0 x 102 to 3.0 x 105 CFU mL-1, with a detection limit of 2.0 x 102 CFU mL-1. The whole process for separation and detection could be completed after bacteria capture, bacteriophage replication, and bacteria lysis within 2

h. Since the isolated bacteriophage recognized the target bacteria with very high specificity, the proposed strategy did not show any signal response to all of the tested interfering bacteria. Furthermore, it excluded the interference from inactivated P. aeruginosa because the bacteriophage could replicate only in viable cells. The proposed strategy had been applied for detection of P. aeruginosa in glucose injection, human urine, and rat plasma. In the further work, this facile bacteriophage-affinity strategy could be extended for detection of other pathogens by utilizing virulent bacteriophage specific to other targets.

Heinrich, S., Sidler, C. L., Azzalin, C. M., and Weis, K. Stem-loop RNA labeling can affect nuclear and cytoplasmic mRNA processing. RNA. 2017; 23(2):134-141; PM: 28096443

ABSTRACT: The binding of sequence-specific RNA-interacting proteins, such as the bacteriophage MS2 or PP7 coat proteins, to their corresponding target sequences has been extremely useful and widely used to visualize single mRNAs in vivo. However, introduction of MS2 stem-loops into yeast mRNAs has recently been shown to lead to the accumulation of RNA fragments, suggesting that the loops impair mRNA decay. This result was questioned, because fragment occurrence was mainly assessed using ensemble methods, and their cellular localization and its implications had not been addressed on a single transcript level. Here, we demonstrate that the introduction of either MS2 stem-loops (MS2SL) or PP7 stem-loops (PP7SL) can affect the processing and subcellular localization of mRNA. We use single-molecule fluorescence in situ hybridization (smFISH) to determine the localization of three independent mRNAs tagged with the stem-loop labeling systems in glucose-rich and glucose starvation conditions. Transcripts containing MS2SL or PP7SL display aberrant localization in both the nucleus and the cytoplasm. These defects are most prominent in glucose starvation conditions, with nuclear mRNA processing being altered and stem-loop fragments abnormally enriching in processing bodies (PBs). The mislocalization of SL-containing RNAs is independent of the presence of the MS2 or PP7 coat protein (MCP or PCP).

Heler, R., Wright, A. V., Vucelja, M., Bikard, D., Doudna, J. A., and Marraffini, L. A. Mutations in Cas9 Enhance the Rate of Acquisition of Viral Spacer Sequences during the CRISPR-Cas Immune Response. Mol.Cell. 1-5-2017; 65(1):168-175; PM: 28017588

ABSTRACT: CRISPR loci and their associated (Cas) proteins encode a prokaryotic immune system that protects against viruses and plasmids. Upon infection, a low fraction of cells acquire short DNA sequences from the invader. These sequences (spacers) are integrated in between the repeats of the CRISPR locus and immunize the host against the matching invader. Spacers specify the targets of the CRISPR immune response through transcription into short RNA guides that direct Cas nucleases to the invading DNA molecules. Here we performed random mutagenesis of the RNA-guided Cas9 nuclease to look for variants that provide enhanced immunity against viral infection. We identified a mutation, I473F, that increases the rate of spacer acquisition by more than two orders of magnitude. Our results highlight the role of Cas9 during CRISPR immunization and provide a useful tool to study this rare process and develop it as a biotechnological application.

Hernandez, A. J. and Richardson, C. C. Kinetics of Lagging-strand DNA Synthesis In Vitro by the Bacteriophage T7 Replication Proteins. J.Vis.Exp. 2-25-2017; (120); PM: 28287575

ABSTRACT: Here we provide protocols for the kinetic examination of lagging-strand DNA synthesis in vitro by the replication proteins of bacteriophage T7. The T7 replisome is one of the simplest replication systems known, composed of only four proteins, which is an attractive feature for biochemical experiments. Special emphasis is placed on the synthesis of ribonucleotide primers by the T7 primase-helicase, which are used by DNA polymerase to initiate DNA synthesis. Because the mechanisms of DNA replication are conserved across evolution, these protocols should be applicable, or useful as a conceptual springboard, to investigators using other model systems. The protocols described here are highly sensitive and an experienced investigator can perform these experiments and obtain data for analysis in about a day. The only specialized piece of equipment required is a rapid-quench flow instrument, but this piece of equipment is relatively common and available from various commercial sources. The major drawbacks of these assays, however, include the use of radioactivity and the relative low throughput.

Hernandez, I. Bacteriophages against Serratia as Fish Spoilage Control Technology. Front Microbiol. 2017; 8:449; PM: 28421038

ABSTRACT: Bacteria of the genus Serratia, mainly S. proteamaculans and S. fonticola, are important spoilage agents in Atlantic horse mackerel (Trachurus trachurus). In order to evaluate whether bacteriophages against Serratia could delay the spoilage process, 11 viral strains active against this genus were isolated from food and best candidate was applied to fresh mackerel filets. All the phages belong to the Siphoviridae and Podoviridae families and were active at multiplicity of infection (MOI) levels below 1:1 in Long & Hammer broth. The ability of phage AZT6 to control Serratia populations in real food was tested in Atlantic horse mackerel extract and applied to fresh mackerel filets. Treatment with high phage concentration (MOI 350:1, initial Serratia population 3.9 +/- 0.3 Log cfu/g) can reduce the Serratia populations up to 90% during fish storage (a maximum of 6 days) at low temperatures (6 degrees C). Bacterial inhibition was dependent on the bacteriophage dosage, and MOI of 10:1 or lower did not significantly affect the Serratia populations.

Hill, R. L. L., Vlach, J., Parker, L. K., Christie, G. E., Saad, J. S., and Dokland, T. Derepression of SaPIbov1 Is Independent of phiNM1 Type 2 dUTPase Activity and Is Inhibited by dUTP and dUMP. J.Mol.Biol. 4-8-2017; PM: 28400210

ABSTRACT: Staphylococcus aureus is an opportunistic human pathogen able to transfer virulence genes to other cells through the mobilization of S. aureus pathogenicity islands (SaPIs). SaPIs are derepressed and packaged into phage-like transducing particles by helper phages like 80alpha or phiNM1. Phages 80alpha and phiNM1 encode structurally distinct dUTPases, Dut80alpha (type 1) and DutNM1 (type 2). Both dUTPases can interact with the SaPIbov1 StI master repressor, leading to derepression and mobilization. That two structurally distinct dUTPases bind the same repressor led us to speculate that dUTPase activity may be important to the derepression process. In type 1 dUTPases, StI binding is inhibited by dUTP. The purpose of this study was to assess the involvement of dUTP binding and dUTPase activity in derepression by DutNM1. DutNM1 activity mutants were created and tested for dUTPase activity using a novel NMR-based assay. We found that all DutNM1 null activity mutants interacted with the SaPIbov1 StI C-terminal domain, formed DutNM1-StI heterodimers, and caused the release of the Pstr promoter. However,

promoter release was inhibited in the presence of dUTP or dUMP. We tested two phiNM1 mutant phages that had null enzyme activity and found that they could still mobilize SaPIbov1. These results show that only the apo form of DutNM1 is active in StI derepression and that dUTPase activity is not necessary for the mobilization of SaPIbov1 by DutNM1.

Hockett, K. L. and Baltrus, D. A. Use of the Soft-agar Overlay Technique to Screen for Bacterially Produced Inhibitory Compounds. J.Vis.Exp. 1-14-2017; (119); PM: 28117830

ABSTRACT: The soft-agar overlay technique was originally developed over 70 years ago and has been widely used in several areas of microbiological research, including work with bacteriophages and bacteriocins, proteinaceous antibacterial agents. This approach is relatively inexpensive, with minimal resource requirements. This technique consists of spotting supernatant from a donor strain (potentially harboring a toxic compound(s)) onto a solidified soft agar overlay that is seeded with a bacterial test strain (potentially sensitive to the toxic compound(s)). We utilized this technique to screen a library of Pseudomonas syringae strains for intraspecific killing. By combining this approach with a precipitation step and targeted gene deletions, multiple toxic compounds produced by the same strain can be differentiated. The two antagonistic agents commonly recovered using this technique are bacteriophages and bacteriocins. These two agents can be differentiated using two simple additional tests. Performing a serial dilution on a supernatant containing bacteriophage will result in individual plaques becoming less in number with greater dilution, whereas serial dilution of a supernatant containing bacteriocin will result a clearing zone that becomes uniformly more turbid with greater dilution. Additionally, a bacteriophage will produce a clearing zone when spotted onto a fresh soft agar overlay seeded with the same strain, whereas a bacteriocin will not produce a clearing zone when transferred to a fresh soft agar lawn, owing to the dilution of the bacteriocin.

Hodgson, K. R., Torok, V. A., and Turnbull, A. R. Bacteriophages as enteric viral indicators in bivalve mollusc management. Food Microbiol. 2017; 65:284-293; PM: 28400015

ABSTRACT: Human enteric viruses, such as norovirus and hepatitis A virus, are spread by a variety of routes including faecal-oral transmission. Contaminated bivalve shellfish are regularly implicated in foodborne viral disease outbreaks internationally. Traditionally indicator bacteria, the coliforms and Escherichia coli, have been used to detect faecal pollution in growing waters and shellfish. However, studies have established that they are inadequate as indicators of the risk of human enteric viruses. Bacteriophages have been identified as potential indicators or surrogates for human enteric viruses due to their similarities in morphology, behaviour in water environments and resistance to disinfectant treatments. The somatic coliphages, male-specific RNA coliphages (FRNA coliphages) and the bacteriophages of Bacteroides are the groups recognised as most suitable for water and shellfish testing. In this review, we discuss the rationale and supporting evidence for the application of bacteriophages as surrogates for human enteric viruses in shellfish under a variety of conditions. There is some evidence to support the validity of using bacteriophage levels to indicate viral risk in shellfish in highly contaminated sites and following adverse sewage events.

Hoekstra, T. P., Depken, M., Lin, S. N., Cabanas-Danes, J., Gross, P., Dame, R. T., Peterman, E. J., and Wuite, G. J. Switching between Exonucleolysis and Replication by T7 DNA Polymerase Ensures High Fidelity. Biophys.J. 2-28-2017; 112(4):575-583; PM: 28256218

ABSTRACT: DNA polymerase catalyzes the accurate transfer of genetic information from one generation to the next, and thus it is vitally important for replication to be faithful. DNA polymerase fulfills the strict requirements for fidelity by a combination of mechanisms: 1) high selectivity for correct nucleotide incorporation, 2) a slowing down of the replication rate after misincorporation, and 3) proofreading by excision of misincorporated bases. To elucidate the kinetic interplay between replication and proofreading, we used high-resolution optical tweezers to probe how DNA-duplex stability affects replication by bacteriophage T7 DNA polymerase. Our data show highly irregular replication dynamics, with frequent pauses and direction reversals as the polymerase cycles through the states that govern the mechanochemistry behind high-fidelity T7 DNA replication. We constructed a kinetic model that incorporates both existing biochemical data and the, to our knowledge, novel states we observed. We fit the model directly to the acquired pause-time and run-time distributions. Our findings indicate that the main pathway for error correction is DNA polymerase dissociation-mediated DNA transfer, followed by biased binding into the exonuclease active site. The number of bases removed by this proofreading mechanism is much larger than the number of erroneous bases that would be expected to be incorporated, ensuring a high-fidelity replication of the bacteriophage T7 genome.

Holt, G. S., Lodge, J. K., McCarthy, A. J., Graham, A. K., Young, G., Bridge, S. H., Brown, A. K., Veses-Garcia, M., Lanyon, C. V., Sails, A., Allison, H. E., and Smith, D. L. Shigatoxin encoding Bacteriophage varphi24B modulates bacterial metabolism to raise antimicrobial tolerance. Sci.Rep. 1-20-2017; 7:40424; PM: 28106081

ABSTRACT: How temperate bacteriophages play a role in microbial infection and disease progression is not fully understood. They do this in part by carrying genes that promote positive evolutionary selection for the lysogen. Using Biolog phenotype microarrays and comparative metabolite profiling we demonstrate the impact of the well-characterised Shiga toxin-prophage varphi24B on its Escherichia coli host MC1061. As a lysogen, the prophage alters the bacterial physiology by increasing the rates of respiration and cell proliferation. This is the first reported study detailing phage-mediated control of the E. coli biotin and fatty acid synthesis that is rate limiting to cell growth. Through varphi24B conversion the lysogen also gains increased antimicrobial tolerance to chloroxylenol and 8-hydroxyquinoline. Distinct metabolite profiles discriminate between MC1061 and the varphi24B lysogen in standard culture, and when treated with 2 antimicrobials. This is also the first reported use of metabolite profiling to characterise the physiological impact of lysogeny under antimicrobial pressure. We propose that temperate phages do not need to carry antimicrobial resistance genes to play a significant role in tolerance to antimicrobials.

Hosseinidoust, Z. Phage-Mediated Gene Therapy. Curr.Gene Ther. 5-10-2017; PM: 28494733

ABSTRACT: Bacteriophages (bacterial viruses) have long been under investigation as vectors for gene therapy. Similar to other viral vectors, the phage coat proteins have evolved over millions of years to protect the viral genome from degradation post injection, offering protection for the valuable therapeutic sequence. However, what sets

phage apart from other viral gene delivery vectors is their safety for human use and the relative ease by which foreign molecules can be expressed on the phage outer surface, enabling highly targeted gene delivery. The latter property also makes phage a popular choice for gene therapy target discovery through directed evolution. Although promising, phage-mediated gene therapy faces several outstanding challenges, the most notable being lower gene delivery efficiency compared to animal viruses, vector stability, and nondesirable immune stimulation. This review presents a critical review of promises and challenges of employing phage as gene delivery vehicles as well as an introduction to the concept of phage-based microbiome therapy as the new frontier and perhaps the most promising application of phage-based for gene therapy.

Hoyland-Kroghsbo, N. M., Paczkowski, J., Mukherjee, S., Broniewski, J., Westra, E., Bondy-Denomy, J., and Bassler, B. L. Quorum sensing controls the Pseudomonas aeruginosa CRISPR-Cas adaptive immune system. Proc.Natl.Acad.Sci.U.S.A. 1-3-2017; 114(1):131-135; PM: 27849583

ABSTRACT: CRISPR-Cas are prokaryotic adaptive immune systems that provide protection against bacteriophage (phage) and other parasites. Little is known about how CRISPR-Cas systems are regulated, preventing prediction of phage dynamics in nature and manipulation of phage resistance in clinical settings. Here, we show that the bacterium Pseudomonas aeruginosa PA14 uses the cell-cell communication process, called quorum sensing, to activate cas gene expression, to increase CRISPR-Cas targeting of foreign DNA, and to promote CRISPR adaptation, all at high cell density. This regulatory mechanism ensures maximum CRISPR-Cas function when bacterial populations are at highest risk for phage infection. We demonstrate that CRISPR-Cas activity and acquisition of resistance can be modulated by administration of pro- and antiquorum-sensing compounds. We propose that quorum-sensing inhibitors could be used to suppress the CRISPR-Cas adaptive immune system to enhance medical applications, including phage therapies.

Hryc, C. F., Chen, D. H., Afonine, P. V., Jakana, J., Wang, Z., Haase-Pettingell, C., Jiang, W., Adams, P. D., King, J. A., Schmid, M. F., and Chiu, W. Accurate model annotation of a near-atomic resolution cryo-EM map. Proc.Natl.Acad.Sci.U.S.A. 3-21-2017; 114(12):3103-3108; PM: 28270620

ABSTRACT: Electron cryomicroscopy (cryo-EM) has been used to determine the atomic coordinates (models) from density maps of biological assemblies. These models can be assessed by their overall fit to the experimental data and stereochemical information. However, these models do not annotate the actual density values of the atoms nor their positional uncertainty. Here, we introduce a computational procedure to derive an atomic model from a cryo-EM map with annotated metadata. The accuracy of such a model is validated by a faithful replication of the experimental cryo-EM map computed using the coordinates and associated metadata. The functional interpretation of any structural features in the model and its utilization for future studies can be made in the context of its measure of uncertainty. We applied this protocol to the 3.3-A map of the mature P22 bacteriophage capsid, a large and complex macromolecular assembly. With this protocol, we identify and annotate previously undescribed molecular interactions between capsid subunits that are crucial to maintain stability in the absence of cementing proteins or cross-linking, as occur in other bacteriophages.

Hughes, G. and Webber, M. A. Novel approaches to the treatment of bacterial biofilm infections. Br.J.Pharmacol. 1-7-2017; PM: 28063237

ABSTRACT: Bacterial infection remains a major challenge to healthcare and is responsible for significant morbidity and mortality. This situation is becoming complicated by an increasingly ageing and susceptible population and large numbers of bacterial isolates, which have developed resistance to antibiotics. Bacteria that form biofilms and colonize or infect medical devices or wounds are particularly hard to treat as biofilms are inherently highly antibiotic resistant. Most infections have a component where bacteria exist as a biofilm and as a result, prevention or treatment of biofilm-associated infections is highly important. A number of novel strategies to kill biofilms have been in development; these include the use of weak organic acids, photo irradiation and the application of bacteriophage. All have promise and are able to effectively kill biofilms in model systems, but for each there are still unanswered questions. This review summarizes the main features of biofilm infections, each of these novel approaches and the evidence that is still lacking before these potential treatments can be incorporated into clinical usage.

Hussain, M. A., Liu, H., Wang, Q., Zhong, F., Guo, Q., and Balamurugan, S. Use of encapsulated bacteriophages to enhance farm to fork food safety. Crit Rev.Food Sci.Nutr. 9-2-2017; 57(13):2801-2810; PM: 26357904

ABSTRACT: Bacteriophages have been successfully applied to control the growth of pathogens in foods and to reduce the colonization and shedding of pathogens by food animals. They are set to play a dominant role in food safety in the future. However, many food-processing operations and the microenvironments in food animals' guts inactivate phages and reduce their infectivity. Encapsulation technologies have been used successfully to protect phages against extreme environments, and have been shown to preserve their activity and enable their release in targeted environments. A number of encapsulation technologies have shown potential for use with bacteriophages. This review discusses the current state of knowledge about the use of encapsulation technologies with bacteriophages to control pathogens in foods and food animals.

Hynes, A. P. and Moineau, S. Phagebook: The Social Network. Mol.Cell. 3-16-2017; 65(6):963-964; PM: 28306511

ABSTRACT: Much like social networks are used to connect with friends or relatives, bacteria communicate with relatives through quorum sensing. Viruses, though, were thought to be asocial-until now. Erez et al. (2017) reveal that viruses are also sharing information with relatives.

Janczuk, M., Richter, L., Hoser, G., Kawiak, J., Los, M., Niedziolka-Jonsson, J., Paczesny, J., and Holyst, R. Bacteriophage-Based Bioconjugates as a Flow Cytometry Probe for Fast Bacteria Detection. Bioconjug.Chem. 2-15-2017; 28(2):419-425; PM: 27990800

ABSTRACT: Robust detection of bacteria can significantly reduce risks of nosocomial infections, which are a serious problem even in developed countries (4.1 million cases each year in Europe). Here we demonstrate utilization of novel multifunctional bioconjugates as specific probes for bacteria detection. Bifunctional magnetic-

fluorescent microparticles are coupled with bacteriophages. The T4 bacteriophage, due to its natural affinity to bacterial receptors, namely, OmpC and LPS, enables specific and efficient detection of Escherichia coli bacteria. Prepared probes are cheap, accessible (even in nonbiological laboratories), as well as versatile and easily tunable for different bacteria species. The magnetic properties of the bioconjugates facilitate the separation of captured target bacteria from other components of complex samples and other bacteria strains. Fluorescence enables simple analysis. We chose flow cytometry as the detection method as it is fast and widely used for biotests. The capture efficiency of the prepared bioconjugates is close to 100% in the range of bacteria concentrations from tens to around 105 CFU/mL. The limit of detection is restricted by flow cytometry capabilities and in our case was around 104 CFU/mL.

Johnson, T. J., Shank, J. M., and Johnson, J. G. Current and Potential Treatments for Reducing Campylobacter Colonization in Animal Hosts and Disease in Humans. Front Microbiol. 2017; 8:487; PM: 28386253

ABSTRACT: Campylobacter jejuni is the leading cause of bacteria-derived gastroenteritis worldwide. In the developed world, Campylobacter is usually acquired by consuming under-cooked poultry, while in the developing world it is often obtained through drinking contaminated water. Once consumed, the bacteria adhere to the intestinal epithelium or mucus layer, causing toxin-mediated inhibition of fluid reabsorption from the intestine and invasion-induced inflammation and diarrhea. Traditionally, severe or prolonged cases of campylobacteriosis have been treated with antibiotics; however, overuse of these antibiotics has led to the emergence of antibiotic-resistant strains. As the incidence of antibiotic resistance, emergence of post-infectious diseases, and economic burden associated with Campylobacter increases, it is becoming urgent that novel treatments are developed to reduce Campylobacter numbers in commercial poultry and campylobacteriosis in humans. The purpose of this review is to provide the current status of present and proposed treatments to combat Campylobacter infection in humans and colonization in animal reservoirs. These treatments include anti-Campylobacter compounds, probiotics, bacteriophage, vaccines, and anti-Campylobacter bacteriocins, all of which may be successful at reducing the incidence of campylobacteriosis in humans and/or colonization loads in poultry. In addition to reviewing treatments, we will also address several proposed targets that may be used in future development of novel anti-Campylobacter treatments.

Jonczyk-Matysiak, E., Weber-Dabrowska, B., Zaczek, M., Miedzybrodzki, R., Letkiewicz, S., Lusiak-Szelchowska, M., and Gorski, A. Prospects of Phage Application in the Treatment of Acne Caused by Propionibacterium acnes. Front Microbiol. 2017; 8:164; PM: 28228751

ABSTRACT: Propionibacterium acnes is associated with purulent skin infections, and it poses a global problem for both patients and doctors. Acne vulgaris (acne) remains a problem due to its chronic character and difficulty of treatment, as well as its large impact on patients' quality of life. Due to the chronic course of the disease, treatment is long lasting, and often ineffective. Currently there are data regarding isolation of P. acnes phages, and there have been numerous studies on phage killing of P. acnes, but no data are available on phage application specifically in acne treatment. In this review, we have summarized the current knowledge on the phages active against P. acnes described so far and their potential application in the treatment of acne associated with P. acnes. The treatment of acne with phages may be important in order to reduce the overuse of antibiotics, which are currently the main acne treatment.

However, more detailed studies are first needed to understand phage functioning in the skin microbiome and the possibility to use phages to combat P. acnes.

Jung, P., Abdelbary, M. M., Kraushaar, B., Fetsch, A., Geisel, J., Herrmann, M., Witte, W., Cuny, C., and Bischoff, M. Impact of bacteriophage Saint3 carriage on the immune evasion capacity and hemolytic potential of Staphylococcus aureus CC398. Vet.Microbiol. 2017; 200:46-51; PM: 26923248

ABSTRACT: Livestock-associated methicillin-resistant Staphylococcus aureus (LA-MRSA) isolates of clonal complex 398 (CC398) are frequently found in Europe, and recent studies highlighted the importance of mobile genetic element (MGE) exchange for host adaptation of this lineage. Of note, one of the MGEs commonly found in human S. aureus isolates, the immune evasion cluster (IEC) harboring bacteriophage Saint3, is very rarely found in LA-MRSA CC398 isolates obtained from farm animals, but more frequently found in LA-MRSA CC398 that were retransmitted to humans. Here, we analyzed with a set of S. aureus CC398 isolates harboring/lacking phiSaint3 how this MGE affects (i) phagocytosis of CC398 isolates by polymorphonuclear neutrophils (PMNs), and (ii) hemolysis of human and livestock-derived erythrocytes. Isolates lacking phiSaint3 were more efficiently phagocytosed by human PMNs in whole blood phagocytosis assays than isolates harboring this bacteriophage, irrespective of their origin. Notably, a similar effect was observed when equine blood was utilized, but not detected with porcine blood. Integration of phiSaint3 into LA-MRSA CC398 strains lacking this MGE confirmed these findings, as phiSaint3-harboring recipients were again less efficiently ingested by PMNs in equine and human blood than their parental strains. Integration of phiSaint3 strongly reduced the hemolytic potential of the culture supernatants against human-derived erythrocytes, and to a smaller extent also against porcine-derived erythrocytes, while phiSaint3 integration only slightly affected the hemolytic capacities against equine-derived red blood cells. The significant protective effect of phiSaint3 against phagocytosis by equine PMNs suggests that the host specificity of the IEC components might be broader than currently assumed.

Kacharia, F. R., Millar, J. A., and Raghavan, R. Emergence of New sRNAs in Enteric Bacteria is Associated with Low Expression and Rapid Evolution. J.Mol.Evol. 2017; 84(4):204-213; PM: 28405712

ABSTRACT: Non-coding small RNAs (sRNAs) are critical to post-transcriptional gene regulation in bacteria. However, unlike for protein-coding genes, the evolutionary forces that shape sRNAs are not understood. We investigated sRNAs in enteric bacteria and discovered that recently emerged sRNAs evolve at significantly faster rates than older sRNAs. Concomitantly, younger sRNAs are expressed at significantly lower levels than older sRNAs. This process could potentially facilitate the integration of newly emerged sRNAs into bacterial regulatory networks. Furthermore, it has previously been difficult to trace the evolutionary histories of sRNAs because rapid evolution obscures their original sources. We overcame this challenge by identifying a recently evolved sRNA in Escherichia coli, which allowed us to determine that novel sRNAs could emerge from vestigial bacteriophage genes, the first known source for sRNA origination.

Kackar, S., Suman, E., and Kotian, M. S. Bacterial and fungal biofilm formation on contact lenses and their susceptibility to lens care solutions. Indian J.Med.Microbiol. 2017; 35(1):80-84; PM: 28303823

ABSTRACT: BACKGROUND: Microbial biofilm formation on contact lenses and lens storage cases may be a risk factor for contact lens-associated corneal infections. Various types of contact lens care solutions are used to reduce microbial growths on lenses. *OBJECTIVES*: The present study aimed at comparing the growths of biofilms on the different contact lenses and lens cases. The study also aimed at determining the effect of lens care solutions and bacteriophage on these biofilms. *MATERIALS AND METHODS*: One type of hard lens and two types of soft lenses were used for the study. The organisms used were Staphylococcus aureus ATCC 25923, Pseudomonas aeruginosa ATCC 27853, Candida albicans ATCC 60193 and Escherichia coli ATCC 25922. Biofilm production was performed by modified O'Toole and Kolter method and effect of lens cleaning solutions and a crude coliphage on biofilms was also studied. Results were visualised using scanning electron microscopy and quantitated by colony counting method and spectrophotometric measurement of optical density (OD). Statistical analysis was done by SPSS 11.5, Kruskal-Wallis test and Chi-square test. *RESULTS*: Soft lens cleaning solutions had a significant inhibitory effect (P = 0.020) on biofilm formation on soft lenses and also lens cases (P < 0.001). Soft lens cleaning solution 2 was more efficient than solution 1. However, no such inhibitory effect was observed with regard to hard lens cleaning solution, but for a significant reduction in the OD values (P < 0.001). There was no significant inhibitory effect by bacteriophages. *CONCLUSION*: This study showed the importance of selecting the appropriate lens cleaning solution to prevent biofilm production on contact lenses.

Kaikabo, A. A., AbdulKarim, S. M., and Abas, F. Evaluation of the efficacy of chitosan nanoparticles loaded PhiKAZ14 bacteriophage in the biological control of colibacillosis in chickens. Poult.Sci. 2-1-2017; 96(2):295-302; PM: 27702916

ABSTRACT: Disease inflicted by avian pathogenic Escherichia coli (APEC) causes economic losses and burden to the poultry industry worldwide. In this study, the efficacy of chitosan nanoparticles loaded PhiKAZ14 (C-PhiKAZ14 NPs) as an oral biological therapy for Colibacillosis was evaluated. C-PhiKAZ14 NPs containing 107 PFU/ml of PhiKAZ14 (Myoviridae; T4-like coliphage) bacteriophage were used to treat experimentally APEC-infected COBB 500 broiler chicks. C-PhiKAZ14 NPs and PhiKAZ14 bacteriophage were administered orally in a single dose. The clinical symptoms, mortality, and pathology in the infected birds were recorded and compared with those of control birds that did not receive C-PhiKAZ14 NPs or naked PhiKAZ14 bacteriophage. The results showed that C-PhiKAZ14 NP intervention decreased mortality from 58.33 to 16.7% with an increase in the protection rate from 42.00 to 83.33%. The bacterial colonization of the intestines of infected birds was significantly higher in the untreated control than in the C-PhiKAZ14 NP-treated group (2.30x109 +/- 0.02 and 0.79x103 +/- 0.10 CFU/mL, respectively) (P </= 0.05). Similarly, a significant difference in the fecal shedding of Escherichia coli was observed on d 7 post challenge between the untreated control and the C-PhiKAZ14 NP-treated group (2.35x109 +/- 0.05 and 1.58x103 +/- 0.06 CFU/mL, respectively) (P </= 0.05). Similar trends were observed from d 14 until d 21 when the experiment was terminated. Treatment with C-PhiKAZ14 NPs improved the body weights of the infected chicks. A difference in body weight on d 7 post challenge was observed between the untreated control and the C-PhiKAZ14 NP-treated group (140 +/- 20 g and 160 +/- 20 g, respectively). The increase was significant (P </= 0.05) on d 21 between the

2 groups (240 +/- 30 g and 600 +/- 80 g, respectively). Consequently, the clinical signs and symptoms were ameliorated upon treatment with C-PhiKAZ14 NPs compared with infected untreated birds. In all, based on the results, it can be concluded that the encapsulation of bacteriophage could enhance bacteriophage therapy and is a valuable approach for controlling APEC infections in poultry.

Kaliniene, L., Simoliunas, E., Truncaite, L., Zajanckauskaite, A., Nainys, J., Kaupinis, A., Valius, M., and Meskys, R. Molecular Analysis of Arthrobacter Myovirus vB_ArtM-ArV1: We Blame It on the Tail. J.Virol. 4-15-2017; 91(8); PM: 28122988

ABSTRACT: This is the first report on a myophage that infects Arthrobacter A novel virus, vB_ArtM-ArV1 (ArV1), was isolated from soil using Arthrobacter sp. strain 68b for phage propagation. Transmission electron microscopy showed its resemblance to members of the family Myoviridae: ArV1 has an isometric head (approximately 74 nm in diameter) and a contractile, nonflexible tail (approximately 192 nm). Phylogenetic and comparative sequence analyses, however, revealed that ArV1 has more genes in common with phages from the family Siphoviridae than it does with any myovirus characterized to date. The genome of ArV1 is a linear, circularly permuted, double-stranded DNA molecule (71,200 bp) with a GC content of 61.6%. The genome includes 101 open reading frames (ORFs) yet contains no tRNA genes. More than 50% of ArV1 genes encode unique proteins that either have no reliable identity to database entries or have homologues only in Arthrobacter phages, both sipho- and myoviruses. Using bioinformatics approaches, 13 ArV1 structural genes were identified, including those coding for head, tail, tail fiber, and baseplate proteins. A further 6 ArV1 ORFs were annotated as encoding putative structural proteins based on the results of proteomic analysis. Phylogenetic analysis based on the alignment of four conserved virion proteins revealed that Arthrobacter myophages form a discrete clade that seems to occupy a position somewhat intermediate between myo- and siphoviruses. Thus, the data presented here will help to advance our understanding of genetic diversity and evolution of phages that constitute the order CaudoviralesIMPORTANCE Bacteriophages, which likely originated in the early Precambrian Era, represent the most numerous population on the planet. Approximately 95% of known phages are tailed viruses that comprise three families: Podoviridae (with short tails), Siphoviridae (with long noncontractile tails), and Myoviridae (with contractile tails). Based on the current hypothesis, myophages, which may have evolved from siphophages, are thought to have first emerged among Gram-negative bacteria, whereas they emerged only later among Gram-positive bacteria. The results of the molecular characterization of myophage vB_ArtM-ArV1 presented here conform to the aforementioned hypothesis, since, at a glance, bacteriophage vB_ArtM-ArV1 appears to be a siphovirus that possesses a seemingly functional contractile tail. Our work demonstrates that such "chimeric" myophages are of cosmopolitan nature and are likely characteristic of the ecologically important soil bacterial genus Arthrobacter.

Kang, D. W., Adams, J. B., Gregory, A. C., Borody, T., Chittick, L., Fasano, A., Khoruts, A., Geis, E., Maldonado, J., Donough-Means, S., Pollard, E. L., Roux, S., Sadowsky, M. J., Lipson, K. S., Sullivan, M. B., Caporaso, J. G., and Krajmalnik-Brown, R. Microbiota Transfer Therapy alters gut ecosystem and improves gastrointestinal and autism symptoms: an open-label study. Microbiome. 1-23-2017; 5(1):10; PM: 28122648

ABSTRACT: BACKGROUND: Autism spectrum disorders (ASD) are complex neurobiological

disorders that impair social interactions and communication and lead to restricted, repetitive, and stereotyped patterns of behavior, interests, and activities. The causes of these disorders remain poorly understood, but gut microbiota, the 1013 bacteria in the human intestines, have been implicated because children with ASD often suffer gastrointestinal (GI) problems that correlate with ASD severity. Several previous studies have reported abnormal gut bacteria in children with ASD. The gut microbiome-ASD connection has been tested in a mouse model of ASD, where the microbiome was mechanistically linked to abnormal metabolites and behavior. Similarly, a study of children with ASD found that oral non-absorbable antibiotic treatment improved GI and ASD symptoms, albeit temporarily. Here, a small open-label clinical trial evaluated the impact of Microbiota Transfer Therapy (MTT) on gut microbiota composition and GI and ASD symptoms of 18 ASD-diagnosed children. *RESULTS*: MTT involved a 2-week antibiotic treatment, a bowel cleanse, and then an extended fecal microbiota transplant (FMT) using a high initial dose followed by daily and lower maintenance doses for 7-8 weeks. The Gastrointestinal Symptom Rating Scale revealed an approximately 80% reduction of GI symptoms at the end of treatment, including significant improvements in symptoms of constipation, diarrhea, indigestion, and abdominal pain. Improvements persisted 8 weeks after treatment. Similarly, clinical assessments showed that behavioral ASD symptoms improved significantly and remained improved 8 weeks after treatment ended. Bacterial and phagedeep sequencing analyses revealed successful partial engraftment of donor microbiota and beneficial changes in the gut environment. Specifically, overall bacterial diversity and the abundance of Bifidobacterium, Prevotella, and Desulfovibrio among other taxa increased following MTT, and these changes persisted after treatment stopped (followed for 8 weeks). *CONCLUSIONS*: This exploratory, extended-duration treatment protocol thus appears to be a promising approach to alter the gut microbiome and virome and improve GI and behavioral symptoms of ASD. Improvements in GI symptoms, ASD symptoms, and the microbiome all persisted for at least 8 weeks after treatment ended, suggesting a long-term impact. *TRIAL REGISTRATION*: This trial was registered on the ClinicalTrials.gov, with the registration number NCT02504554.

Keen, E. C., Bliskovsky, V. V., Malagon, F., Baker, J. D., Prince, J. S., Klaus, J. S., and Adhya, S. L. Novel "Superspreader" Bacteriophages Promote Horizontal Gene Transfer by Transformation. MBio. 1-17-2017; 8(1); PM: 28096488

ABSTRACT: Bacteriophages infect an estimated 1023 to 1025 bacterial cells each second, many of which carry physiologically relevant plasmids (e.g., those encoding antibiotic resistance). However, even though phage-plasmid interactions occur on a massive scale and have potentially significant evolutionary, ecological, and biomedical implications, plasmid fate upon phage infection and lysis has not been investigated to date. Here we show that a subset of the natural lytic phage population, which we dub "superspreaders," releases substantial amounts of intact, transformable plasmid DNA upon lysis, thereby promoting horizontal gene transfer by transformation. Two novel Escherichia coli phage superspreaders, SUSP1 and SUSP2, liberated four evolutionarily distinct plasmids with equal efficiency, including two close relatives of prominent antibiotic resistance vectors in natural environments. SUSP2 also mediated the extensive lateral transfer of antibiotic resistance in unbiased communities of soil bacteria from Maryland and Wyoming. Furthermore, the addition of SUSP2 to cocultures of kanamycin-resistant E. coli and kanamycin-sensitive Bacillus sp. bacteria resulted in roughly 1,000-fold more kanamycin-resistant Bacillus sp. bacteria than arose in phage-free controls. Unlike many other lytic phages, neither SUSP1 nor SUSP2 encodes homologs to known hydrolytic

endonucleases, suggesting a simple potential mechanism underlying the superspreading phenotype. Consistent with this model, the deletion of endonuclease IV and the nucleoid-disrupting protein ndd from coliphage T4, a phage known to extensively degrade chromosomal DNA, significantly increased its ability to promote plasmid transformation. Taken together, our results suggest that phage superspreaders may play key roles in microbial evolution and ecology but should be avoided in phage therapy and other medical applications. IMPORTANCE: Bacteriophages (phages), viruses that infect bacteria, are the planet's most numerous biological entities and kill vast numbers of bacteria in natural environments. Many of these bacteria carry plasmids, extrachromosomal DNA elements that frequently encode antibiotic resistance. However, it is largely unknown whether plasmids are destroyed during phage infection or released intact upon phage lysis, whereupon their encoded resistance could be acquired and manifested by other bacteria (transformation). Because phages are being developed to combat antibiotic-resistant bacteria and because transformation is a principal form of horizontal gene transfer, this question has important implications for biomedicine and microbial evolution alike. Here we report the isolation and characterization of two novel Escherichia coli phages, dubbed "superspreaders," that promote extensive plasmid transformation and efficiently disperse antibiotic resistance genes. Our work suggests that phage superspreaders are not suitable for use in medicine but may help drive bacterial evolution in natural environments.

Khan, Mirzaei M., Haileselassie, Y., Navis, M., Cooper, C., Sverremark-Ekstrom, E., and Nilsson, A. S. Corrigendum: Morphologically Distinct Escherichia coli Bacteriophages Differ in Their Efficacy and Ability to Stimulate Cytokine Release In Vitro. Front Microbiol. 2016; 7:2145; PM: 28053602

ABSTRACT: [This corrects the article on p. 437 in vol. 7, PMID: 27065990.].

Kick, B., Hensler, S., Praetorius, F., Dietz, H., and Weuster-Botz, D. Specific growth rate and multiplicity of infection affect high-cell-density fermentation with bacteriophage M13 for ssDNA production. Biotechnol.Bioeng. 2017; 114(4):777-784; PM: 27748519

ABSTRACT: The bacteriophage M13 has found frequent applications in nanobiotechnology due to its chemically and genetically tunable protein surface and its ability to self-assemble into colloidal membranes. Additionally, its single-stranded (ss) genome is commonly used as scaffold for DNA origami. Despite the manifold uses of M13, upstream production methods for phage and scaffold ssDNA are underexamined with respect to future industrial usage. Here, the high-cell-density phage production with Escherichia coli as host organism was studied in respect of medium composition, infection time, multiplicity of infection, and specific growth rate. The specific growth rate and the multiplicity of infection were identified as the crucial state variables that influence phage amplification rate on one hand and the concentration of produced ssDNA on the other hand. Using a growth rate of 0.15 h-1 and a multiplicity of infection of 0.05 pfu cfu-1 in the fed-batch production process, the concentration of pure isolated M13 ssDNA usable for scaffolded DNA origami could be enhanced by 54% to 590 mg L-1 . Thus, our results help enabling M13 production for industrial uses in nanobiotechnology. Biotechnol. Bioeng. 2017;114: 777-784. (c) 2016 Wiley Periodicals, Inc.

Kim, J., Vu, B., Kourentzi, K., Willson, R. C., and Conrad, J. C. Increasing Binding Efficiency via Reporter Shape and Flux in a Viral Nanoparticle Lateral-Flow Assay. ACS Appl.Mater.Interfaces. 3-1-2017; 9(8):6878-6884; PM: 28150489

ABSTRACT: To identify factors controlling the performance of reporter particles in a sensitive lateral-flow assay (LFA), we investigated the effect of the flux and shape of filamentous bacteriophage (phage) on the performance of phage LFAs. Phage of three different lengths and diameters were modified with biotin and AlexaFluor 555 as binding and read-out elements, respectively. The binding efficiencies of the functionalized phage were tested in a fibrous glass LFA membrane modified with avidin. The total binding rate, quantified using real-time particle counting and particle image velocimetry, decreased monotonically with the average bulk flux of phage through the membrane. At the pore scale, more phage bound in regions with faster local flow, confirming that both average and local flux increased binding. The number of bound phage increased with the aspect ratio of the phage and scaled with the phage surface area, consistent with a binding interaction controlled by the number of recognition elements on the surface. Together, these results indicate that increasing the likelihood that recognition elements on the surface of phage encounter the fibers enhances the assay binding efficiency and suggests one origin for the improved performance of nonspherical phage reporters.

Kim, J. S., Hosseindoust, A., Lee, S. H., Choi, Y. H., Kim, M. J., Lee, J. H., Kwon, I. K., and Chae, B. J. Bacteriophage cocktail and multi-strain probiotics in the feed for weanling pigs: effects on intestine morphology and targeted intestinal coliforms and Clostridium. Animal. 2017; 11(1):45-53; PM: 27353334

ABSTRACT: Two experiments were conducted to investigate the effects of dietary supplementation of bacteriophage cocktail, probiotics and a combination of these two supplements on performance and gut health of weanling pigs. In Experiment 1, 150 weaned piglets were randomly allotted to three treatments on the basis of BW. The dietary treatments included a basal diet supplemented with 0 (control), 1.0 and 1.5 g/kg bacteriophage cocktail. Pigs fed 1.0 and 1.5 g/kg bacteriophage product had greater ($P<0.05$) average daily gain (ADG), apparent total tract digestibility of dry matter from day 22 to 35, ileal Lactobacillus spp., villus height (duodenum and jejunum), and fewer coliforms (ileum) and Clostridium spp. (ileum). In Experiment 2, 200 weaned piglets were randomly allotted to four treatments. Dietary treatments included basal diet, basal diet supplemented with 3.0 g/kg fermented probiotic product (P), 1.0 g/kg bacteriophage cocktail (B) and combination of 1.0 g/kg bacteriophage cocktail and 3.0 g/kg fermented probiotic product. Pigs fed bacteriophage cocktail diets had greater ($P<0.05$) overall ADG, gain to feed ratio (G : F), fecal score from day 8 to day 21, and pigs fed bacteriophage cocktail diets had fewer coliforms (ileum) Clostridium spp. (ileum and cecum). Probiotics significantly increased G : F, colonization of Lactobacillus spp. in ileum. At day 35, bacteriophage treatment group showed greater ($P<0.05$) villus height of the duodenum, but a deeper crypt in duodenum. The present results indicate that the bacteriophage cocktail had a potential to enhance the performance and gut health of weanling pigs, however their combination with probiotics did not show an interaction.

Kim, Y., de la, Torre A., Leal, A. A., and Finkelstein, I. J. Efficient modification of lambda-DNA substrates for single-molecule studies. Sci.Rep. 5-18-2017; 7(1):2071; PM: 28522818

ABSTRACT: Single-molecule studies of protein-nucleic acid interactions frequently require site-specific modification of long DNA substrates. The bacteriophage lambda is a convenient source of high quality long (48.5 kb) DNA. However, introducing specific sequences, tertiary structures, and chemical modifications into lambda-DNA remains technically challenging. Most current approaches rely on multi-step ligations with low yields and incomplete products. Here, we describe a molecular toolkit for rapid preparation of modified lambda-DNA. A set of PCR cassettes facilitates the introduction of recombinant DNA sequences into the lambda-phage genome with 90-100% yield. Extrahelical structures and chemical modifications can be inserted at user-defined sites via an improved nicking enzyme-based strategy. As a proof-of-principle, we explore the interactions of S. cerevisiae Proliferating Cell Nuclear Antigen (yPCNA) with modified DNA sequences and structures incorporated within lambda-DNA. Our results demonstrate that S. cerevisiae Replication Factor C (yRFC) can load yPCNA onto 5'-ssDNA flaps, (CAG)13 triplet repeats, and homoduplex DNA. However, yPCNA remains trapped on the (CAG)13 structure, confirming a proposed mechanism for triplet repeat expansion. We anticipate that this molecular toolbox will be broadly useful for other studies that require site-specific modification of long DNA substrates.

Koberg, S., Brinks, E., Fiedler, G., Husing, C., Cho, G. S., Hoeppner, M. P., Heller, K. J., Neve, H., and Franz, C. M. Genome Sequence of Klebsiella pneumoniae Bacteriophage PMBT1 Isolated from Raw Sewage. Genome Announc. 2-23-2017; 5(8); PM: 28232430

ABSTRACT: A bacteriophage virulent for extended-spectrum beta-lactamase (ESBL)-producing Klebsiella pneumoniae strain 182 was isolated from sewage. The double-stranded DNA (dsDNA) genome showed high similarity to the genomes of other Klebsiella pneumoniae phages. It comprises 175,206 bp with a mol% G+C content of 41.9 and contains 276 putative open reading frames (ORFs) and one tRNA.

Koganti, S., Alhmidi, H., Tomas, M. E., Cadnum, J. L., Sass, C., Jencson, A. L., and Donskey, C. J. Evaluation of an Ethanol-Based Spray Disinfectant for Decontamination of Cover Gowns Prior to Removal. Infect.Control Hosp.Epidemiol. 2017; 38(3):364-366 PM: 27917733

ABSTRACT: An ethanol-based spray disinfectant significantly reduced bacteriophage MS2 contamination on material from gowns meeting ASTM standard 1671 for resistance to blood and viral penetration and on a cover gown worn by personnel. Effectiveness of disinfection was affected by the type of gown material and the correctness of fit. Infect Control Hosp Epidemiol 2017;38:364-366.

Kong, M., Shin, J. H., Heu, S., Park, J. K., and Ryu, S. Lateral flow assay-based bacterial detection using engineered cell wall binding domains of a phage endolysin. Biosens.Bioelectron. 5-4-2017; 96:173-177 PM: 28494369

ABSTRACT: The development of a cost-effective and efficient bacterial detection assay is essential for diagnostic fields, particularly in resource-poor settings. Although antibodies have been widely used for bacterial capture, the production of soluble antibodies is still expensive and time-consuming. Here, we developed a nitrocellulose-based lateral flow assay using cell wall binding domains (CBDs) from phage as a recognition element and colloidal gold nanoparticles as a colorimetric signal for the detection of a model

pathogenic bacterium, Bacillus cereus (B. cereus). To improve conjugation efficiency and detection sensitivity, cysteine-glutathione-S-transferase-tagged CBDs and maltose-binding protein-tagged CBDs were produced in Escherichia coli (E. coli) and incorporated in our assays. The sensitivity of the strip to detect B. cereus was 1x104 CFU/mL and the overall assay time was 20min. The assay showed superior results compared to the antibody-based approach, and did not show any significant cross-reactivity. This proof of concept study indicates that the lateral flow assay using engineered CBDs hold considerable promise as simple, rapid, and cost-effective biosensors for whole cell detection.

Kozlowska, K. I., Tymecka-Mulik, J., and Wegrzyn, G. Purified Stx and lambda phage initiator O proteins bind specifically to two different origins of replication in vitro. Protein Expr.Purif. 2017; 131:16-26; PM: 27826079

ABSTRACT: The O protein is a crucial factor initiating the DNA replication of lambdoid bacteriophage. Efficient DNA replication of Shiga toxin-converting phage is necessary for effective production of Shiga toxin - main virulence factor of STEC strains. We developed an improved protocol for overproduction, bacterial cell lysis and purification of lambdaO protein. With use of this method we have also isolated O proteins of Stx-phage P27 and 933W that were never purified before. Purified proteins were tested for their DNA binding activity and revealed a sequence specific interactions.

Kremer, P. H., Lees, J. A., Koopmans, M. M., Ferwerda, B., Arends, A. W., Feller, M. M., Schipper, K., Valls, Seron M., van der, Ende A., Brouwer, M. C., van de, Beek D., and Bentley, S. D. Benzalkonium tolerance genes and outcome in Listeria monocytogenes meningitis. Clin.Microbiol.Infect. 2017; 23(4):265-265; PM: 27998823

ABSTRACT: OBJECTIVES: Listeria monocytogenes is a food-borne pathogen that can cause meningitis. The listerial genotype ST6 has been linked to increasing rates of unfavourable outcome over time. We investigated listerial genetic variation and the relation with clinical outcome in meningitis. *METHODS*: We sequenced 96 isolates from adults with listerial meningitis included in two prospective nationwide cohort studies by whole genome sequencing, and evaluated associations between bacterial genetic variation and clinical outcome. We validated these results by screening listerial genotypes of 445 cerebrospinal fluid and blood isolates from patients over a 30-year period from the Dutch national surveillance cohort. *RESULTS*: We identified a bacteriophage, phiLMST6 co-occurring with a novel plasmid, pLMST6, in ST6 isolates to be associated with unfavourable outcome in patients (p 2.83e-05). The plasmid carries a benzalkonium chloride tolerance gene, emrC, conferring decreased susceptibility to disinfectants used in the food-processing industry. Isolates harbouring emrC were growth inhibited at higher levels of benzalkonium chloride (median 60 mg/L versus 15 mg/L; p <0.001), and had higher MICs for amoxicillin and gentamicin compared with isolates without emrC (both p <0.001). Transformation of pLMST6 into naive strains led to benzalkonium chloride tolerance and higher MICs for gentamicin. *CONCLUSIONS*: These results show that a novel plasmid, carrying the efflux transporter emrC, is associated with increased incidence of ST6 listerial meningitis in the Netherlands. Suggesting increased disease severity, our findings warrant consideration of disinfectants used in the food-processing industry that select for resistance mechanisms and may, inadvertently, lead to increased risk of poor disease outcome.

Kubota, S., Kawaki, H., and Takigawa, M. Protocols for Screening Peptide Motifs Binding to CCN Family Proteins. Methods Mol.Biol. 2017; 1489:155-167; PM: 27734375

ABSTRACT: Function of CCN family proteins is determined by the interactions with multiple cofactors that are present in microenvironment. Therefore, finding out these cofactors is critically important in understanding the molecular function of the CCN family members. For this objective, bacteriophage random peptide display library is a quite feasible tool. In this library, each filamentous bacteriophage is designed to display an oligopeptide of random 12-16 amino acid residues on its surface. Bacteriophage clones that possess the peptides that bind to a CCN family protein are selected through several cycles of a process designated biopanning or affinity selection. By determining the nucleotide sequence of the DNA that encodes the displayed peptide, oligopeptides that specifically bind to the CCN family member can be specified. Obtained peptide sequences can be utilized for designing peptide aptamers for the CCN family protein, or as a key sequence to find out new CCN family cofactor candidates in silico.

Kudr, J., Richtera, L., Xhaxhiu, K., Hynek, D., Heger, Z., Zitka, O., and Adam, V. Carbon dots based FRET for the detection of DNA damage. Biosens.Bioelectron. 6-15-2017; 92:133-139; PM: 28213325

ABSTRACT: Here, we aimed our attention at the synthesis of carbon dots (C-dots) with the ability to interact with DNA to suggest an approach for the detection of DNA damage. Primarily, C-dots modified with amine moieties were synthesized using the one-step microwave pyrolysis of citric acid in the presence of diethylenetriamine. The C-dots showed strong photoluminescence with a quantum yield of 4%. In addition, the C-dots (2.8+/-0.8nm) possessed a good colloidal stability and exhibited a positive surface charge (zeta=36mV) at a neutral pH. An interaction study of the C-dots and the DNA fragment of lambda bacteriophage was performed, and the DNA binding resulted in changes to the photoluminescent and absorption properties of the C-dots. A binding of the C-dots to DNA was also observed as a change to DNA electrophoretic mobility and a decreased ability to intercalate ethidium bromide (EtBr). Moreover, the Forster (or fluorescence) resonance energy transfer (FRET) between the C-dots and EtBr was studied, in which the C-dots serve as an excitation energy donor and the EtBr serves as an acceptor. When DNA was damaged using ultraviolet (UV) radiation (lambda=254nm) and hydroxyl radicals, the intensity of the emitted photoluminescence at 612nm significantly decreased. The concept was proved on analysis of the genomic DNA from PC-3 cells and DNA isolated from melanoma tissues.

Kulabhusan, P. K., Rajwade, J. M., Sahul Hameed, A. S., and Paknikar, K. M. Lateral flow assay for rapid detection of white spot syndrome virus (WSSV) using a phage-displayed peptide as bio-recognition probe. Appl.Microbiol.Biotechnol. 3-27-2017; PM: 28349164

ABSTRACT: White spot disease caused by the white spot syndrome virus (WSSV) has a major socio-economic impact on shrimp farming in India. It has been realized that a field-usable diagnostic capable of rapid detection of WSSV can prevent huge economic losses in disease outbreaks. In this work, we explored the possibility of using a peptide as bio-recognition probe in a field-usable device for the detection of WSSV from infected shrimps and prawns. A commercially available random phage-display library was screened against rVP28 (a major structural protein of WSSV, expressed as a recombinant

protein in Escherichia coli). A bacteriophage clone VP28-4L was obtained, and its binding to purified rVP28 protein as well as WSSV from infected shrimp Litopaeneus vannamei tissue was confirmed by ELISA and western blot. The apparent equilibrium dissociation constant (Kd,app) was calculated to be 810 nM. VP28-4L did not show cross-reactivity with any other shrimp viruses. A 12-mer peptide (pep28, with the sequence 'TFQAFDLSPFPS') displayed on the VP28-4L was synthesized, and its diagnostic potential was evaluated in a lateral flow assay (LFA). Visual detection of WSSV could be achieved using biotinylated-pep28 and streptavidin-conjugated gold nanoparticles. In LFA, 12.5 mug/mL of the virus could be detected from L. vannamei gill tissue homogenate within 20 min. Pep28 thus becomes an attractive candidate in bio-recognition of WSSV in field-usable diagnostic platforms benefitting the aquaculture sector.

Kulczyk, A. W., Moeller, A., Meyer, P., Sliz, P., and Richardson, C. C. Cryo-EM structure of the replisome reveals multiple interactions coordinating DNA synthesis. Proc.Natl.Acad.Sci.U.S.A. 3-7-2017; 114(10):E1848-E1856; PM: 28223502

ABSTRACT: We present a structure of the approximately 650-kDa functional replisome of bacteriophage T7 assembled on DNA resembling a replication fork. A structure of the complex consisting of six domains of DNA helicase, five domains of RNA primase, two DNA polymerases, and two thioredoxin (processivity factor) molecules was determined by single-particle cryo-electron microscopy. The two molecules of DNA polymerase adopt a different spatial arrangement at the replication fork, reflecting their roles in leading- and lagging-strand synthesis. The structure, in combination with biochemical data, reveals molecular mechanisms for coordination of leading- and lagging-strand synthesis. Because mechanisms of DNA replication are highly conserved, the observations are relevant to other replication systems.

Kunkel, S. A., Azimi, P., Zhao, H., Stark, B. C., and Stephens, B. Quantifying the size-resolved dynamics of indoor bioaerosol transport and control. Indoor.Air. 2-11-2017; PM: 28190263

ABSTRACT: Understanding the bioaerosol dynamics of droplets and droplet nuclei emitted during respiratory activities is important for understanding how infectious diseases are transmitted and potentially controlled. To this end, we conducted experiments to quantify the size-resolved dynamics of indoor bioaerosol transport and control in an unoccupied apartment unit operating under four different HVAC particle filtration conditions. Two model organisms (Escherichia coli K12 and bacteriophage T4) were aerosolized under alternating low and high flow rates to roughly represent constant breathing and periodic coughing. Size-resolved aerosol sampling and settle plate swabbing were conducted in multiple locations. Samples were analyzed by DNA extraction and quantitative polymerase chain reaction (qPCR). DNA from both organisms was detected during all test conditions in all air samples up to 7 m away from the source, but decreased in magnitude with the distance from the source. A greater fraction of T4 DNA was recovered from the aerosol size fractions smaller than 1 mum than E. coli K12 at all air sampling locations. Higher efficiency HVAC filtration also reduced the amount of DNA recovered in air samples and on settle plates located 3-7 m from the source.

Kurabi, A., Beasley, K. A., Chang, L., McCann, J., Pak, K., and Ryan, A. F. Peptides actively transported across the tympanic membrane: Functional and structural properties. PLoS.One. 2017; 12(2):e0172158; PM:28234923

ABSTRACT: Otitis media (OM) is the most common infectious disease of children under six, causing more antibiotic prescriptions and surgical procedures than any other pediatric condition. By screening a bacteriophage (phage) library genetically engineered to express random peptides on their surfaces, we discovered unique peptides that actively transport phage particles across the intact tympanic membrane (TM) and into the middle ear (ME). Herein our goals were to characterize the physiochemical peptide features that may underlie trans-TM phage transport; assess morphological and functional effects of phage peptides on the ME and inner ear (IE); and determine whether peptide-bearing phage transmigrate from the ME into the IE. Incubation of five peptide-bearing phage on the TM for over 4hrs resulted in demonstrably superior transport of one peptide, in level and in exponential increase over time. This suggests a preferred peptide motif for TM active transport. Functional and structural comparisons revealed unique features of this peptide: These include a central lysine residue, isoelectric point of 0.0 at physiological pH and a hydrophobic C-terminus. When the optimal peptide was applied to the TM independent of phage, similar transport was observed, indicating that integration into phage is not required. When 109 particles of the four different trans-TM phage were applied directly into the ME, no morphological effects were detected in the ME or IE when compared to saline or wild-type (WT) phage controls. Comparable, reversible hearing loss was observed for saline controls, WT phage and trans-TM peptide phage, suggesting a mild conductive hearing loss due to ME fluid. Perilymph titers after ME incubation established that few copies of trans-TM peptide phage crossed into the IE. The results suggest that, within the parameters tested, trans-TM peptides are safe and could be used as potential agents for noninvasive delivery of drugs, particles and gene therapy vectors to the ME.

Kutyshenko, V. P., Prokhorov, D. A., Mikoulinskaia, G. V., Molochkov, N. V., Paskevich, S. I., and Uversky, V. N. Evidence for the residual tertiary structure in the urea-unfolded form of bacteriophage T5 endolysin. J.Biomol.Struct.Dyn. 2017; 35(6):1331-1338; PM: 27109308

ABSTRACT: Using high-resolution NMR spectroscopy, we studied peculiarities of the unfolding process of the bacteriophage T5 endolysin (EndoT5) by strong denaturants. It was shown that in the absence of zinc ions this protein is mostly unfolded in the solution of 8 M urea or 6 M guanidine hydrochloride. However, in the presence of zinc ions EndoT5 unfolding can be achieved only in acidic solutions (at pH < 4.0), whereas at pH > 4.0 NMR spectra of the metal-bound protein (Zn2+-Ca2+-EndoT5 or Zn2+-EndoT5 complexes) exhibit a few chemical shifts characteristic of the native or native-like proteins. Our data, including the pH-titration curve with the pK of ~5, suggested involvement of the zinc-binding histidines in the stabilization of this protein. Up-field signals that appear in the NMR spectra of apo-EndoT5 in the presence of high concentrations of strong denaturants are probably derived from the amino acid residues included in the formation of structured hydrophobic cluster, which likely corresponds to the 81-93 region of EndoT5 and contains some residual tertiary structure. It is possible also that this hydrophobic fragment serves as a foundation for the formation of structured cluster in the unfolded state.

Kwiatek, M., Parasion, S., Rutyna, P., Mizak, L., Gryko, R., Niemcewicz, M., Olender, A., and Lobocka, M. Isolation of bacteriophages and their application to control Pseudomonas aeruginosa in planktonic and biofilm models. Res.Microbiol. 2017; 168(3):194-207; PM: 27818282

ABSTRACT: Pseudomonas aeruginosa is frequently identified as a cause of diverse infections and chronic diseases. It forms biofilms and has natural resistance to several antibiotics. Strains of this pathogen resistant to new-generation beta-lactams have emerged. Due to the difficulties associated with treating chronic P. aeruginosa infections, bacteriophages are amongst the alternative therapeutic options being actively researched. Two obligatorily lytic P. aeruginosa phages, vB_PaeM_MAG1 (MAG1) and vB_PaeP_MAG4 (MAG4), have been isolated and characterized. These phages belong to the PAK_P1likevirus genus of the Myoviridae family and the LIT1virus genus of the Podoviridae family, respectively. They adsorb quickly to their hosts (approximately 90% in 5 min), have a short latent period (15 min), and are stable during storage. Each individual phage propagated in approximately 50% of P. aeruginosa strains tested, which increased to 72.9% when phages were combined into a cocktail. While MAG4 reduced biofilm more effectively after a short time of treatment, MAG1 was more effective after a longer time and selected less for phage-resistant clones. A MAG1-encoded homolog of YefM antitoxin of the bacterial toxin-antitoxin system may contribute to the superiority of MAG1 over MAG4.

Kwon, S. J., Kim, D., Lee, I., Kim, J., and Dordick, J. S. In vitro gene expression-coupled bacterial cell chip for screening species-specific antimicrobial enzymes. Biotechnol.Bioeng. 3-28-2017; PM: 28369698

ABSTRACT: Targeting infectious bacterial pathogens is important for reducing the evolution of antibiotic-resistant bacteria and preserving the endogenous human microbiome. Cell lytic enzymes including bacteriophage endolysins, bacterial autolysins, and other bacteriolysins are useful antibiotic alternatives due to their exceptional target selectivity, which may be used to lysins rapidly kill target bacteria and their high specificity permit the normal commensal microflora to be left undisturbed. Genetic information of numerous lysins is currently available, but the identification of their antimicrobial function and specificity has been limited because most lysins are often poorly expressed and exhibit low solubilities. Here, we report the development of bacterial cell chip for rapidly accessing the function of diverse genes that are suggestive of encoding lysins. This approach can be used to evaluate rapidly the species-specific antimicrobial activity of diverse lysins synthesized from in vitro transcription and translation (TNT) of plasmid DNA. In addition, new potent lysins can be assessed that are not expressed in hosts and display low solubility. As a result of evaluating the species-specific antimicrobial function of 11 (un)known lysins with an in vitro TNT-coupled bacterial cell chip, a potent recombinant lysin against Staphylococcus strains, SA1, was identified. The SA1 was highly potent against not only S. aureus, but also both lysostaphin-resistant S. simulans and S. epidermidis cells. To this end, the SA1 may be applicable to treat both methicillin-resistant S. aureus (MRSA) and lysostaphin-resistant MRSA mutants. Biotechnol. Bioeng. 2017;9999: 1-10. (c) 2017 Wiley Periodicals, Inc.

Lal, T. M., Sano, M., and Ransangan, J. Isolation and Characterization of Large Marine Bacteriophage (Myoviridae), VhKM4 Infecting Vibrio harveyi. J.Aquat.Anim Health. 2017; 29(1):26-30; PM: 28166465

ABSTRACT: The causative agent responsible for vibriosis in tropical fish aquaculture, Vibrio harveyi, has become a major bacterial pathogen. Studies suggest that this bacterium has developed resistance to antibiotics commonly used in aquaculture. In view of this situation and the requirement for the proposed postantibiotic era, bacteriophage therapy seems to be a promising control strategy for fish vibriosis. In this study, a lytic Vibrio phage VhKM4 belonging to a member of large, marine Myoviridae was successfully isolated. It exhibited bacteriolysis to both V. harveyi VHJR7 and V. parahaemolyticus ATCC 17802. The latent period of the VhKM4 phage was recorded at 60 min. It also recorded average burst size of approximately 52 plaque-forming units per infected cell. A strong bacteriolytic activity at low multiplicity of infection of 0.01 indicates the effectiveness of this large marine myovirid against fish pathogenic strain of V. harveyi VHJR7. Received June 16, 2016; accepted October 7, 2016.

Lambert, S., Yang, Q., De, Angeles R., Chang, J. R., Ortega, M., Davis, C., and Catalano, C. E. Molecular Dissection of the Forces Responsible for Viral Capsid Assembly and Stabilization by Decoration Proteins. Biochemistry. 2-7-2017; 56(5):767-778; PM: 28029785

ABSTRACT: Complex double-stranded DNA viruses utilize a terminase enzyme to package their genomes into a preassembled procapsid shell. DNA packaging triggers a major conformational change in the proteins assembled into the shell and most often subsequent addition of a decoration protein that is required to stabilize the structure. In bacteriophage lambda, DNA packaging drives a procapsid expansion transition to afford a larger but fragile shell. The gpD decoration protein adds to the expanded shell as trimeric spikes at each of the 140 three-fold axes. The spikes provide mechanical strength to the shell such that it can withstand the tremendous internal forces generated by the packaged DNA in addition to environmental insults. Hydrophobic, electrostatic, and aromatic-proline noncovalent interactions have been proposed to mediate gpD trimer spike assembly at the expanded shell surface. Here, we directly examine each of these interactions and demonstrate that hydrophobic interactions play the dominant role. In the course of this study, we unexpectedly found that Trp308 in the lambda major capsid protein (gpE) plays a critical role in shell assembly. The gpE-W308A mutation affords a soluble, natively folded protein that does not further assemble into a procapsid shell, despite the fact that it retains binding interactions with the scaffolding protein, the shell assembly chaparone protein. The data support a model in which the lambda procapsid shell assembles via cooperative interaction of monomeric capsid proteins, as observed in the herpesviruses and phages such as P22. The significance of the results with respect to capsid assembly, maturation, and stability is discussed.

Landry, M. P., Ando, H., Chen, A. Y., Cao, J., Kottadiel, V. I., Chio, L., Yang, D., Dong, J., Lu, T. K., and Strano, M. S. Single-molecule detection of protein efflux from microorganisms using fluorescent single-walled carbon nanotube sensor arrays. Nat.Nanotechnol. 2017; 12(4):368-377; PM: 28114298

ABSTRACT: A distinct advantage of nanosensor arrays is their ability to achieve ultralow detection limits in solution by proximity placement to an analyte. Here, we demonstrate label-free detection of individual proteins from Escherichia coli (bacteria) and Pichia pastoris (yeast) immobilized in a microfluidic chamber, measuring protein efflux from single organisms in real time. The array is fabricated using non-covalent conjugation of an aptamer-anchor polynucleotide sequence to near-infrared emissive single-walled

carbon nanotubes, using a variable chemical spacer shown to optimize sensor response. Unlabelled RAP1 GTPase and HIV integrase proteins were selectively detected from various cell lines, via large near-infrared fluorescent turn-on responses. We show that the process of E. coli induction, protein synthesis and protein export is highly stochastic, yielding variability in protein secretion, with E. coli cells undergoing division under starved conditions producing 66% fewer secreted protein products than their non-dividing counterparts. We further demonstrate the detection of a unique protein product resulting from T7 bacteriophage infection of E. coli, illustrating that nanosensor arrays can enable real-time, single-cell analysis of a broad range of protein products from various cell types.

Latka, A., Maciejewska, B., Majkowska-Skrobek, G., Briers, Y., and Drulis-Kawa, Z. Bacteriophage-encoded virion-associated enzymes to overcome the carbohydrate barriers during the infection process. Appl.Microbiol.Biotechnol. 2017; 101(8):3103-3119; PM: 28337580

ABSTRACT: Bacteriophages are bacterial viruses that infect the host after successful receptor recognition and adsorption to the cell surface. The irreversible adherence followed by genome material ejection into host cell cytoplasm must be preceded by the passage of diverse carbohydrate barriers such as capsule polysaccharides (CPSs), O-polysaccharide chains of lipopolysaccharide (LPS) molecules, extracellular polysaccharides (EPSs) forming biofilm matrix, and peptidoglycan (PG) layers. For that purpose, bacteriophages are equipped with various virion-associated carbohydrate active enzymes, termed polysaccharide depolymerases and lysins, that recognize, bind, and degrade the polysaccharide compounds. We discuss the existing diversity in structural locations, variable architectures, enzymatic specificities, and evolutionary aspects of polysaccharide depolymerases and virion-associated lysins (VALs) and illustrate how these aspects can correlate with the host spectrum. In addition, we present methods that can be used for activity determination and the application potential of these enzymes as antibacterials, antivirulence agents, and diagnostic tools.

Lavysh, D., Sokolova, M., Slashcheva, M., Forstner, K. U., and Severinov, K. Transcription Profiling of Bacillus subtilis Cells Infected with AR9, a Giant Phage Encoding Two Multisubunit RNA Polymerases. MBio. 2-14-2017; 8(1); PM: 28196958

ABSTRACT: Bacteriophage AR9 is a recently sequenced jumbo phage that encodes two multisubunit RNA polymerases. Here we investigated the AR9 transcription strategy and the effect of AR9 infection on the transcription of its host, Bacillus subtilis Analysis of whole-genome transcription revealed early, late, and continuously expressed AR9 genes. Alignment of sequences upstream of the 5' ends of AR9 transcripts revealed consensus sequences that define early and late phage promoters. Continuously expressed AR9 genes have both early and late promoters in front of them. Early AR9 transcription is independent of protein synthesis and must be determined by virion RNA polymerase injected together with viral DNA. During infection, the overall amount of host mRNAs is significantly decreased. Analysis of relative amounts of host transcripts revealed notable differences in the levels of some mRNAs. The physiological significance of up- or downregulation of host genes for AR9 phage infection remains to be established. AR9 infection is significantly affected by rifampin, an inhibitor of host RNA polymerase transcription. The effect is likely caused by the antibiotic-induced killing of host cells, while phage genome transcription is solely performed by viral RNA polymerases. *IMPORTANCE*: Phages regulate the timing of the expression of their own genes to coordinate processes in the infected cell and maximize the release of viral progeny. Phages also alter the levels

of host transcripts. Here we present the results of a temporal analysis of the host and viral transcriptomes of Bacillus subtilis infected with a giant phage, AR9. We identify viral promoters recognized by two virus-encoded RNA polymerases that are a unique feature of the phiKZ-related group of phages to which AR9 belongs. Our results set the stage for future analyses of highly unusual RNA polymerases encoded by AR9 and other phiKZ-related phages.

Leavitt, J. C., Heitkamp, A. J., Bhattacharjee, A. S., Gilcrease, E. B., and Casjens, S. R. Genome Sequence of Escherichia coli Tailed Phage Utah. Genome Announc. 3-30-2017; 5(13); PM:28360173

ABSTRACT: Escherichia coli bacteriophage Utah is a member of the chi-like tailed phage cluster in the Siphoviridae family. We report here the complete 59,024-bp sequence of the genome of phage Utah.

Lee, C. Y., Kim, S. J., Park, B. C., and Han, J. H. Effects of dietary supplementation of bacteriophages against enterotoxigenic Escherichia coli (ETEC) K88 on clinical symptoms of post-weaning pigs challenged with the ETEC pathogen. J.Anim Physiol Anim Nutr.(Berl). 2017; 101(1):88-95; PM: 27271838

ABSTRACT: The present study was performed to investigate the effects of dietary supplementation of bacteriophages (phages) against enterotoxigenic Escherichia coli (ETEC) K88 as a therapy against the ETEC infection in post-weaning pigs. Two groups of post-weaning pigs aged 35 days, eight animals per group, were challenged with 3.0 x 1010 colony forming units of ETEC K88, a third group given the vehicle. The unchallenged group and one challenged group were fed a basal nursery diet for 14 days while the remaining challenged group was fed the basal diet supplemented with 1.0 x 107 plaque forming units of the phage per kg. Average daily gain (ADG), goblet cell density and villous height:crypt depth (VH:CD) ratio in the intestine were less in the challenged group than in the unchallenged group within the animals fed the basal diet ($p < 0.05$); the reverse was true for rectal temperature, faecal consistency score (FCS), E. coli adhesion score (EAS) in the intestine, serum interleukin-8 (IL-8) and tumour necrosis factor-alpha (TNF-alpha) concentrations and digesta pH in the stomach, caecum and colon. The ETEC infection symptom within the challenged animals was alleviated by the dietary phage supplementation ($p < 0.05$) in ADG, FCS, EAS in the jejunum, serum TNF-alpha concentration, digesta pH in the colon, goblet cell density in the ileum and colon and VH:CD ratio in the ileum. Moreover, the infection symptom tended to be alleviated ($p < 0.10$) by the phage supplementation in rectal temperature, EAS in the ileum and caecum, and VH:CD ratio in the duodenum and jejunum. However, EAS in the colon, digesta pH in the stomach and caecum, and goblet cell density in the jejunum did not change due to the dietary phage. Overall, results indicate that the phage therapy is effective for alleviation of acute ETEC K88 infection in post-weaning pigs.

Lee, H. C., Jung, S. H., Hwang, H. J., Kang, D., De, S., Dudekula, D. B., Martindale, J. L., Park, B., Park, S. K., Lee, E. K., Lee, J. H., Jeong, S., Han, K., Park, H. J., Ko, Y. G., Gorospe, M., and Lee, J. S. WIG1 is crucial for AGO2-mediated ACOT7 mRNA silencing via miRNA-dependent and -independent mechanisms. Nucleic Acids Res. 5-3-2017; PM: 28472401

ABSTRACT: RNA-binding proteins (RBPs) are involved in mRNA splicing, maturation,

transport, translation, storage and turnover. Here, we identified ACOT7 mRNA as a novel target of human WIG1. ACOT7 mRNA decay was triggered by the microRNA miR-9 in a WIG1-dependent manner via classic recruitment of Argonaute 2 (AGO2). Interestingly, AGO2 was also recruited to ACOT7 mRNA in a WIG1-dependent manner in the absence of miR-9, which indicates an alternative model whereby WIG1 controls AGO2-mediated gene silencing. The WIG1-AGO2 complex attenuated translation initiation via an interaction with translation initiation factor 5B (eIF5B). These results were confirmed using a WIG1 tethering system based on the MS2 bacteriophage coat protein and a reporter construct containing an MS2-binding site, and by immunoprecipitation of WIG1 and detection of WIG1-associated proteins using liquid chromatography-tandem mass spectrometry. We also identified WIG1-binding motifs using photoactivatable ribonucleoside-enhanced crosslinking and immunoprecipitation analyses. Altogether, our data indicate that WIG1 governs the miRNA-dependent and the miRNA-independent recruitment of AGO2 to lower the stability of and suppress the translation of ACOT7 mRNA.

Lee, I. M., Tu, I. F., Yang, F. L., Ko, T. P., Liao, J. H., Lin, N. T., Wu, C. Y., Ren, C. T., Wang, A. H., Chang, C. M., Huang, K. F., and Wu, S. H. Structural basis for fragmenting the exopolysaccharide of Acinetobacter baumannii by bacteriophage PhiAB6 tailspike protein. Sci.Rep. 2-17-2017; 7:42711; PM: 28209973

ABSTRACT: With an increase in antibiotic-resistant strains, the nosocomial pathogen Acinetobacter baumannii has become a serious threat to global health. Glycoconjugate vaccines containing fragments of bacterial exopolysaccharide (EPS) are an emerging therapeutic to combat bacterial infection. Herein, we characterize the bacteriophage PhiAB6 tailspike protein (TSP), which specifically hydrolyzed the EPS of A. baumannii strain 54149 (Ab-54149). Ab-54149 EPS exhibited the same chemical structure as two antibiotic-resistant A. baumannii strains. The PhiAB6 TSP-digested products comprised oligosaccharides of two repeat units, typically with stoichiometric pseudaminic acid (Pse). The 1.48-1.89-A resolution crystal structures of an N-terminally-truncated PhiAB6 TSP and its complexes with the semi-hydrolyzed products revealed a trimeric beta-helix architecture that bears intersubunit carbohydrate-binding grooves, with some features unusual to the TSP family. The structures suggest that Pse in the substrate is an important recognition site for PhiAB6 TSP. A region in the carbohydrate-binding groove is identified as the determinant of product specificity. The structures also elucidated a retaining mechanism, for which the catalytic residues were verified by site-directed mutagenesis. Our findings provide a structural basis for engineering the enzyme to produce desired oligosaccharides, which is useful for the development of glycoconjugate vaccines against A. baumannii infection.

Lee, J. H., Fan, B., Samdin, T. D., Monteiro, D. A., Desai, M. S., Scheideler, O., Jin, H. E., Kim, S., and Lee, S. W. Phage-Based Structural Color Sensors and Their Pattern Recognition Sensing System. ACS Nano. 4-25-2017; 11(4):3632-3641; PM: 28355060

ABSTRACT: The mammalian olfactory system provides great inspiration for the design of intelligent sensors. To this end, we have developed a bioinspired phage nanostructure-based color sensor array and a smartphone-based sensing network system. Using a M13 bacteriophage (phage) as a basic building block, we created structural color matrices that are composed of liquid-crystalline bundled nanofibers from self-assembled phages. The phages were engineered to express cross-responsive receptors on their major coat

protein (pVIII), leading to rapid, detectable color changes upon exposure to various target chemicals, resulting in chemical- and concentration-dependent color fingerprints. Using these sensors, we have successfully detected 5-90% relative humidity with 0.2% sensitivity. In addition, after modification with aromatic receptors, we were able to distinguish between various structurally similar toxic chemicals including benzene, toluene, xylene, and aniline. Furthermore, we have developed a method of interpreting and disseminating results from these sensors using smartphones to establish a wireless system. Our phage-based sensor system has the potential to be very useful in improving national security and monitoring the environment and human health.

Lee, J. Y., Li, Z., and Miller, E. S. Vibrio Phage KVP40 Encodes a Functional NAD+ Salvage Pathway. J.Bacteriol. 5-1-2017; 199(9); PM: 28167526

ABSTRACT: The genome of T4-type Vibrio bacteriophage KVP40 has five genes predicted to encode proteins of pyridine nucleotide metabolism, of which two, nadV and natV, would suffice for an NAD+ salvage pathway. NadV is an apparent nicotinamide phosphoribosyltransferase (NAmPRTase), and NatV is an apparent bifunctional nicotinamide mononucleotide adenylyltransferase (NMNATase) and nicotinamide-adenine dinucleotide pyrophosphatase (Nudix hydrolase). Genes encoding the predicted salvage pathway were cloned and expressed in Escherichia coli, the proteins were purified, and their enzymatic properties were examined. KVP40 NadV NAmPRTase is active in vitro, and a clone complements a Salmonella mutant defective in both the bacterial de novo and salvage pathways. Similar to other NAmPRTases, the KVP40 enzyme displayed ATPase activity indicative of energy coupling in the reaction mechanism. The NatV NMNATase activity was measured in a coupled reaction system demonstrating NAD+ biosynthesis from nicotinamide, phosphoribosyl pyrophosphate, and ATP. The NatV Nudix hydrolase domain was also shown to be active, with preferred substrates of ADP-ribose, NAD+, and NADH. Expression analysis using reverse transcription-quantitative PCR (qRT-PCR) and enzyme assays of infected Vibrio parahaemolyticus cells demonstrated nadV and natV transcription during the early and delayed-early periods of infection when other KVP40 genes of nucleotide precursor metabolism are expressed. The distribution and phylogeny of NadV and NatV proteins among several large double-stranded DNA (dsDNA) myophages, and also those from some very large siphophages, suggest broad relevance of pyridine nucleotide scavenging in virus-infected cells. NAD+ biosynthesis presents another important metabolic resource control point by large, rapidly replicating dsDNA bacteriophages.IMPORTANCE T4-type bacteriophages enhance DNA precursor synthesis through reductive reactions that use NADH/NADPH as the electron donor and NAD+ for ADP-ribosylation of proteins involved in transcribing and translating the phage genome. We show here that phage KVP40 encodes a functional pyridine nucleotide scavenging pathway that is expressed during the metabolic period of the infection cycle. The pathway is conserved in other large, dsDNA phages in which the two genes, nadV and natV, share an evolutionary history in their respective phage-host group.

Lee, S., Hata, A., Yamashita, N., and Tanaka, H. Evaluation of Virus Reduction by Ultrafiltration with Coagulation-Sedimentation in Water Reclamation. Food Environ.Virol. 4-28-2017; PM: 28455611

ABSTRACT: The evaluation of virus reduction in water reclamation processes is essential for proper assessment and management of the risk of infection by enteric viruses.

Ultrafiltration (UF) with coagulation-sedimentation (CS) is potentially effective for efficient virus removal. However, its performance at removing indigenous viruses has not been evaluated. In this study, we evaluated the reduction of indigenous viruses by UF with and without CS in a pilot-scale water reclamation plant in Okinawa, Japan, by measuring the concentration of viruses using the real-time polymerase chain reaction (qPCR). Aichi virus (AiV) and pepper mild mottle virus (PMMoV) were targeted in addition to the main enteric viruses of concern for risk management, namely, norovirus (NoV) genogroups I and II (GI and GII) and rotavirus (RoV). PMMoV, which is a plant pathogenic virus and is present at high concentrations in water contaminated by human feces, has been suggested as a useful viral indicator. We also investigated the reduction of a spiked model virus (F-specific RNA bacteriophage MS2) to measure the effect of viral inactivation by both qPCR and plaque assay. Efficiencies of removal of NoV GI, NoV GII, RoV, and AiV by UF with and without CS were >0.5 to 3.7 log10, although concentrations were below the detection limit in permeate water. PMMoV was the most prevalent virus in both feed and permeate water following UF, but CS pretreatment could not significantly improve its removal efficiency (mean removal efficiency: UF, 3.1 log10; CS + UF, 3.4 log10; t test, $P > 0.05$). CS increased the mean removal efficiency of spiked MS2 by only 0.3 log10 by qPCR (t-test, $P > 0.05$), but by 2.8 log10 by plaque assay (t-test, $P < 0.01$). This difference indicates that the virus was inactivated during CS + UF. Our results suggest that PMMoV could be used as an indicator of removal efficiency in water reclamation processes, but cultural assay is essential to understanding viral fate.

Lee, S., Ihara, M., Yamashita, N., and Tanaka, H. Improvement of virus removal by pilot-scale coagulation-ultrafiltration process for wastewater reclamation: Effect of optimization of pH in secondary effluent. Water Res. 5-1-2017; 114:23-30 PM: 28226246

ABSTRACT: Reclaimed water (i.e., reused advanced-treated wastewater) offers an alternative water resource. To reduce the health risks associated with its use, efficient virus removal such as with advanced wastewater treatment processes is important. Virus removal by coagulation followed by ultrafiltration (UF) for the treatment of drinking water has been well examined. But its efficacy in wastewater reclamation purpose using secondary treated effluent (SE) from wastewater treatment plant (WWTP) as feed water is unclear. Here, we optimized the virus removal efficiency of coagulation-UF in pilot-scale wastewater reclamation plants using SE as feed water, using the F-specific RNA bacteriophage MS2 as a model virus, at two wastewater treatment plants in Japan. We investigated how using coagulation as a pretreatment for UF improved virus removal efficiency. The efficiency varied greatly between SEs. To reveal the cause of the variation, we conducted laboratory-scale batch coagulation experiments. The efficiency of viral coagulation was negatively correlated with the concentration of dissolved organic matter in the feed water. The optimum pH for coagulation differed between SEs, and the efficiency of coagulation could be dramatically improved by optimizing the pH. We confirmed that the virus removal efficiency in the pilot-scale facility actually could be improved by adjusting the pH. In addition, we confirmed that coagulation-sedimentation-UF with pH adjustment could operate stably for more than 30 days at the pilot scale, with a high virus removal rate. Thus, the wastewater reclamation process described here offers promise in terms of reduced health risks and practical operation.

Lee, S., Kim, M. G., Lee, H. S., Heo, S., Kwon, M., and Kim, G. Isolation and Characterization of Listeria phages for Control of Growth of Listeria monocytogenes in Milk. Korean J.Food Sci.Anim Resour. 2017; 37(2):320-328 PM: 28515656

ABSTRACT: In this study, two Listeria bacteriophages, LMP1 and LMP7, were isolated from chicken feces as a means of biocontrol of L. monocytogenes. Both bacteriophages had a lytic effect on L. monocytogenes ATCC 7644, 15313, 19114, and 19115. Phages LMP1 and LMP7 were able to inhibit the growth of L. monocytogenes ATCC 7644 and 19114 in tryptic soy broth at 10 degrees C and 30 degrees C. Nevertheless, LMP1 was more effective than LMP7 at inhibiting L. monocytogenes ATCC 19114. On the contrary, LMP7 was more effective than LMP1 at inhibiting L. monocytogenes ATCC 7644. The morphology of LMP1 and LMP7 resembled that of members of the Siphoviridae family. The growth of L. monocytogenes ATCC 7644 was inhibited by both LMP1 and LMP7 in milk; however, the growth of L. monocytogenes ATCC 19114 was only inhibited by LMP1 at 30 degrees C. The lytic activity of bacteriophages was also evaluated at 4 degrees C in milk in order to investigate the potential use of these phages in refrigerated products. In conclusion, these two bacteriophages exhibit different host specificities and characteristics, suggesting that they can be used as a component of a phage cocktail to control L. monocytogenes in the food industry.

Lee, T. J., Yoo, J. Y., Shu, D., Li, H., Zhang, J., Yu, J. G., Jaime-Ramirez, A. C., Acunzo, M., Romano, G., Cui, R., Sun, H. L., Luo, Z., Old, M., Kaur, B., Guo, P., and Croce, C. M. RNA Nanoparticle-Based Targeted Therapy for Glioblastoma through Inhibition of Oncogenic miR-21. Mol.Ther. 1-18-2017; PM: 28109960

ABSTRACT: Targeted inhibition of oncogenic miRNA-21 has been proposed to treat glioblastoma by rescuing tumor suppressors, PTEN and PDCD4. However, systemic delivery of anti-miR-21 sequences requires a robust and efficient delivery platform to successfully inhibit this druggable target. Three-way-junction (3WJ)-based RNA nanoparticles (RNP), artificially derived from pRNA of bacteriophage phi29 DNA packaging motor, was recently shown to target glioblastoma. Here, we report that multi-valent folate (FA)-conjugated 3WJ RNP constructed to harbor anti-miR-21 LNA sequences (FA-3WJ-LNA-miR21) specifically targeted and delivered anti-miR-21 LNA and knocked down miR-21 expression in glioblastoma cells in vitro and in vivo with favorable biodistribution. Systemically injected FA-3WJ-LNA-miR21 RNP efficiently rescued PTEN and PDCD4, resulting in glioblastoma cell apoptosis and tumor growth regression. Overall survival rate was also significantly improved by FA-3WJ-LNA-miR21 RNP. These results are indicative of the clinical benefit of FA-3WJ RNP-based gene therapy for the successful targeted therapy of developing and even recurring glioblastoma.

Leigh, B., Karrer, C., Cannon, J. P., Breitbart, M., and Dishaw, L. J. Isolation and Characterization of a Shewanella Phage-Host System from the Gut of the Tunicate, Ciona intestinalis. Viruses. 3-22-2017; 9(3); PM: 28327522

ABSTRACT: Outnumbering all other biological entities on earth, bacteriophages (phages) play critical roles in structuring microbial communities through bacterial infection and subsequent lysis, as well as through horizontal gene transfer. While numerous studies have examined the effects of phages on free-living bacterial cells, much less is known regarding the role of phage infection in host-associated biofilms, which help to stabilize adherent microbial communities. Here we report the cultivation and characterization of a novel strain of Shewanella fidelis from the gut of the marine tunicate Ciona intestinalis, inducible prophages from the S. fidelis genome, and a strain-specific lytic phage recovered from surrounding seawater. In vitro biofilm assays demonstrated that lytic

phage infection affects biofilm formation in a process likely influenced by the accumulation and integration of the extracellular DNA released during cell lysis, similar to the mechanism that has been previously shown for prophage induction.

Leung, R. L. C., Robinson, M. D. M., Ajabali, A. A. A., Karunanithy, G., Lyons, B., Raj, R., Raoufmoghaddam, S., Mohammed, S., Claridge, T. D. W., Baldwin, A. J., and Davis, B. G. Monitoring the Disassembly of Virus-like Particles by 19F-NMR. J.Am.Chem.Soc. 4-19-2017; 139(15):5277-5280; PM: 28350443

ABSTRACT: Virus-like particles (VLPs) are stable protein cages derived from virus coats. They have been used extensively as biomolecular platforms, e.g., nanocarriers or vaccines, but a convenient in situ technique is lacking for tracking functional status. Here, we present a simple way to monitor disassembly of 19F-labeled VLPs derived from bacteriophage Qbeta by 19F NMR. Analysis of resonances, under a range of conditions, allowed determination not only of the particle as fully assembled but also as disassembled, as well as detection of a degraded state upon digestion by cells. This in turn allowed mutational redesign of disassembly and testing in both bacterial and mammalian systems as a strategy for the creation of putative, targeted-VLP delivery systems.

Leung, S. S., Parumasivam, T., Gao, F. G., Carter, E. A., Carrigy, N. B., Vehring, R., Finlay, W. H., Morales, S., Britton, W. J., Kutter, E., and Chan, H. K. Effects of storage conditions on the stability of spray dried, inhalable bacteriophage powders. Int.J.Pharm. 4-15-2017; 521(1-2):141-149; PM: 28163231

ABSTRACT: This study aimed to develop inhalable powders containing phages active against antibiotic-resistant Pseudomonas aeruginosa for pulmonary delivery. A Pseudomonas phage, PEV2, was spray dried into powder matrices comprising of trehalose (0-80%), mannitol (0-80%) and l-leucine (20%). The resulting powders were stored at various relative humidity (RH) conditions (0, 22 and 60% RH) at 4 degrees C. The phage stability and in vitro aerosol performance of the phage powders were examined at the time of production and after 1, 3 and 12 months storage. After spray drying, a total of 1.3 log titer reduction in phage was observed in the formulations containing 40%, 60% and 80% trehalose, whereas 2.4 and 5.1 log reductions were noted in the formulations containing 20% and no trehalose, respectively. No further reduction in titer occurred for powders stored at 0 and 22% RH even after 12 months, except the formulation containing no trehalose. The 60% RH storage condition had a destructive effect such that no viable phages were detected after 3 and 12 months. When aerosolised, the total lung doses for formulations containing 40%, 60% and 80% trehalose were similar (in the order of 105 pfu). The results demonstrated that spray drying is a suitable method to produce stable phage powders for pulmonary delivery. A powder matrix containing >/=40% trehalose provided good phage preservation and aerosol performances after storage at 0 and 22% RH at 4 degrees C for 12 months.

Li, E., Wei, X., Ma, Y., Yin, Z., Li, H., Lin, W., Wang, X., Li, C., Shen, Z., Zhao, R., Yang, H., Jiang, A., Yang, W., Yuan, J., and Zhao, X. Corrigendum: Isolation and characterization of a bacteriophage phiEap-2 infecting multidrug resistant Enterobacter aerogenes. Sci.Rep. 5-9-2017; 7:46805; PM: 28485399

No Abstract Available.

Liana, A. E., Marquis, C. P., Gunawan, C., Gooding, J. J., and Amal, R. T4 bacteriophage conjugated magnetic particles for E. coli capturing: Influence of bacteriophage loading, temperature and tryptone. Colloids Surf.B Biointerfaces. 3-1-2017; 151:47-57; PM: 27974276

ABSTRACT: This work demonstrates the use of bacteriophage conjugated magnetic particles (Fe3O4) for the rapid capturing and isolation of Escherichia coli. The investigation of T4 bacteriophage adsorption to silane functionalised Fe3O4 with amine (NH2), carboxylic (COOH) and methyl (CH3) surface functional groups reveals the domination of net electrostatic and hydrophobic interactions in governing bacteriophage adsorption. The bare Fe3O4 and Fe3O4-NH2 with high T4 loading captured 3-fold more E. coli (approximately 70% capturing efficiency) compared to the low loading T4 on Fe3O4-COOH, suggesting the significance of T4 loading in E. coli capturing efficiency. Importantly, it is further revealed that E. coli capture is highly dependent on the incubation temperature and the presence of tryptone in the media. Effective E. coli capturing only occurs at 37 degrees C in tryptone-containing media with the absence of either conditions resulted in poor bacteria capture. The incubation temperature dictates the capturing ability of Fe3O4/T4, whereby T4 and E. coli need to establish an irreversible binding that occurred at 37 degrees C. The presence of tryptophan-rich tryptone in the suspending media was also critical, as shown by a 3-fold increase in E. coli capture efficiency of Fe3O4/T4 in tryptone-containing media compared to that in tryptone-free media. This highlights for the first time that successful bacteria capturing requires not only an optimum tailoring of the particle's surface physicochemical properties for favourable bacteriophage loading, but also an in-depth understanding of how factors, such as temperature and solution chemistry influence the subsequent bacteriophage-bacteria interactions.

Lim, J. A., Heu, S., Park, J., and Roh, E. Genomic characterization of bacteriophage vB_PcaP_PP2 infecting Pectobacterium carotovorum subsp. carotovorum, a new member of a proposed genus in the subfamily Autographivirinae. Arch.Virol. 4-13-2017; PM: 28409265

ABSTRACT: Bacteriophage vB_PcaP_PP2 (PP2) is a novel virulent phage that infects the plant-pathogenic bacterium Pectobacterium carotovorum subsp. carotovorum. PP2 phage has a 41,841-bp double-stranded DNA encoding 47 proteins, and it was identified as a member of the family Podoviridae by transmission electron microscopy. Nineteen of its open reading frames (ORFs) show homology to functional proteins, and 28 ORFs have been characterized as hypothetical proteins. PP2 phage is homologous to Cronobacter phage vB_CskP_GAP227 and Dev-CD-23823. Based on phylogenetic analysis, PP2 and its homologous bacteriophages form a new group within the subfamily Autographivirinae in the family Podoviridae, suggesting the need to establish a new genus. No lysogenic-cycle-related genes or bacterial toxins were identified.

Lim, S. W., Lance, S. T., Stedman, K. M., and Abate, A. R. PCR-activated cell sorting as a general, cultivation-free method for high-throughput identification and enrichment of virus hosts. J.Virol.Methods. 2017; 242:14-21; PM: 28042018

ABSTRACT: Characterizing virus-host relationships is critical for understanding the impact of a virus on an ecosystem, but is challenging with existing techniques, particularly for uncultivable species. We present a general, cultivation-free approach for identifying phage-associated bacterial cells. Using PCR-activated cell sorting, we interrogate millions of individual bacteria for the presence of specific phage nucleic acids. If the nucleic acids are present, the bacteria are recovered via sorting and their genomes analyzed. This allows targeted recovery of all possible host species in a diverse population associated with a specific phage, and can be easily targeted to identify the hosts of different phages by modifying the PCR primers used for detection. Moreover, this technique allows quantification of free phage particles, as benchmarked against the "gold standard" of virus enumeration, the plaque assay.

Lino, C. A., Caldeira, J. C., and Peabody, D. S. Display of single-chain variable fragments on bacteriophage MS2 virus-like particles. J.Nanobiotechnology. 2-13-2017; 15(1):13; PM: 28193211

ABSTRACT: BACKGROUND: Virus-like particles (VLPs) of the RNA bacteriophage MS2 have many potential applications in biotechnology. MS2 VLPs provide a platform for peptide display and affinity selection (i.e. biopanning). They are also under investigation as vehicles for targeted drug delivery, using display of receptor-specific peptides or nucleic acid aptamers to direct their binding to specific cell-surface receptors. However, there are few molecules more suited to the precise targeting and binding of a cellular receptor than antibodies. *RESULTS*: Here we describe a strategy for display of four different functional single-chain variable fragments (scFvs) on the surface of the MS2 VLP. Each scFv is validated both for its presence on the surface of the VLP and for its ability to bind its cognate antigen. *CONCLUSIONS*: This work demonstrates the suitability of the MS2 VLP platform to display genetically fused scFvs, allowing for many potential applications of these VLPs and paving the way for future work with libraries of scFvs displayed in a similar manner on the VLP surface. These libraries can then be biopanned and novel scFv binders to targets can be readily discovered.

Liu, S., Tafoya, S., and Bustamante, C. Deciphering the Molecular Mechanism of the Bacteriophage phi29 DNA Packaging Motor. Methods Mol.Biol. 2017; 1486:343-355; PM: 27844435

ABSTRACT: The past decade has seen an explosion in the use of single-molecule approaches to study complex biological processes. One such approach-optical trapping-is particularly well suited for investigating molecular motors, a diverse group of macromolecular complexes that convert chemical energy into mechanical work, thus playing key roles in virtually every aspect of cellular life. Here we describe how to use high-resolution optical tweezers to investigate the mechanism of the bacteriophage phi29 DNA packaging motor, a ring-shaped ATPase responsible for genome packing during viral assembly. This system illustrates how to use single-molecule techniques to uncover novel, often unexpected, principles of motor operation.

Liu, Z., Wang, M., Meng, X., Li, Y., Wang, D., Jiang, Y., Shao, H., and Zhang, Y. Isolation and Genome Sequencing of a Novel Pseudoalteromonas Phage PH1. Curr.Microbiol. 2017; 74(2):212-218; PM: 27942842

ABSTRACT: The family Pseudoalteromonas is highly adaptable to dissimilar ecological habitats and plays an important ecological role in the marine environment. In this study, a new Pseudoalteromonas phage PH1 was isolated from the Yellow Sea. To better understand the bacteriophage, its biological properties, including morphology, host range, growth phenotype, thermal and pH stability, and nucleic acid composition, were investigated in detail. The result showed that the phage PH1 is a Podoviridae-phage with an icosahedral head (60 nm of diameter) and a short tail (26 nm in length). The phage PH1 genome consists of 42,685 bp length double-stranded DNA with a G+C content of 42.24% and is predicted to have 55 open reading frames (ORFs) with an average length of 740 bp nucleotides each. The phage PH1 genome adds a new Podoviridae-phage genome to marine bacteriophage dataset, which will provide useful basic information for further molecular research on interaction mechanisms between bacteriophages and their hosts.

Loison, L., Gayon, J., and Burian, R. M. The Contributions - and Collapse - of Lamarckian Heredity in Pasteurian Molecular Biology: 1. Lysogeny, 1900-1960. J.Hist Biol. 2017; 50(1):5-52; PM: 26732271

ABSTRACT: This article shows how Lamarckism was essential in the birth of the French school of molecular biology. We argue that the concept of inheritance of acquired characters positively shaped debates surrounding bacteriophagy and lysogeny in the Pasteurian tradition during the interwar period. During this period the typical Lamarckian account of heredity treated it as the continuation of protoplasmic physiology in daughter cells. Felix d'Herelle applied this conception to argue that there was only one species of bacteriophage and Jules Bordet applied it to develop an account of bacteriophagy as a transmissible form of autolysis and to analyze the new phenomenon of lysogeny. In a long-standing controversy with Bordet, Eugene Wollman deployed a more morphological understanding of the inheritance of acquired characters, yielding a particulate, but still Lamarckian, account of lysogeny. We then turn to Andre Lwoff who, with several colleagues, completed Wollman's research program from 1949 to 1953. We examine how he gradually set aside the Lamarckian background, finally removing inheritance of acquired characters from the resulting account of bacteriophagy and lysogeny. In the conclusion, we emphasize the complex dual role of Lamarckism as it moved from an assumed explanatory framework to a challenge that the nascent molecular biology had to overcome.

Lokareddy, R. K., Sankhala, R. S., Roy, A., Afonine, P. V., Motwani, T., Teschke, C. M., Parent, K. N., and Cingolani, G. Portal protein functions akin to a DNA-sensor that couples genome-packaging to icosahedral capsid maturation. Nat.Commun. 1-30-2017; 8:14310; PM: 28134243

ABSTRACT: Tailed bacteriophages and herpesviruses assemble infectious particles via an empty precursor capsid (or 'procapsid') built by multiple copies of coat and scaffolding protein and by one dodecameric portal protein. Genome packaging triggers rearrangement of the coat protein and release of scaffolding protein, resulting in dramatic procapsid lattice expansion. Here, we provide structural evidence that the portal protein of the bacteriophage P22 exists in two distinct dodecameric conformations: an asymmetric assembly in the procapsid (PC-portal) that is competent for high affinity binding to the large terminase packaging protein, and a symmetric ring

in the mature virion (MV-portal) that has negligible affinity for the packaging motor. Modelling studies indicate the structure of PC-portal is incompatible with DNA coaxially spooled around the portal vertex, suggesting that newly packaged DNA triggers the switch from PC- to MV-conformation. Thus, we propose the signal for termination of 'Headful Packaging' is a DNA-dependent symmetrization of portal protein.

Lood, R., Molina, H., and Fischetti, V. A. Determining bacteriophage endopeptidase activity using either fluorophore-quencher labeled peptides combined with liquid chromatography-mass spectrometry (LC-MS) or Forster resonance energy transfer (FRET) assays. PLoS.One. 2017; 12(3):e0173919; PM: 28296948

ABSTRACT: The necessity of identifying novel methods to combat infections caused by antibiotic resistant bacteria is increasing each year. Recent advancements in the development of peptidoglycan hydrolases (e.g. lysins) from bacterial viruses (bacteriophages) have revealed the efficiency of this class of enzymes in treating serious bacterial infections. Though promising results have been obtained regarding the lethal action of lysin on bacterial pathogens both in vitro and in vivo, an often-overlooked factor in these studies is precisely identifying their peptidoglycan cleavage site. This knowledge would be useful for following the activity of the enzyme during development, without the need for whole-organism lytic assays. However, more importantly, it would enable the selection of lysins with different cleavage activities that would act synergistically for enhanced efficacy. Here, we have developed two new methods to accurately identify the cleavage site of lysins using liquid chromatography mass spectrometry (LC-MS) on peptidoglycan-like fluorophore-quencher modified synthetic peptides, as well as determining the enzymatic action and kinetics of the enzymes on modified peptides in a Forster resonance energy transfer (FRET) assay. These methods should facilitate progress within the lysin field, accelerating the development of therapeutic lysins to combat antibiotic resistant bacterial infections.

Lu, R., Zhang, C., Piatkovsky, M., Ulbricht, M., Herzberg, M., and Nguyen, T. H. Improvement of virus removal using ultrafiltration membranes modified with grafted zwitterionic polymer hydrogels. Water Res. 6-1-2017; 116:86-94; PM: 28324709

ABSTRACT: Potable water reuse has been adopted by cities suffering water scarcity in recent years. The microbial safety in water reuse, especially with respect to pathogenic viruses, is still a concern for water consumers. Membrane filtration can achieve sufficient removal of pathogenic viruses without disinfection byproducts, but the required energy is intensive. In this study, we graft-polymerized zwitterionic SPP ([3-(methacryloylamino) propyl] dimethyl (3-sulfopropyl) ammonium hydroxide) on a 150 kDa ultrafiltration polyethersulfone membrane to achieve a significantly higher virus removal. The redox-initiated graft-polymerization was performed in an aqueous solution during filtration of the monomer and initiators, allowing for functionalizing the membrane pores with hydrophilic polySPP. Bacteriophage MS2 and human adenovirus type 2 (HAdV-2) were used as surrogates for pathogenic human norovirus and human adenovirus. The grafting resulted in approximately 18% loss of the membrane permeability but an increase of 4 log10 in HAdV-2 removal and 3 log10 in MS2 removal. The pristine and the grafted membranes were both conditioned with soluble microbial products (SMP) extracted from a full-scale membrane bioreactor (MBR) in order to test the virus removal after fouling the membranes. After fouling, the HAdV-2 removal by the grafted membrane was 1 log10 higher than that of the pristine membrane. For MS2, the grafted membrane after fouling

with SMP achieved an additional 5 log10 removal compared to the unmodified membrane. The simple graft-polymerization functionalization of commercialized membrane achieving enhanced virus removal efficiency highlights the promise of membrane filtration for pathogen control in potable water reuse.

Lusiak-Szelachowska, M., Zaczek, M., Weber-Dabrowska, B., Miedzybrodzki, R., Letkiewicz, S., Fortuna, W., Rogoz, P., Szufnarowski, K., Jonczyk-Matysiak, E., Olchawa, E., Walaszek, K. M., and Gorski, A. Antiphage activity of sera during phage therapy in relation to its outcome. Future.Microbiol. 2017; 12:109-117; PM: 27643529

ABSTRACT: AIM: The aim was to study the association between the phage neutralization of patients' sera and the clinical outcome of phage therapy (PT). *PATIENTS*: About 62 patients with various bacterial infections receiving PT as well as 30 healthy volunteers were studied. *MATERIALS & METHODS*: Antiphage activity of sera (AAS) was examined using the phage neutralization test of different types of phages before and during PT in relation to the route of phage administration and correlated with the results of PT. *RESULTS & CONCLUSION*: The analysis of the association between AAS level and clinical results indicated that the level of AAS is not correlated with the outcome of PT.

Ma, Q., Guo, Z., Gao, C., Zhu, R., Wang, S., Yu, L., Qin, W., Xia, X., Gu, J., Yan, G., and Lei, L. Enhancement of the direct antimicrobial activity of Lysep3 against Escherichia coli by inserting cationic peptides into its C terminus. Antonie Van Leeuwenhoek. 2017; 110(3):347-355; PM: 27943012

ABSTRACT: Phage lysins are considered promising antimicrobials against resistant bacterial infections. Some lysins have been reported for the prevention and treatment of Gram-positive bacterial infection. Gram-negative bacterial phage lysins, however, can only destroy the bacterial cell wall from inside because of the obstruction of the bacterial outer membrane that prevents direct hydrolysis of the bacterial wall peptidoglycan from the outside, severely restricting the development of lysins against Gram-negative bacteria. In this study, genetic engineering techniques were used to fuse a 5 cationic amino acid polypeptide (KRKRK), a 10 cationic amino acid polypeptide (KRKRKRKRKR), a 15 cationic amino acid polypeptide (KRKRKRKRKRKRKRK), and a polypeptide including both cationic and hydrophobic amino acids (KRKRKFFVAIIP) to the C-terminus of the Escherichia coli phage lysin Lysep3 to obtain four fusion lysins (5aa, 10aa, 15aa, Mix). The bactericidal effects of those four lysins on E. coli were then compared in vitro. Our results showed that the fusion of hydrophobic and positively charged amino acids, Mix, can kill E. coli effectively; the fusion of positively charged amino acids alone at the C-terminus (5aa, 10aa, 15aa) also showed bactericidal activity against E. coli from the outside, with the bactericidal activity gradually increasing with the positive charge at the C-terminus of the lysin. Collectively, improving the positive charge at the C-terminus of E. coli bacteriophage lysin Lysep3 increases its bactericidal ability from outside E. coli, providing a new practical method for the development of anti-Gram-negative bacterial lysins.

Mac, Mahon J., Pillai, S. C., Kelly, J. M., and Gill, L. W. Solar photocatalytic disinfection of E. coli and bacteriophages MS2, PhiX174 and PR772 using TiO2, ZnO and ruthenium based complexes in a continuous flow system. J.Photochem.Photobiol.B. 4-2-2017; 170:79-90; PM: 28399477

ABSTRACT: The performance of photocatalytic treatment processes were assessed using different photocatalysts against E. coli and bacteriophages MS2, PhiX174 and PR772, in a recirculating continuous flow compound parabolic collector system under real sunlight conditions. Suspended TiO2 and ZnO nanoparticle powders and Tris(2,2'-bipyridyl)dichlororuthenium(II) hexahydrate in solution were tested separately, as well as in combination, using E. coli. For a 3-log reduction of E. coli in distilled water, inactivation rates in terms of cumulative dose were in the order Ru(bpy)3Cl2>(TiO2 & Ru(bpy)3Cl2)>(ZnO & Ru(bpy)3Cl2)>ZnO>TiO2>photolysis. Reactivation of E. coli was observed following all trials despite the detection limit being reached, although the reactivated colonies were observed to be under stress and much slower growing when compared to original colonies. Treatment with Ru(bpy)3Cl2 was also compared against standard photolysis of bacteriophages MS2, PhiX174 and PR772 with the order of photolytic inactivation for a 3-log reduction in terms of cumulative UV-A dose being PhiX174>PR772>MS2. However, MS2 was found to be the most susceptible bacteriophage to treatment with Ru(bpy)3Cl2, with complete removal of the phage observed within the first 15min of exposure. Ru(bpy)3Cl2 also significantly improved inactivation rates for PR772 and PhiX174.

Maciejewska, B., Roszniowski, B., Espaillat, A., Kesik-Szeloch, A., Majkowska-Skrobek, G., Kropinski, A. M., Briers, Y., Cava, F., Lavigne, R., and Drulis-Kawa, Z. Klebsiella phages representing a novel clade of viruses with an unknown DNA modification and biotechnologically interesting enzymes. Appl.Microbiol.Biotechnol. 2017; 101(2):673-684; PM: 27766357

ABSTRACT: Lytic bacteriophages and phage-encoded endolysins (peptidoglycan hydrolases) provide a source for the development of novel antimicrobial strategies. In the present study, we focus on the closely related (96 % DNA sequence identity) environmental myoviruses vB_KpnM_KP15 (KP15) and vB_KpnM_KP27 (KP27) infecting multidrug-resistant Klebsiella pneumoniae and Klebsiella oxytoca strains. Their genome organisation and evolutionary relationship are compared to Enterobacter phage phiEap-3 and Klebsiella phages Matisse and Miro. Due to the shared and distinct evolutionary history of these phages, we propose to create a new phage genus "Kp15virus" within the Tevenvirinae subfamily. In silico genome analysis reveals two unique putative homing endonucleases of KP27 phage, probably involved in unrevealed mechanism of DNA modification and resistance to restriction digestion, resulting in a broader host spectrum. Additionally, we identified in KP15 and KP27 a complete set of lysis genes, containing holin, antiholin, spanin and endolysin. By turbidimetric assays on permeabilized Gram-negative strains, we verified the ability of the KP27 endolysin to destroy the bacterial peptidoglycan. We confirmed high stability, absence of toxicity on a human epithelial cell line and the enzymatic specificity of endolysin, which was found to possess endopeptidase activity, cleaving the peptide stem between L-alanine and D-glutamic acid.

Mahony, J., Oliveira, J., Collins, B., Hanemaaijer, L., Lugli, G. A., Neve, H., Ventura, M., Kouwen, T. R., Cambillau, C., and van, Sinderen D. Genetic and functional characterisation of the lactococcal P335 phage-host interactions. BMC.Genomics. 2-10-2017; 18(1):146; PM: 28183268

ABSTRACT: BACKGROUND: Despite continuous research efforts, bacterio(phages) infecting Lactococcus lactis starter strains persist as a major threat to dairy fermentations.

The lactococcal P335 phages, which are currently classified into four sub-groups (I-IV), are the second most frequently isolated phage group in an industrial dairy context. *RESULTS*: The current work describes the isolation and comparative genomic analysis of 17 novel P335 group phages. Detailed analysis of the genomic region of P335 phages encoding the so-called "baseplate", which includes the receptor binding protein (RBP) was combined with a functional characterization of the RBP of sub-group III and IV phages. Additionally, calcium-dependence assays revealed a specific requirement for calcium by sub-group IV phages while host range analysis highlighted a higher number of strains with CWPS type A (11 of 39 strains) are infected by the P335 phages assessed in this study than those with a C (five strains), B (three of 39 strains) or unknown (one of 39 strains) CWPS type. *CONCLUSIONS*: These analyses revealed significant divergence among RBP sequences, apparently reflecting their unique interactions with the host and particularly for strains with a type A CWPS. The implications of the genomic architecture of lactococcal P335 phages on serving as a general model for Siphoviridae phages are discussed.

Mahony, J., Moscarelli, A., Kelleher, P., Lugli, G. A., Ventura, M., Settanni, L., and van, Sinderen D. Phage Biodiversity in Artisanal Cheese Wheys Reflects the Complexity of the Fermentation Process. Viruses. 3-16-2017; 9(3); PM:28300778

ABSTRACT: Dairy fermentations constitute a perfect "breeding ground" for bacteriophages infecting starter cultures, particularly strains of Lactococcus lactis. In modern fermentations, these phages typically belong to one of three groups, i.e., the 936, P335, and c2 phage groups. Traditional production methods present fewer chemical and physical barriers to phage proliferation compared to modern production systems, while the starter cultures used are typically complex, variable, and undefined. In the current study, a variety of cheese whey, animal-derived rennet, and vat swab samples from artisanal cheeses produced in Sicily were analysed for the presence of lactococcal phages to assess phage diversity in such environments. The complete genomes of 18 representative phage isolates were sequenced, allowing the identification of 10 lactococcal 949 group phages, six P087 group phages, and two members of the 936 group phages. The genetic diversity of these isolates was examined using phylogenetic analysis as well as a focused analysis of the receptor binding proteins, which dictate specific interactions with the host-encoded receptor. Thermal treatments at 63 degrees C and 83 degrees C indicate that the 949 phages are particularly sensitive to thermal treatments, followed by the P087 and 936 isolates, which were shown to be much less sensitive to such treatments. This difference may explain the relatively low frequency of isolation of the so-called "rare" 949 and P087 group phages in modern fermentations.

Mandali, S., Gupta, K., Dawson, A. R., Van Duyne, G. D., and Johnson, R. C. Control of Recombination Directionality by the Listeria Phage A118 Protein Gp44 and the Coiled-Coil Motif of Its Serine Integrase. J.Bacteriol. 6-1-2017; 199(11); PM:28289084

ABSTRACT: The serine integrase of phage A118 catalyzes integrative recombination between attP on the phage and a specific attB locus on the chromosome of Listeria monocytogenes, but it is unable to promote excisive recombination between the hybrid attL and attR sites found on the integrated prophage without assistance by a recombination directionality factor (RDF). We have identified and characterized the phage-encoded RDF Gp44, which activates the A118 integrase for excision and inhibits integration. Gp44 binds to the C-terminal DNA binding domain of integrase, and we

have localized the primary binding site to be within the mobile coiled-coil (CC) motif but distinct from the distal tip of the CC that is required for recombination. This interaction is sufficient to inhibit integration, but a second interaction involving the N-terminal end of Gp44 is also required to activate excision. We provide evidence that these two contacts modulate the trajectory of the CC motifs as they extend out from the integrase core in a manner dependent upon the identities of the four att sites. Our results support a model whereby Gp44 shapes the Int-bound complexes to control which att sites can synapse and recombine.*IMPORTANCE*: Serine integrases mediate directional recombination between bacteriophage and bacterial chromosomes. These highly regulated site-specific recombination reactions are integral to the life cycle of temperate phage and, in the case of Listeria monocytogenes lysogenized by A118 family phage, are an essential virulence determinant. Serine integrases are also utilized as tools for genetic engineering and synthetic biology because of their exquisite unidirectional control of the DNA exchange reaction. Here, we identify and characterize the recombination directionality factor (RDF) that activates excision and inhibits integration reactions by the phage A118 integrase. We provide evidence that the A118 RDF binds to and modulates the trajectory of the long coiled-coil motif that extends from the large carboxyl-terminal DNA binding domain and is postulated to control the early steps of recombination site synapsis.

Manthey, G. M., Clear, A. D., Liddell, L. C., Negritto, M. C., and Bailis, A. M. Homologous recombination in budding yeast expressing the human RAD52 gene reveals a Rad51-independent mechanism of conservative double-strand break repair. Nucleic Acids Res. 2-28-2017; 45(4):1879-1888 PM: 27923995

ABSTRACT: RAD52 is a homologous recombination (HR) protein that is conserved from bacteriophage to humans. Simultaneously attenuating expression of both the RAD52 gene, and the HR and tumor suppressor gene, BRCA2, in human cells synergistically reduces HR - indicating that RAD52 and BRCA2 control independent mechanisms of HR. We have expressed the human RAD52 gene (HsRAD52) in budding yeast strains lacking the endogenous RAD52 gene and found that HsRAD52 supports repair of DNA double-strand breaks (DSB) by a mechanism of HR that conserves genome structure. Importantly, this mechanism of HR is independent of RAD51, which encodes the central strand exchange protein in yeast required for conservative HR. In contrast, BRCA2 exerts its effect on HR in human cells together with HsRAD51, potentially explaining the synergistic effect of attenuating the expression of both HsRAD52 and BRCA2. This suggests that multiple mechanisms of conservative DSB repair may contribute to tumor suppression in human cells.

Marcus, J. I., Hassoun, S., and Nair, N. U. Computational prediction of functional abortive RNA in E. coli. Genomics. 3-24-2017; PM: 28347827

ABSTRACT: Failure by RNA polymerase to break contacts with promoter DNA results in release of bound RNA and re-initiation of transcription. These abortive RNAs were assumed to be non-functional but have recently been shown to affect termination in bacteriophage T7. Little is known about the functional role of these RNA in other genetic models. Using a computational approach, we investigated whether abortive RNA could exert function in E. coli. Fragments generated from 3780 transcription units were used as

query sequences within their respective transcription units to search for possible binding sites. Sites that fell within known regulatory features were then ranked based upon the free energy of hybridization to the abortive. We further hypothesize about mechanisms of regulatory action for a select number of likely matches. Future experimental validation of these putative abortive-mRNA pairs may confirm our findings and promote exploration of functional abortive RNAs (faRNAs) in natural and synthetic systems.

Marets, N., Kuo, D., Torrey, J. R., Sakamoto, T., Henmi, M., Katayama, H., and Kato, T. Highly Efficient Virus Rejection with Self-Organized Membranes Based on a Crosslinked Bicontinuous Cubic Liquid Crystal. Adv.Healthc.Mater. 5-9-2017; PM: 28485109

ABSTRACT: To remove viruses from water, the use of self-assembling liquid crystals is presented as a novel method for the synthesis of membranes with a regular pore size (below 1 nm) and controlled pore structures. Nanostructured bicontinuous cubic liquid-crystalline (LC) thin films are photopolymerized onto a polysulfone support layer. It is found that these membranes reject the virus, Qbeta bacteriophage (approximately 20 nm diameter) by >99.9999%. Prepressurization of the membrane appears to enhance their virus rejection properties. This is the first example of nanostructured LC membranes that are used for virus rejection, for which they show great potential.

Marshall, R., Maxwell, C. S., Collins, S. P., Beisel, C. L., and Noireaux, V. Short DNA containing chi sites enhances DNA stability and gene expression in E. coli cell-free transcription-translation systems. Biotechnol.Bioeng. 5-5-2017; PM: 28475211

ABSTRACT: E. coli cell-free transcription-translation (TXTL) systems offer versatile platforms for advanced biomanufacturing and for prototyping synthetic biological parts and devices. Production and testing could be accelerated with the use of linear DNA, which can be rapidly and cheaply synthesized. However, linear DNA is efficiently degraded in TXTL preparations from Escherichia coli. Here, we show that double-stranded DNA encoding chi sites-eight base-pair sequences preferentially bound by the RecBCD recombination machinery-stabilizes linear DNA and greatly enhances the TXTL-based expression and activity of a fluorescent reporter gene, simple regulatory cascades, and T7 bacteriophage particles. The chi-site DNA and the DNA-binding lambda protein Gam yielded similar enhancements, and DNA with as few as four chi sites was sufficient to ensure robust gene expression in TXTL. Given the affordability and scalability of producing the short chi-site DNA, this generalized strategy is expected to advance the broad use of TXTL systems across its many applications. This article is protected by copyright. All rights reserved.

Marvin, D. A. Fibre diffraction studies of biological macromolecules. Prog.Biophys.Mol.Biol. 4-24-2017; PM: 28442432

ABSTRACT: Two fundamental structures in molecular biology, DNA and the alpha-helix, were determined using X-ray fibre diffraction data, and yet fibre diffraction occupies an obscure niche in structural biology. Relatively few structures are appropriate for the technique, and it seldom supplies data of the quality common in protein crystallography; however, it has proven indispensable in some cases. Here we outline some aspects of helix diffraction mathematics, and then illustrate the application of fibre diffraction by three case studies: DNA, filamentous bacterial viruses, and bacterial pili. These examples

are illustrative, not exhaustive, and reviews of other important structures such as plant viruses, polysaccharides and amyloids are also cited, as appropriate. Finally we describe in more detail the methods currently used to obtain and analyze fibre diffraction patterns of biological macromolecules, to give a technique-oriented tutorial which may be useful to researchers who find that they require fibre diffraction for their work.

Mattiacio, J. L., Brewer, M., and Dewhurst, S. Display of HIV-1 Envelope Protein on Lambda Phage Scaffold as a Vaccine Platform. Methods Mol.Biol. 2017; 1581:245-253; PM: 28374253

ABSTRACT: The generation of a strong antibody response to target antigens is a major goal for vaccine development. Here we describe the display of the human immunodeficiency virus (HIV) envelope spike protein (Env) on a virus-like scaffold provided by the lambda phage capsid. Phage vectors, in general, have advantages over mammalian virus vectors due to their genetic tractability, inexpensive production, suitability for scale-up, as well as their physical stability, making them an attractive vaccine platform.

McMinn, B. R., Ashbolt, N. J., and Korajkic, A. Bacteriophages as indicators of fecal pollution and enteric virus removal. Lett.Appl.Microbiol. 3-17-2017; PM: 28304098

ABSTRACT: Bacteriophages are an attractive alternative to fecal indicator bacteria (FIB), particularly as surrogates of enteric virus fate and transport, due to their closer morphological and biological properties. Based on a review of published data, we summarize densities of coliphages (F+ and somatic), Bacteroides spp. and enterococci bacteriophages (phages) in individual human waste, raw wastewater, ambient fresh and marine waters and removal through wastewater treatment processes utilizing traditional treatments. We also provide comparisons with FIB and enteric viruses whenever possible. Lastly, we examine fate and transport characteristics in the aquatic environment and provide an overview of the environmental factors affecting their survival. In summary, concentrations of bacteriophages in various sources were consistently lower than FIB, but more reflective of infectious enteric virus levels. Overall, our investigation indicates that bacteriophages may be adequate viral surrogates, especially in built systems, such as wastewater treatment plants. This article is protected by copyright. All rights reserved.

Meaden, S. and Koskella, B. Adaptation of the pathogen, Pseudomonas syringae, during experimental evolution on a native vs. alternative host plant. Mol.Ecol. 2017; 26(7):1790-1801; PM: 28207977

ABSTRACT: The specialization and distribution of pathogens among species has substantial impact on disease spread, especially when reservoir hosts can maintain high pathogen densities or select for increased pathogen virulence. Theory predicts that optimal within-host growth rate will vary among host genotypes/species and therefore that pathogens infecting multiple hosts should experience different selection pressures depending on the host environment in which they are found. This should be true for pathogens with broad host ranges, but also those experiencing opportunistic infections on novel hosts or that spill over among host populations. There is very little empirical data, however, regarding how adaptation to one host might directly influence infectivity and growth on another. We took an experimental evolution approach to examine short-term

adaptation of the plant pathogen, Pseudomonas syringae pathovar tomato, to its native tomato host compared with an alternative host, Arabidopsis, in either the presence or absence of bacteriophages. After four serial passages (20 days of selection in planta), we measured bacterial growth of selected lines in leaves of either the focal or alternative host. We found that passage through Arabidopsis led to greater within-host bacterial densities in both hosts than did passage through tomato. Whole genome resequencing of evolved isolates identified numerous single nucleotide polymorphisms based on our novel draft assembly for strain PT23. However, there was no clear pattern of clustering among plant selection lines at the genetic level despite the phenotypic differences observed. Together, the results emphasize that previous host associations can influence the within-host growth rate of pathogens.

Meng, X., Wang, M., You, S., Wang, D., Li, Y., Liu, Z., Gao, Y., Liu, L., Zhang, Y., Yan, Z., Liu, C., Jiang, Y., and Shao, H. Characterization and Complete Genome Sequence of a Novel Siphoviridae Bacteriophage BS5. Curr.Microbiol. 4-20-2017; PM: 28424939

ABSTRACT: A novel Siphoviridae family Phage BS5, which infects Pseudoalteromonas atlantica, was isolated from the surface waters of the Yellow Sea. Morphological study by transmission electron microscopy revealed that the novel phage belongs to Siphoviridae. The complete genome sequence of PBS5 contained a linear, double-strand 39949-bp DNA molecule with a G + C content of 40.6% and 65 putative open reading frames. Twelve conserved domains were detected by BLASTP in NCBI, and of these the functions of 5 were known. The genome was grouped into four modules as follows: phage structure, phage packaging, DNA replication and regulation, and some additional functions.16 S rDNA sequence analysis was also applied to identify the host bacteria. After initial characterization of bacteriophage PBS5, it was found that the optimal pH was 7.0, the optimal temperature was 30 degrees C, and the burst size was about 95 virions per cell. This information will provide an important benchmark for further research on the interaction between bacteriophages and their hosts.

Miedzybrodzki, R., Klak, M., Jonczyk-Matysiak, E., Bubak, B., Wojcik, A., Kaszowska, M., Weber-Dabrowska, B., Lobocka, M., and Gorski, A. Means to Facilitate the Overcoming of Gastric Juice Barrier by a Therapeutic Staphylococcal Bacteriophage A5/80. Front Microbiol. 2017; 8:467; PM: 28386250

ABSTRACT: In this article we compare the efficacy of different pharmacological agents (ranitidine, and omeprazole) to support phage transit from stomach to distal portions of the gastrointestinal tract in rats. We show that a temporal modification of environment in the animal stomach may protect Twort-like therapeutic antistaphylococcal phage A5/80 (from bacteriophage collection of the Hirszfeld Institute of Immunology and Experimental Therapy PAS in Wroclaw, Poland) from the inactivation by gastric juice effectively enough to enable a significant fraction of orally administered A5/80 to pass to the intestine. Interestingly, we found that yogurt may be a relatively strong in enhancing phage transit. Given the immunomodulating activities of phages our data may suggest that phages and yogurt can act synergistically in mediating their probiotic activities and enhancing the effectiveness of oral phage therapy. We also demonstrate that orally applied phages of similar size, morphology, and sensitivity to acidic environment may differ in their translocation into the bloodstream. This was evident in mice in which a therapeutic staphylococcal phage A5/80 reached the blood upon oral administration combined with antacid agent whilst T4 phage was not detected even when applied in

103 times higher dose. Our findings also suggest that phage penetration from digestive tract to the blood may be species-specific.

Mikalova, L., Bosak, J., Hribkova, H., Dedicova, D., Benada, O., Smarda, J., and Smajs, D. Novel Temperate Phages of Salmonella enterica subsp. salamae and subsp. diarizonae and Their Activity against Pathogenic S. enterica subsp. enterica Isolates. PLoS.One. 2017; 12(1):e0170734; PM: 28118395

ABSTRACT: Forty strains of Salmonella enterica (S. enterica) subspecies salamae (II), arizonae (IIIa), diarizonae (IIIb), and houtenae (IV) were isolated from human or environmental samples and tested for bacteriophage production. Production of bacteriophages was observed in 15 S. enterica strains (37.5%) belonging to either the subspecies salamae (8 strains) or diarizonae (7 strains). Activity of phages was tested against 52 pathogenic S. enterica subsp. enterica isolates and showed that phages produced by subsp. salamae had broader activity against pathogenic salmonellae compared to phages from the subsp. diarizonae. All 15 phages were analyzed using PCR amplification of phage-specific regions and 9 different amplification profiles were identified. Five phages (SEN1, SEN4, SEN5, SEN22, and SEN34) were completely sequenced and classified as temperate phages. Phages SEN4 and SEN5 were genetically identical, thus representing a single phage type (i.e. SEN4/5). SEN1 and SEN4/5 fit into the group of P2-like phages, while the SEN22 phage showed sequence relatedness to P22-like phages. Interestingly, while phage SEN34 was genetically distantly related to Lambda-like phages (Siphoviridae), it had the morphology of the Myoviridae family. Based on sequence analysis and electron microscopy, phages SEN1 and SEN4/5 were members of the Myoviridae family and phage SEN22 belonged to the Podoviridae family.

Mills, S., Griffin, C., O'Connor, P. M., Serrano, L. M., Meijer, W. C., Hill, C., and Ross, R. P. A Multi-Bacteriocin Cheese Starter System comprising Nisin and Lacticin 3147 in Lactococcus lactis, in Combination with Plantaricin from Lactobacillus plantarum. Appl.Environ.Microbiol. 5-5-2017; PM: 28476774

ABSTRACT: Functional starter cultures demonstrating superior technological and food safety properties are advantageous to the food fermentation industry. We evaluated the efficacy of single and double bacteriocin-producing starters of Lactococcus lactis capable of producing the Class I bacteriocins, nisin A and/or lacticin 3147 in terms of starter performance. Single producers were generated by mobilising the conjugative, bacteriophage resistance plasmid pMRC01, encoding lacticin genetic determinants, or the conjugative transposon Tn5276, encoding nisin genetic determinants, to the commercial starter L. lactis CSK2775. The effect of bacteriocin co-production was examined by superimposing pMRC01 into the newly constructed nisin transconjugant. Transconjugants were improved with regard to antimicrobial activity and bacteriophage insensitivity when compared to the recipient strain and the double producer was immune to both bacteriocins. Bacteriocin production in the starter was stable, although the recipient strain proved to be a more efficient acidifier than transconjugant derivatives. Overall, combining Class I bacteriocins (the double-producer or a combination of single producers) proved as effective as individual bacteriocins for controlling Listeria innocua growth in laboratory-scale cheeses. However, using the double producer in combination with the Class II bacteriocin producer Lactobacillus plantarum, or the lacticin producer with the Class II producer, proved most effective for

reducing bacterial load. As emergence of bacteriocin tolerance was reduced 10-fold in the presence of nisin and lacticin, we suggest that the double producer in conjunction with the Class II producer could serve as a protective culture providing a food-grade, multi-hurdle approach to control pathogenic growth in a variety of industrial applications.IMPORTANCE We generated a suite of single and double-bacteriocin producing starter cultures capable of generating the Class I bacteriocins lacticin 3147 or nisin or both bacteriocins simultaneously via conjugation. The transconjugants exhibited improved bacteriophage resistance and antimicrobial activity. The single producers proved as effective as the double-bacteriocin producer at reducing Listeria numbers in laboratory-scale cheese. However, combining the double producer or the lacticin producing starter with a Class II bacteriocin producer, Lactobacillus plantarum LMG P-26358, proved most effective at reducing Listeria numbers, and was significantly better than a combination of the three bacteriocin producing strains, as the double producer is not inhibited by either of the Class I bacteriocins. Since the simultaneous use of lacticin and nisin should reduce the emergence of bacteriocin tolerant derivatives this study suggests that a protective starter system produced by bacteriocin stacking is a worthwhile multi-hurdle approach for food safety applications.

Miranda, J. A. and Steward, G. F. Variables influencing the efficiency and interpretation of reverse transcription quantitative PCR (RT-qPCR): An empirical study using Bacteriophage MS2. J.Virol.Methods. 2017; 241:1-10; PM: 27940257

ABSTRACT: Reverse transcription, quantitative PCR (RT-qPCR) is a sensitive method for quantification of specific RNA targets, but the first step of the assay, reverse transcription, is notoriously variable and sensitive to reaction conditions. In this study, we used purified Bacteriophage MS2 genomic RNA as a model virus target to test two different RT enzymes (SuperScript II and SuperScript III), two RT-priming strategies (gene-specific primers and random hexamers), and varying background RNA concentrations (0-50ngmul-1) to determine how these variables influence the efficiency of reverse transcription over a range of target concentrations (101-107 copies mul-1). The efficiency of the RT reaction was greatly improved by increasing both background RNA and primer concentrations, but the benefit provided by background RNA was source dependent. At a given target concentration, similar RT efficiencies were achieved with gene-specific primers and random hexamers, but the latter required much higher concentrations. With random hexamers, we observed a systematic variation in RT reaction efficiency as a function of target concentration. Using an RNA standard curve that was also subject to RT effectively normalized for this systematic variability, but the assay accuracy depended critically on the length of the standard RNA extending to the 3' end of the qPCR target site. Our results shed some light on previous contradictory conclusions in the literature, and provide insights that may aid in the design of RT-qPCR assays and the design of synthetic RNA standards when full-length material is not available.

Mizuno, A. Destruction of biological particles using non-thermal plasma. J.Clin.Biochem.Nutr. 2017; 60(1):12-24; PM: 28163377

ABSTRACT: Mechanism of inactivation of bio-particles exposed to non-thermal plasma (NTP), namely, dielectric barrier discharge (DBD), and plasma jet (PJ), has been studied using E. coli, B. subtilis spore, S. cerevisiae and bacteriophages. States of different biological components were monitored during the course of inactivation. Analysis of green fluorescent protein, GFP, introduced into E. coli. or B. subtiles spore cells proved

that radicals generated by NTP penetrate into microbes, destroying the cell membrane and finally damage the genes. We have evaluated the damage of the bacteriophages. Bacteriophage lambda having double stranded DNA was exposed to DBD, then DNA was purified and subjected to in vitro DNA packaging reactions. The re-packaged phages consist of the DNA from discharged phages and brand-new coat proteins were proved to be active, indicating that the damage of coat proteins is responsible for inactivation. M13 phages having single stranded DNA were also examined with the same manner. In this case, damage to the DNA was as severe as that of the coat proteins. For practical applications, DBD showed very intense sterilization ability for B. Subtilis spore with the D-value of less than 10 s. This result indicates a possibility of application of NTP for quick sterilization.

Modell, J. W., Jiang, W., and Marraffini, L. A. CRISPR-Cas systems exploit viral DNA injection to establish and maintain adaptive immunity. Nature. 4-6-2017; 544(7648):101-104; PM: 28355179

ABSTRACT: Clustered regularly interspaced short palindromic repeats (CRISPR)-Cas systems provide protection against viral and plasmid infection by capturing short DNA sequences from these invaders and integrating them into the CRISPR locus of the prokaryotic host. These sequences, known as spacers, are transcribed into short CRISPR RNA guides that specify the cleavage site of Cas nucleases in the genome of the invader. It is not known when spacer sequences are acquired during viral infection. Here, to investigate this, we tracked spacer acquisition in Staphylococcus aureus cells harbouring a type II CRISPR-Cas9 system after infection with the staphylococcal bacteriophage varphi12. We found that new spacers were acquired immediately after infection preferentially from the cos site, the viral free DNA end that is first injected into the cell. Analysis of spacer acquisition after infection with mutant phages demonstrated that most spacers are acquired during DNA injection, but not during other stages of the viral cycle that produce free DNA ends, such as DNA replication or packaging. Finally, we showed that spacers acquired from early-injected genomic regions, which direct Cas9 cleavage of the viral DNA immediately after infection, provide better immunity than spacers acquired from late-injected regions. Our results reveal that CRISPR-Cas systems exploit the phage life cycle to generate a pattern of spacer acquisition that ensures a successful CRISPR immune response.

Moreau, P., Diggle, S. P., and Friman, V. P. Bacterial cell-to-cell signaling promotes the evolution of resistance to parasitic bacteriophages. Ecol.Evol. 2017; 7(6):1936-1941; PM: 28331600

ABSTRACT: The evolution of host-parasite interactions could be affected by intraspecies variation between different host and parasite genotypes. Here we studied how bacterial host cell-to-cell signaling affects the interaction with parasites using two bacteria-specific viruses (bacteriophages) and the host bacterium Pseudomonas aeruginosa that communicates by secreting and responding to quorum sensing (QS) signal molecules. We found that a QS-signaling proficient strain was able to evolve higher levels of resistance to phages during a short-term selection experiment. This was unlikely driven by demographic effects (mutation supply and encounter rates), as nonsignaling strains reached higher population densities in the absence of phages in our selective environment. Instead, the evolved nonsignaling strains suffered relatively higher growth reduction in the absence of the phage, which could have constrained the phage resistance evolution. Complementation experiments with synthetic signal molecules

showed that the Pseudomonas quinolone signal (PQS) improved the growth of nonsignaling bacteria in the presence of a phage, while the activation of las and rhl quorum sensing systems had no effect. Together, these results suggest that QS-signaling can promote the evolution of phage resistance and that the loss of QS-signaling could be costly in the presence of phages. Phage-bacteria interactions could therefore indirectly shape the evolution of intraspecies social interactions and PQS-mediated virulence in P. aeruginosa.

Morley, D., Broniewski, J. M., Westra, E. R., Buckling, A., and van, Houte S. Host diversity limits the evolution of parasite local adaptation. Mol.Ecol. 2017; 26(7):1756-1763; PM: 27862566

ABSTRACT: Specificity in the interactions between hosts and their parasites can lead to local adaptation. However, the degree of local adaptation is predicted to depend upon the diversity of resistance alleles within the host population; increasing host diversity should decrease mean parasite infectivity and hence reduce local adaptation. In this study, we empirically test this prediction using the highly specific interactions between bacteria with clustered regularly interspaced short palindromic repeats/CRISPR-associated (CRISPR/Cas) immunity and their bacteriophage. Bacteria acquire immunity to phage by incorporating a phage-derived spacer sequence into CRISPR loci on the host genome, and phage can escape the CRISPR-mediated immunity of a specific clone by mutating the targeted sequence. We found that high levels of CRISPR allele diversity that naturally evolve in host populations exposed to phage (because each bacterial clone captures a unique phage-derived sequence) prevents phage from becoming locally adapted. By manipulating the number of CRISPR alleles in the host population, we show that phage can become locally adapted to their bacterial hosts but only when CRISPR allele diversity is low.

Motlagh, A. M., Bhattacharjee, A. S., Coutinho, F. H., Dutilh, B. E., Casjens, S. R., and Goel, R. K. Insights of Phage-Host Interaction in Hypersaline Ecosystem through Metagenomics Analyses. Front Microbiol. 2017; 8:352; PM: 28316597

ABSTRACT: Bacteriophages, as the most abundant biological entities on Earth, place significant predation pressure on their hosts. This pressure plays a critical role in the evolution, diversity, and abundance of bacteria. In addition, phages modulate the genetic diversity of prokaryotic communities through the transfer of auxiliary metabolic genes. Various studies have been conducted in diverse ecosystems to understand phage-host interactions and their effects on prokaryote metabolism and community composition. However, hypersaline environments remain among the least studied ecosystems and the interaction between the phages and prokaryotes in these habitats is poorly understood. This study begins to fill this knowledge gap by analyzing bacteriophage-host interactions in the Great Salt Lake, the largest prehistoric hypersaline lake in the Western Hemisphere. Our metagenomics analyses allowed us to comprehensively identify the bacterial and phage communities with Proteobacteria, Firmicutes, and Bacteroidetes as the most dominant bacterial species and Siphoviridae, Myoviridae, and Podoviridae as the most dominant viral families found in the metagenomic sequences. We also characterized interactions between the phage and prokaryotic communities of Great Salt Lake and determined how these interactions possibly influence the community diversity, structure, and biogeochemical cycles. In addition, presence of prophages and their interaction with the prokaryotic host was studied and showed the possibility of prophage induction and subsequent infection of

prokaryotic community present in the Great Salt Lake environment under different environmental stress factors. We found that carbon cycle was the most susceptible nutrient cycling pathways to prophage induction in the presence of environmental stresses. This study gives an enhanced snapshot of phage and prokaryote abundance and diversity as well as their interactions in a hypersaline complex ecosystem, which can pave the way for further research studies.

Mumford, R. and Friman, V. P. Bacterial competition and quorum-sensing signalling shape the eco-evolutionary outcomes of model in vitro phage therapy. Evol.Appl. 2017; 10(2):161-169; PM: 28127392

ABSTRACT: The rapid rise of antibiotic resistance has renewed interest in phage therapy - the use of bacteria-specific viruses (phages) to treat bacterial infections. Even though phages are often pathogen-specific, little is known about the efficiency and eco-evolutionary outcomes of phage therapy in polymicrobial infections. We studied this experimentally by exposing both quorum-sensing (QS) signalling PAO1 and QS-deficient lasR Pseudomonas aeruginosa genotypes (differing in their ability to signal intraspecifically) to lytic PT7 phage in the presence and absence of two bacterial competitors: Staphylococcus aureus and Stenotrophomonas maltophilia-two bacteria commonly associated with P. aeruginosa in polymicrobial cystic fibrosis lung infections. Both the P. aeruginosa genotype and the presence of competitors had profound effects on bacteria and phage densities and bacterial resistance evolution. In general, competition reduced the P. aeruginosa frequencies leading to a lower rate of resistance evolution. This effect was clearer with QS signalling PAO1 strain due to lower bacteria and phage densities and relatively larger pleiotropic growth cost imposed by both phages and competitors. Unexpectedly, phage selection decreased the total bacterial densities in the QS-deficient lasR pathogen communities, while an increase was observed in the QS signalling PAO1 pathogen communities. Together these results suggest that bacterial competition can shape the eco-evolutionary outcomes of phage therapy.

Murray, T. D., Schroeder, B. K., Schneider, W. L., Luster, D. G., Sechler, A., Rogers, E. E., and Subbotin, S. A. Rathayibacter toxicus, Other Rathayibacter Species Inducing Bacterial Head Blight of Grasses, and the Potential for Livestock Poisonings. Phytopathology. 5-15-2017; HYTO02170047RVW; PM: 28414631

ABSTRACT: Rathayibacter toxicus, a Select Agent in the United States, is one of six recognized species in the genus Rathayibacter and the best known due to its association with annual ryegrass toxicity, which occurs only in parts of Australia. The Rathayibacter species are unusual among phytopathogenic bacteria in that they are transmitted by anguinid seed gall nematodes and produce extracellular polysaccharides in infected plants resulting in bacteriosis diseases with common names such as yellow slime and bacterial head blight. R. toxicus is distinguished from the other species by producing corynetoxins in infected plants; toxin production is associated with infection by a bacteriophage. These toxins cause grazing animals feeding on infected plants to develop convulsions and abnormal gate, which is referred to as "staggers," and often results in death of affected animals. R. toxicus is the only recognized Rathayibacter species to produce toxin, although reports of livestock deaths in the United States suggest a closely related toxigenic species may be present. A closely related but undescribed species, Rathayibacter sp. EV, originally isolated from Ehrharta villosa var. villosa in South Africa, is suspected of producing toxin. Many of the diseases caused by Rathayibacter species occur in arid areas and the extracellular polysaccharide they

produce is believed to aid in their survival between crops. For example, R. "agropyri" was isolated from infected plant material after being stored for 50 years in a herbarium. Similarly, the anguinid vectors associated with these bacteria form seed galls in infected plants and are capable of surviving for very long periods of time under dry conditions. The addition of R. toxicus to the list of Select Agents has raised concern over its potential introduction and a realization that current diagnostic methods are inadequate to distinguish among Rathayibacter species. In addition, little is known about the Rathayibacter species and their seed gall nematode vectors present in the United States.

Mustaev, A., Roberts, J., and Gottesman, M. Transcription elongation. Transcription. 2-8-2017; e1289294; PM: 28301288

ABSTRACT: This review is focused on recent progress in understanding how Escherichia coli RNAP polymerase translocates along the DNA template and the factors that affect this movement. We discuss the fundamental aspects of RNAP translocation, template signals that influence forward or backward movement, and host or phage factors that modulate translocation.

Naka, K., Qi, D., Yonesaki, T., and Otsuka, Y. RnlB Antitoxin of the Escherichia coli RnlA-RnlB Toxin-Antitoxin Module Requires RNase HI for Inhibition of RnlA Toxin Activity. Toxins.(Basel). 1-11-2017; 9(1); PM: 28085056

ABSTRACT: The Escherichia coli RnlA-RnlB toxin-antitoxin system is related to the anti-phage mechanism. Under normal growth conditions, an RnlA toxin with endoribonuclease activity is inhibited by binding of its cognate RnlB antitoxin. After bacteriophage T4 infection, RnlA is activated by the disappearance of RnlB, resulting in the rapid degradation of T4 mRNAs and consequently no T4 propagation when T4 dmd encoding a phage antitoxin against RnlA is defective. Intriguingly, E. coli RNase HI, which plays a key role in DNA replication, is required for the activation of RnlA and stimulates the RNA cleavage activity of RnlA. Here, we report an additional role of RNase HI in the regulation of RnlA-RnlB system. Both RNase HI and RnlB are associated with NRD (one of three domains of RnlA). The interaction between RnlB and NRD depends on RNase HI. Exogenous expression of RnlA in wild-type cells has no effect on cell growth because of endogenous RnlB and this inhibition of RnlA toxicity requires RNase HI and NRD. These results suggest that RNase HI recruits RnlB to RnlA through NRD for inhibiting RnlA toxicity and thus plays two contrary roles in the regulation of RnlA-RnlB system.

Nanda, S., Golemi-Kotra, D., McDermott, J. C., Dalai, A. K., Gokalp, I., and Kozinski, J. A. Fermentative production of butanol: Perspectives on synthetic biology. N.Biotechnol. 7-25-2017; 37(Pt B):210-221; PM: 28286167

ABSTRACT: Apprehensions relating to global warming, climate change, pollution, rising energy demands as well as fluctuating crude oil prices and supply are leading to a shift in global interest to find suitable alternatives to fossil fuels. This review aims to highlight the many different facets of butanol as an advanced next-generation transportation biofuel. Butanol has fuel properties almost on a par with gasoline, such as high energy content, low vapor pressure, non-hygroscopic nature, less volatility, flexible fuel blends and high octane number. The paper reviews some recent advances in acetone-butanol-ethanol fermentation with special emphasis on the primary challenges encountered in butanol

fermentation, including butanol toxicity, solvent intolerance and bacteriophage contamination. The mechanisms for butanol recovery techniques have been covered along with their benefits and limitations. A comprehensive discussion of genetic and metabolic engineering of butanol-producing microorganisms is made for the prospective development of industrially-relevant strains that can overcome the technical challenges involved in efficient butanol production.

Nandy, P., Young, M., Haugen, S. P., Katzenmeyer-Pleuss, K., Gordon, E. A., Retta, S. M., Wood, S. C., and Lucas, A. D. Evaluation of one-way valves used in medical devices for prevention of cross-contamination. Am.J.Infect.Control. 3-27-2017; PM: 28359612

ABSTRACT: BACKGROUND: One-way valves used in day use devices (used on multiple patients throughout a day without reprocessing between patients) are intended to reduce the potential for cross-contamination between patients resulting from the backflow of patient fluids. One-way valves are typically designed to withstand high levels of back pressure before failure; however, they may not be explicitly designed as a means of infection control as used in medical device applications. *METHODS*: Five different medical grade one-way valves were placed in low pressure configurations. After flushing in the intended direction of flow, bacteriophage, bacteria, or dye was placed patient side for 24 hours. The upstream device side of the valve was then evaluated for microbial growth or presence of visible dye. *RESULTS*: Leakage (ie, backflow) of the microorganisms occurred with a variety of one-way valve designs across a range of fluid properties tested. *CONCLUSIONS*: This study describes testing of the one-way valves (component-level testing) for the potential of cross-contamination. Although day use medical device systems may use numerous other factors to prevent patient cross-contamination, this work demonstrates that one-way valves themselves may not prevent leakage of contaminated fluid if the fluid is able to reach the upstream side of the one-way valve.

Neamah, M. M., Mir-Sanchis, I., Lopez-Sanz, M., Acosta, S., Baquedano, I., Haag, A. F., Marina, A., Ayora, S., and Penades, J. R. Sak and Sak4 recombinases are required for bacteriophage replication in Staphylococcus aureus. Nucleic Acids Res. 5-5-2017; PM: 28475766

ABSTRACT: DNA-single strand annealing proteins (SSAPs) are recombinases frequently encoded in the genome of many bacteriophages. As SSAPs can promote homologous recombination among DNA substrates with an important degree of divergence, these enzymes are involved both in DNA repair and in the generation of phage mosaicisms. Here, analysing Sak and Sak4 as representatives of two different families of SSAPs present in phages infecting the clinically relevant bacterium Staphylococcus aureus, we demonstrate for the first time that these enzymes are absolutely required for phage reproduction. Deletion of the genes encoding these enzymes significantly reduced phage replication and the generation of infectious particles. Complementation studies revealed that these enzymes are required both in the donor (after prophage induction) and in the recipient strain (for infection). Moreover, our results indicated that to perform their function SSAPs require the activity of their cognate single strand binding (Ssb) proteins. Mutational studies demonstrated that the Ssb proteins are also required for phage replication, both in the donor and recipient strain. In summary, our results expand the functions attributed to the Sak and Sak4 proteins, and demonstrate that both SSAPs and Ssb proteins are essential for the life cycle of temperate staphylococcal phages.

Needham, D. M., Sachdeva, R., and Fuhrman, J. A. Ecological dynamics and co-occurrence among marine phytoplankton, bacteria and myoviruses shows microdiversity matters. ISME.J. 4-11-2017; PM: 28398348

ABSTRACT: Numerous ecological processes, such as bacteriophage infection and phytoplankton-bacterial interactions, often occur via strain-specific mechanisms. Therefore, studying the causes of microbial dynamics should benefit from highly resolving taxonomic characterizations. We sampled daily to weekly over 5 months following a phytoplankton bloom off Southern California and examined the extent of microdiversity, that is, significant variation within 99% sequence similarity clusters, operational taxonomic units (OTUs), of bacteria, archaea, phytoplankton chloroplasts (all via 16S or intergenic spacer (ITS) sequences) and T4-like-myoviruses (via g23 major capsid protein gene sequence). The extent of microdiversity varied between genes (ITS most, g23 least) and only temporally common taxa were highly microdiverse. Overall, 60% of taxa exhibited microdiversity; 59% of these had subtypes that changed significantly as a proportion of the parent taxon, indicating ecologically distinct taxa. Pairwise correlations between prokaryotes and myoviruses or phytoplankton (for example, highly microdiverse Chrysochromulina sp.) improved when using single-base variants. Correlations between myoviruses and SAR11 increased in number (172 vs 9, Spearman>0.65) and became stronger (0.61 vs 0.58, t-test: P<0.001) when using SAR11 ITS single-base variants vs OTUs. Whole-community correlation between SAR11 and myoviruses was much improved when using ITS single-base variants vs OTUs, with Mantel rho=0.49 vs 0.27; these results are consistent with strain-specific interactions. Mantel correlations suggested >1 mum (attached/large) prokaryotes are a major myovirus source. Consideration of microdiversity improved observation of apparent host and virus networks, and provided insights into the ecological and evolutionary factors influencing the success of lineages, with important implications to ecosystem resilience and microbial function.The ISME Journal advance online publication, 11 April 2017; doi:10.1038/ismej.2017.29.

Newton-Northup, J. and Deutscher, S. L. Characterization of In Vivo Selected Bacteriophage for the Development of Novel Tumor-Targeting Agents with Specific Pharmacokinetics and Imaging Applications. Methods Mol.Biol. 2017; 1572:445-465; PM: 28299705

ABSTRACT: Bacteriophage (phage) display technology is a powerful strategy for the identification of peptide-based tumor targeting agents for drug discovery. Phage selections performed in vitro often result in many phage clones/peptides with similar properties and often similar sequence. However, these phage and corresponding peptides are selected, validated, and characterized outside the complicated milieu of a living animal. Thus, there is no guarantee that peptides from in vitro selections will successfully meet the requirements of an in vivo targeting compound. In comparison, in vivo phage display selections have the distinct advantage of identifying phage clones with robust pharmacokinetics and tumor/tissue targeting ability. This capacity has allowed for the identification of peptides with specific in vivo localization and/or clearance profiles. However, in vivo phage display selections also have the potential to result in an array of phage clones with various and unknown targets and little to no sequence similarity. Given these shortcomings, we have developed methods to select phage peptide display libraries in living mice to identify phage (and corresponding synthesized peptides) with specific clearance and/or tumor-targeting propensity. Additionally, we describe the use of labeled phage clones for the efficient screening of

selected phage/peptides to aid in the identification and characterization of a phage clone with an optimal and specific pharmacokinetic profile.

Noppe, W. and Deckmyn, H. Development and screening of epoxy-spacer-phage cryogels for affinity chromatography: Enhancing the binding capacity. J.Sep.Sci. 5-4-2017; PM: 28470771

ABSTRACT: Macroporous epoxy cryogels can be used as an alternative for classical matrices in affinity chromatography. Due to the structural properties of cryogels, with pores of up to 100 mum, crude samples can be processed at high speed without previous manipulations such as clarification or centrifugation. Also, we previously used a peptide-expressing M13 bacteriophage as an affinity ligand. These ligands show high specificity towards the target to be purified. Combination of both, leads to a relative cost-effective one-step chromatographic set-up delivering a high purity sample (>95%), however, so far with limited capacity. To increase the binding capacity of the affinity columns, we now inserted spacers between the chromatographic matrix and the phage ligand. Both linear spacers, di-amino-alkanes (C2-C10) and branched polyethyleneimine spacers with different molecular weights (800 Da - 10 kDa) were analyzed. Two types of peptide expressing phage ligands, a linear 15-mer and a cyclic 6-mer, were used for screening. Up to a tenfold increase in binding capacity was observed depending on the combination of phage ligand and spacer type. This article is protected by copyright. All rights reserved.

Nyambe, S., Burgess, C., Whyte, P., O'Kiely, P., and Bolton, D. The fate of verocytotoxigenic Escherichia coli C600phi3538(Deltavtx2 ::cat) and its vtx2 prophage during grass silage preparation. J.Appl.Microbiol. 2017; 122(5):1197-1206; PM: 28245080

ABSTRACT: AIMS: Silage is grass, preserved by fermentation and used as winter feed for cattle. The impact of a range of current grass silage preparation practices on the survival of Escherichia coli C600phi3538(Deltavtx2 ::cat) and on the induction, release and infectivity of free phage were investigated. *METHODS AND RESULTS*: Wilted and fresh grass samples, from plots with and without slurry application, were ensiled with or without formic acid. Each treatment combination was inoculated with approximately 6 log10 CFU per g E. coli C600phi3538(Deltavtx2 ::cat) (donor strain) and E. coli C600::kanamycinR (recipient strain) in test-tube model silos and incubated in the dark at 15 degrees C. The physico-chemical (pH, ammonia, ethanol, lactic acid and volatile fatty acids) and microbiological (total viable counts, TVC, total Enterobacteriaceae counts, TEC, E. coli counts, ECC and lactic acid bacteria, LAB) properties of each fermentation were monitored throughout the experiment as were the concentrations of E. coli C600phi3538(Deltavtx2 ::cat), E. coli C600::kanamycinR , free phage and transductants, using culture and PCR-based methods. Over the course of the experiment the pH of the grass samples typically decreased by 2 pH units. TVC, TEC and ECC decreased by up to 2.3, 6.4 and 6.2 log10 CFU per g, respectively, while the LAB counts remained relatively stable at 5.2-7.1 log10 CFU per g. Both donor and recipient strains decreased by approximately 5 log10 CFU per g. Free phages were detected in all treatments and transductants were detected and confirmed by PCR in the silo containing wilted grass, pretreated with slurry and ensiled without formic acid. *CONCLUSIONS*: Verocytotoxigenic E. coli may survive the ensiling process and the conditions encountered are sufficient to induce vtx2 bacteriophage leading to low levels of phage-mediated vtx2 gene transfer. *SIGNIFICANCE AND IMPACT OF THE STUDY*: These

studies suggest that the ensiling of grass may create an environment which facilitates the emergence of new verocytotoxigenic E. coli.

O'Brien, E., Munir, M., Marsh, T., Heran, M., Lesage, G., Tarabara, V. V., and Xagoraraki, I. Diversity of DNA viruses in effluents of membrane bioreactors in Traverse City, MI (USA) and La Grande Motte (France). Water Res. 3-15-2017; 111:338-345; PM: 28107747

ABSTRACT: This study assesses diversity of DNA viruses in the effluents of two membrane bioreactor (MBR) wastewater treatment plants (WWTPs): an MBR in the United States and an MBR in France. Viral diversity of these effluents is compared to that of a conventional activated sludge WWTP in the U.S. Diversity analysis indicates Herpesvirales to be the most abundant order of potentially pathogenic human DNA viruses in wastewater treated effluent in all utilities. Other potentially pathogenic human viruses detected include Adenoviridae, Parvoviridae, and Polyomaviridae. Bacteriophage order Caudovirales comprises the majority of DNA virus sequences in the effluent of all utilities. The choice of treatment process (MBR versus activated sludge reactor) utilized had no impact on effluent DNA viral diversity. In contrast, the type of disinfection applied had an impact on the viral diversity present in the effluent.

Oechslin, F., Piccardi, P., Mancini, S., Gabard, J., Moreillon, P., Entenza, J. M., Resch, G., and Que, Y. A. Synergistic Interaction Between Phage Therapy and Antibiotics Clears Pseudomonas Aeruginosa Infection in Endocarditis and Reduces Virulence. J.Infect.Dis. 3-1-2017; 215(5):703-712; PM: 28007922

ABSTRACT: Background: Increasing antibiotic resistance warrants therapeutic alternatives. Here we investigated the efficacy of bacteriophage-therapy (phage) alone or combined with antibiotics against experimental endocarditis (EE) due to Pseudomonas aeruginosa, an archetype of difficult-to-treat infection. *Methods*: In vitro fibrin clots and rats with aortic EE were treated with an antipseudomonas phage cocktail alone or combined with ciprofloxacin. Phage pharmacology, therapeutic efficacy, and resistance were determined. *Results*: In vitro, single-dose phage therapy killed 7 log colony-forming units (CFUs)/g of fibrin clots in 6 hours. Phage-resistant mutants regrew after 24 hours but were prevented by combination with ciprofloxacin (2.5 x minimum inhibitory concentration). In vivo, single-dose phage therapy killed 2.5 log CFUs/g of vegetations in 6 hours ($P < .001$ vs untreated controls) and was comparable with ciprofloxacin monotherapy. Moreover, phage/ciprofloxacin combinations were highly synergistic, killing >6 log CFUs/g of vegetations in 6 hours and successfully treating 64% (n = 7/11) of rats. Phage-resistant mutants emerged in vitro but not in vivo, most likely because resistant mutations affected bacterial surface determinants important for infectivity (eg, the pilT and galU genes involved in pilus motility and LPS formation). *Conclusions*: Single-dose phage therapy was active against P. aeruginosa EE and highly synergistic with ciprofloxacin. Phage-resistant mutants had impaired infectivity. Phage-therapy alone or combined with antibiotics merits further clinical consideration.

Oh, H., Seo, D. J., Jeon, S. B., Park, H., Jeong, S., Chun, H. S., Oh, M., and Choi, C. Isolation and Characterization of Bacillus cereus Bacteriophages from Foods and Soil. Food Environ.Virol. 2-15-2017; PM: 28205130

ABSTRACT: The aim of this study was to isolate and characterize Bacillus cereus

bacteriophages of various origins. Twenty-seven bacteriophages against B. cereus were isolated from various Korean traditional fermented foods and soils. Plaque size, transmission electron microscopy, virulence profile, and in vitro lytic activity of bacteriophage isolates were examined. Transmission electron microscopy confirmed B. cereus bacteriophages belonging to the family Siphoviridae. Among B. cereus bacteriophages with broad host range, 18 isolates (66.7%) did not harbor any B. cereus virulence factors. Among them, bacteriophage strain CAU150036, CAU150038, CAU150058, CAU150064, CAU150065, and CAU150066 effectively inhibited B. cereus in vitro within 1 h. Therefore, they are considered potential candidates for controlling the contamination of B. cereus in food or other applications.

Oliveira, H., Pinto, G., Oliveira, A., Noben, J. P., Hendrix, H., Lavigne, R., Lobocka, M., Kropinski, A. M., and Azeredo, J. Characterization and genomic analyses of two newly isolated Morganella phages define distant members among Tevenvirinae and Autographivirinae subfamilies. Sci.Rep. 4-7-2017; 7:46157; PM: 28387353

ABSTRACT: Morganella morganii is a common but frequent neglected environmental opportunistic pathogen which can cause deadly nosocomial infections. The increased number of multidrug-resistant M. morganii isolates motivates the search for alternative and effective antibacterials. We have isolated two novel obligatorily lytic M. morganii bacteriophages (vB_MmoM_MP1, vB_MmoP_MP2) and characterized them with respect to specificity, morphology, genome organization and phylogenetic relationships. MP1's dsDNA genome consists of 163,095 bp and encodes 271 proteins, exhibiting low DNA (<40%) and protein (<70%) homology to other members of the Tevenvirinae. Its unique property is a >10 kb chromosomal inversion that encompass the baseplate assembly and head outer capsid synthesis genes when compared to other T-even bacteriophages. MP2 has a dsDNA molecule with 39,394 bp and encodes 55 proteins, presenting significant genomic (70%) and proteomic identity (86%) but only to Morganella bacteriophage MmP1. MP1 and MP2 are then novel members of Tevenvirinae and Autographivirinae, respectively, but differ significantly from other tailed bacteriophages of these subfamilies to warrant proposing new genera. Both bacteriophages together could propagate in 23 of 27 M. morganii clinical isolates of different origin and antibiotic resistance profiles, making them suitable for further studies on a development of bacteriophage cocktail for potential therapeutic applications.

Ozaki, T., Abe, N., Kimura, K., Suzuki, A., and Kaneko, J. Genomic analysis of Bacillus subtilis lytic bacteriophage varphiNIT1 capable of obstructing natto fermentation carrying genes for the capsule-lytic soluble enzymes poly-gamma-glutamate hydrolase and levanase. Biosci.Biotechnol.Biochem. 2017; 81(1):135-146; PM: 27885938

ABSTRACT: Bacillus subtilis strains including the fermented soybean (natto) starter produce capsular polymers consisting of poly-gamma-glutamate and levan. Capsular polymers may protect the cells from phage infection. However, bacteriophage varphiNIT1 carries a gamma-PGA hydrolase gene (pghP) that help it to counteract the host cell's protection strategy. varphiNIT had a linear double stranded DNA genome of 155,631-bp with a terminal redundancy of 5,103-bp, containing a gene encoding an active levan hydrolase. These capsule-lytic enzyme genes were located in the possible foreign gene cluster regions between central core and terminal redundant regions, and were expressed at the late phase of the phage lytic cycle. All tested natto origin

Spounavirinae phages carried both genes for capsule degrading enzymes similar to varphiNIT1. A comparative genomic analysis revealed the diversity among varphiNIT1 and Bacillus phages carrying pghP-like and levan-hydrolase genes, and provides novel understanding on the acquisition mechanism of these enzymatic genes.

Pan, Y. J., Lin, T. L., Chen, C. C., Tsai, Y. T., Cheng, Y. H., Chen, Y. Y., Hsieh, P. F., Lin, Y. T., and Wang, J. T. Klebsiella Phage PhiK64-1 Encodes Multiple Depolymerases for Multiple Host Capsular Types. J.Virol. 3-15-2017; 91(6); PM: 28077636

ABSTRACT: The genome of the multihost bacteriophage PhiK64-1, capable of infecting Klebsiella capsular types K1, K11, K21, K25, K30, K35, K64, and K69, as well as new capsular types KN4 and KN5, was analyzed and revealed that 11 genes (S1-1, S1-2, S1-3, S2-1, S2-2, S2-3, S2-4, S2-5, S2-6, S2-7, and S2-8) encode proteins with amino acid sequence similarity to tail fibers/spikes or lyases. S2-5 previously was shown to encode a K64 capsule depolymerase (K64dep). Specific capsule-degrading activities of an additional eight putative capsule depolymerases (S2-4 against K1, S1-1 against K11, S1-3 against K21, S2-2 against K25, S2-6 against K30/K69, S2-3 against K35, S1-2 against KN4, and S2-1 against KN5) was demonstrated by expression and purification of the recombinant proteins. Consistent with the capsular type-specific depolymerization activity of these gene products, phage mutants of S1-2, S2-2, S2-3, or S2-6 lost infectivity for KN4, K25, K35, or K30/K69, respectively, indicating that capsule depolymerase is crucial for infecting specific hosts. In conclusion, we identified nine functional capsule depolymerase-encoding genes in a bacteriophage and correlated activities of the gene products to all ten hosts of this phage, providing an example of type-specific host infection mechanisms in a multihost bacteriophage.IMPORTANCE We currently identified eight novel capsule depolymerases in a multihost Klebsiella bacteriophage and correlated the activities of the gene products to all hosts of this phage, providing an example of carriage of multiple depolymerases in a phage with a wide capsular type host spectrum. Moreover, we also established a recombineering system for modification of Klebsiella bacteriophage genomes and demonstrated the importance of capsule depolymerase for infecting specific hosts. Based on the powerful tool for modification of phage genome, further studies can be conducted to improve the understanding of mechanistic details of Klebsiella phage infection. Furthermore, the newly identified capsule depolymerases will be of great value for applications in capsular typing.

Pang, H., Lambertini, E., Buchanan, R. L., Schaffner, D. W., and Pradhan, A. K. Quantitative Microbial Risk Assessment for Escherichia coli O157:H7 in Fresh-Cut Lettuce. J.Food Prot. 2017; 80(2):302-311; PM: 28221978

ABSTRACT: Leafy green vegetables, including lettuce, are recognized as potential vehicles for foodborne pathogens such as Escherichia coli O157:H7. Fresh-cut lettuce is potentially at high risk of causing foodborne illnesses, as it is generally consumed without cooking. Quantitative microbial risk assessments (QMRAs) are gaining more attention as an effective tool to assess and control potential risks associated with foodborne pathogens. This study developed a QMRA model for E. coli O157:H7 in fresh-cut lettuce and evaluated the effects of different potential intervention strategies on the reduction of public health risks. The fresh-cut lettuce production and supply chain was modeled from field production, with both irrigation water and soil as initial contamination sources, to consumption at home. The baseline model (with no interventions) predicted a mean probability of 1 illness per 10 million servings and a mean of 2,160 illness cases per year in

the United States. All intervention strategies evaluated (chlorine, ultrasound and organic acid, irradiation, bacteriophage, and consumer washing) significantly reduced the estimated mean number of illness cases when compared with the baseline model prediction (from 11.4- to 17.9-fold reduction). Sensitivity analyses indicated that retail and home storage temperature were the most important factors affecting the predicted number of illness cases. The developed QMRA model provided a framework for estimating risk associated with consumption of E. coli O157:H7-contaminated fresh-cut lettuce and can guide the evaluation and development of intervention strategies aimed at reducing such risk.

Pankert, T., Jegou, T., Caudron-Herger, M., and Rippe, K. Tethering RNA to chromatin for fluorescence microscopy based analysis of nuclear organization. Methods. 2-14-2017; PM: 28213279

ABSTRACT: Nuclear RNAs emerge as important factors to orchestrate the dynamic organization of the nucleus into functional subcompartments. By tethering RNAs to distinct genomic loci, RNA-dependent chromatin changes can be dissected by fluorescence microscopic analysis. Here we describe how this approach is implemented in mammalian cells. It involves two high-affinity protein-nucleic acid interactions that can be established with a number of different protein domains and DNA and RNA sequences. A prototypic system is described here in detail: It consists of the binding of MS2 bacteriophage coat protein to its RNA recognition sequence and the interaction between the bacterial LacI repressor protein to its target lacO operator DNA sequence. Via these interactions RNAs tagged with the MS2 recognition sequences can be recruited to a locus with integrated lacO repeats. By inducing RNA-chromatin binding a number of RNA-dependent activities can be dissected: (i) The RNA-induced compaction or decondensation of chromatin, (ii) identification of RNA-interacting chromatin modifiers that set epigenetic signals such as posttranslational histone modifications, and (iii) nuclear relocation of a genomic locus targeted by the tethered RNA. Thus, a variety of RNA-dependent activities can be evaluated with the MS2-LacI system, which are crucial for understanding how RNA shapes nuclear organization.

Parmar, K. M., Hathi, Z. J., and Dafale, N. A. Control of Multidrug-Resistant Gene Flow in the Environment Through Bacteriophage Intervention. Appl.Biochem.Biotechnol. 2017; 181(3):1007-1029; PM: 27723009

ABSTRACT: The spread of multidrug-resistant (MDR) bacteria is an emerging threat to the environment and public wellness. Inappropriate use and indiscriminate release of antibiotics in the environment through un-metabolized form create a scenario for the emergence of virulent pathogens and MDR bugs in the surroundings. Mechanisms underlying the spread of resistance include horizontal and vertical gene transfers causing the transmittance of MDR genes packed in different host, which pass across different food webs. Several controlling agents have been used for combating pathogens; however, the use of lytic bacteriophages proves to be one of the most eco-friendly due to their specificity, killing only target bacteria without damaging the indigenous beneficial flora of the habitat. Phages are part of the natural microflora present in different environmental niches and are remarkably stable in the environment. Diverse range of phage products, such as phage enzymes, phage peptides having antimicrobial properties, and phage cocktails also have been used to eradicate pathogens along with whole phages. Recently, the ability of phages to control pathogens has extended

from the different areas of medicine, agriculture, aquaculture, food industry, and into the environment. To avoid the arrival of pre-antibiotic epoch, phage intervention proves to be a potential option to eradicate harmful pathogens generated by the MDR gene flow which are uneasy to cure by conventional treatments.

Parmar, K. M., Gaikwad, S. L., Dhakephalkar, P. K., Kothari, R., and Singh, R. P. Intriguing Interaction of Bacteriophage-Host Association: An Understanding in the Era of Omics. Front Microbiol. 2017; 8:559; PM: 28439260

ABSTRACT: Innovations in next-generation sequencing technology have introduced new avenues in microbial studies through "omics" approaches. This technology has considerably augmented the knowledge of the microbial world without isolation prior to their identification. With an enormous volume of bacterial "omics" data, considerable attempts have been recently invested to improve an insight into virosphere. The interplay between bacteriophages and their host has created a significant influence on the biogeochemical cycles, microbial diversity, and bacterial population regulation. This review highlights various concepts such as genomics, transcriptomics, proteomics, and metabolomics to infer the phylogenetic affiliation and function of bacteriophages and their impact on diverse microbial communities. Omics technologies illuminate the role of bacteriophage in an environment, the influences of phage proteins on the bacterial host and provide information about the genes important for interaction with bacteria. These investigations will reveal some of bio-molecules and biomarkers of the novel phage which demand to be unveiled.

Patel, A. N., Anne, A., Chovin, A., Demaille, C., Grelet, E., Michon, T., and Taofifenua, C. Scaffolding of Enzymes on Virus Nanoarrays: Effects of Confinement and Virus Organization on Biocatalysis. Small. 2017; 13(13); PM: 28098963

ABSTRACT: Organizing active enzyme molecules on nanometer-sized scaffolds is a promising strategy for designing highly efficient supported catalytic systems for biosynthetic and sensing applications. This is achieved by designing model nanoscale enzymatic platforms followed by thorough analysis of the catalytic activity. Herein, the virus fd bacteriophage is considered as an enzyme nanocarrier to study the scaffolding effects on enzymatic activity. Nanoarrays of randomly oriented, or directionally patterned, fd bacteriophage virus are functionalized with the enzyme glucose oxidase (GOx), using an immunological assembly strategy, directly on a gold electrode support. The scaffolding process on the virus capsid is monitored in situ by AFM (atomic force microscopy) imaging, while cyclic voltammetry is used to interrogate the catalytic activity of the resulting functional GOx-fd nanoarrays. Kinetic analysis reveals the ability to modulate the activity of GOx via nanocarrier patterning. The results evidence, for the first time, enhancement of the enzymatic activity due to scaffolding on a filamentous viral particle.

Pereira, C., Moreirinha, C., Teles, L., Rocha, R. J., Calado, R., Romalde, J. L., Nunes, M. L., and Almeida, A. Application of phage therapy during bivalve depuration improves Escherichia coli decontamination. Food Microbiol. 2017; 61:102-112; PM: 27697159

ABSTRACT: The present study investigated the potential application of the bacteriophage (or phage) phT4A, ECA2 and the phage cocktail phT4A/ECA2 to decrease the concentration of Escherichia coli during the depuration of natural and

artificially contaminated cockles. Depuration in static seawater at multiplicity of infection (MOI) of 1 with single phage suspensions of phT4A and ECA2 was the best condition, as it decreased by approximately 2.0 log CFU/g the concentration of E. coli in artificially contaminated cockles after a 4 h of treatment. When naturally contaminated cockles were treated in static seawater with single phage suspensions and the phage cocktail, similar decreases in the concentration of E. coli (approximately 0.7 log CFU/g) were achieved. However, when employing the phage cocktail, a longer treatment time was required to obtain comparable results to those achieved when using single phage suspensions. When naturally contaminated cockles were depurated with phage phT4A in a recirculated seawater system (mimicking industrial depuration conditions), a 0.6 log CFU/g reduction of E. coli was achieved after a 2 h of treatment. When the depuration process was performed without phage addition, a 4 h treatment was necessary to obtain a similar decrease. By combining phage therapy and depuration procedures, a reduction in bivalves depuration period can be achieved for, thus decreasing the cost associated with this procedure and even enhance the quality and safety of depurated bivalves destined for human consumption.

Peters, D. L., Stothard, P., and Dennis, J. J. The isolation and characterization of Stenotrophomonas maltophilia T4-like bacteriophage DLP6. PLoS.One. 2017; 12(3):e0173341; PM: 28291834

ABSTRACT: Increasing isolation of the extremely antibiotic resistant bacterium Stenotrophomonas maltophilia has caused alarm worldwide due to the limited treatment options available. A potential treatment option for fighting this bacterium is 'phage therapy', the clinical application of bacteriophages to selectively kill bacteria. Bacteriophage DLP6 (vB_SmoM-DLP6) was isolated from a soil sample using clinical isolate S. maltophilia strain D1571 as host. Host range analysis of phage DLP6 against 27 clinical S. maltophilia isolates shows successful infection and lysis in 13 of the 27 isolates tested. Transmission electron microscopy of DLP6 indicates that it is a member of the Myoviridae family. Complete genome sequencing and analysis of DLP6 reveals its richly recombined evolutionary history, featuring a core of both T4-like and cyanophage genes, which suggests that it is a member of the T4-superfamily. Unlike other T4-superfamily phages however, DLP6 features a transposase and ends with 229 bp direct terminal repeats. The isolation of this bacteriophage is an exciting discovery due to the divergent nature of DLP6 in relation to the T4-superfamily of phages.

Petrenko, V. A. and Gillespie, J. W. Paradigm shift in bacteriophage-mediated delivery of anticancer drugs: from targeted 'magic bullets' to self-navigated 'magic missiles'. Expert.Opin.Drug Deliv. 2017; 14(3):373-384; PM: 27466706

ABSTRACT: INTRODUCTION: New phage-directed nanomedicines have emerged recently as a result of the in-depth study of the genetics and structure of filamentous phage and evolution of phage display and phage nanobiotechnology. This review focuses on the progress made in the development of the cancer-targeted nanomaterials and discusses the trends in using phage as a bioselectable molecular navigation system. Areas covered: The merging of phage display technologies with nanotechnology in recent years has proved promising in different areas of medicine and technology, such as medical diagnostics, molecular imaging, vaccine development and targeted drug/gene delivery, which is the focus of this review. The authors used data obtained from their research group and sourced using Science Citation Index (Web of Science)

and NCBI PubMed search resources. *Expert opinion*: First attempts of adapting traditional concepts of direct targeting of tumor using phage-targeted nanomedicines has shown minimal improvements. With discovery and study of biological and technical barriers that prevent anti-tumor drug delivery, a paradigm shift from traditional drug targeting to nanomedicine navigation systems is required. The advanced bacteriophage-driven self-navigation systems are thought to overcome those barriers using more precise, localized phage selection methods, multi-targeting 'promiscuous' ligands and advanced multifunctional nanomedicine platforms.

Petrovic, A., Kostanjsek, R., Rakhely, G., and Knezevic, P. The First Siphoviridae Family Bacteriophages Infecting Bordetella bronchiseptica Isolated from Environment. Microb.Ecol. 2017; 73(2):368-377; PM: 27628741

ABSTRACT: Bordetella bronchiseptica is a well-known etiological agent of kennel cough in dogs and cats and one of the two causative agents of atrophic rhinitis, a serious swine disease. The aim of the study was to isolate B. bronchiseptica bacteriophages from environmental samples for the first time. A total of 29 phages from 65 water samples were isolated using the strain ATCC 10580 as a host. The lytic spectra of the phages were examined at 25 and 37 degrees C, using 12 strains of B. bronchiseptica. All phages were able to plaque on 25.0 % to 41.7 % of the strains. The selected phages showed similar morphology (Siphoviridae, morphotype B2), but variation of RFLP patterns and efficacy of plating on various strains. The partial genome sequence of phage vB_BbrS_CN1 showed its similarity to phages from genus Yuavirus. Using PCR, it was confirmed that the phages do not originate from the host strain, and environmental origin was additionally confirmed by the analysis of host genome sequence in silico and plating heated and unheated samples in parallel. Accordingly, this is the first isolation of B. bronchiseptica phages from environment and the first isolation and characterization of phages of B. bronchiseptica belonging to family Siphoviridae.

Pfreundt, U., Spungin, D., Hou, S., Voss, B., Berman-Frank, I., and Hess, W. R. Genome of a giant bacteriophage from a decaying Trichodesmium bloom. Mar.Genomics. 2-22-2017; PM: 28237778

ABSTRACT: De-novo assembly of a metagenomic dataset obtained from a decaying cyanobacterial Trichodesmium bloom from the New Caledonian lagoon resulted in a complete giant phage genome of 257,908bp, obtained independently with multiple assembly tools. Noteworthy, gammaproteobacteria were an abundant fraction in the sequenced samples. Mapping of the raw reads with 99% accuracy to the giant phage genome resulted in an average coverage of 262X. The closest sequenced relatives, albeit still distant, are the Pseudomonas phages PaBG from Lake Baikal and Lu11 isolated from a soil sample from the Philippines. The phage reported here might belong to the same family within the Myoviridae as PaBG and Lu11 and would thus be its first marine member, indicating a more widespread occurrence of this group. We named this phage NCTB (New Caledonia Trichodesmium Bloom) after its origin.

Phelps, C., Israels, B., Jose, D., Marsh, M. C., von Hippel, P. H., and Marcus, A. H. Using microsecond single-molecule FRET to determine the assembly pathways of T4 ssDNA binding protein onto model DNA replication forks. Proc.Natl.Acad.Sci.U.S.A. 5-2-2017; 114(18):E3612-E3621; PM: 28416680

ABSTRACT: DNA replication is a core biological process that occurs in prokaryotic cells at high speeds (approximately 1 nucleotide residue added per millisecond) and with high fidelity (fewer than one misincorporation event per 107 nucleotide additions). The ssDNA binding protein [gene product 32 (gp32)] of the T4 bacteriophage is a central integrating component of the replication complex that must continuously bind to and unbind from transiently exposed template strands during DNA synthesis. We here report microsecond single-molecule FRET (smFRET) measurements on Cy3/Cy5-labeled primer-template (p/t) DNA constructs in the presence of gp32. These measurements probe the distance between Cy3/Cy5 fluorophores that label the ends of a short (15-nt) segment of ssDNA attached to a model p/t DNA construct and permit us to track the stochastic interconversion between various protein bound and unbound states. The length of the 15-nt ssDNA lattice is sufficient to accommodate up to two cooperatively bound gp32 proteins in either of two positions. We apply a unique multipoint time correlation function analysis to the microsecond-resolved smFRET data obtained to determine and compare the kinetics of various possible reaction pathways for the assembly of cooperatively bound gp32 protein onto ssDNA sequences located at the replication fork. The results of our analysis reveal the presence and translocation mechanisms of short-lived intermediate bound states that are likely to play a critical role in the assembly mechanisms of ssDNA binding proteins at replication forks and other ss duplex junctions.

Piya, D., Vara, L., Russell, W. K., Young, R., and Gill, J. J. The multi-component antirestriction system of phage P1 is linked to capsid morphogenesis. Mol.Microbiol. 5-16-2017; PM: 28509398

ABSTRACT: Bacterial Type I restriction-modification (R-M) systems present a major barrier to foreign DNA entering the bacterial cell. The temperate phage P1 packages several proteins into the virion that protect the phage DNA from host restriction. Isogenic P1 deletion mutants were used to reconstitute the previously described restriction phenotypes associated with darA and darB. While P1DeltadarA and P1DeltadarB produced the expected phenotypes, deletions of adjacent genes hdf and ddrA also produced darA-like phenotypes and deletion of ulx produced a darB-like phenotype, implicating several new proteins of previously unknown function in the P1 dar antirestriction system. Interestingly, disruption of ddrB decreased P1's sensitivity to EcoB and EcoK restriction. Proteomic analysis of purified virions suggests that packaging of antirestriction components into P1 virions follows a distinct pathway that begins with the incorporation of DarA and Hdf and concludes with DarB and Ulx. Electron microscopy analysis showed that hdf and darA mutants also produce abnormally high proportions of virions with aberrant small heads, which suggests Hdf and DarA play a role in capsid morphogenesis. The P1 antirestriction system is more complex than previously realized and is comprised of multiple proteins including DdrA, DdrB, Hdf, and Ulx in addition to DarA and DarB. This article is protected by copyright. All rights reserved.

Pokhilko, A., Zhao, J., Stark, W. M., Colloms, S. D., and Ebenhoh, O. A simplified mathematical model of directional DNA site-specific recombination by serine integrases. J.R.Soc.Interface. 2017; 14(126); PM: 28077763

ABSTRACT: Serine integrases catalyse site-specific recombination to integrate and excise bacteriophage genomes into and out of their host's genome. These enzymes exhibit remarkable directionality; in the presence of the integrase alone, recombination

between attP and attB DNA sites is efficient and irreversible, giving attL and attR products which do not recombine further. However, in the presence of the bacteriophage-encoded recombination directionality factor (RDF), integrase efficiently promotes recombination between attL and attR to re-form attP and attB The DNA substrates and products of both reactions are approximately isoenergetic, and no cofactors (such as adenosine triphosphate) are required for recombination. The thermodynamic driving force for directionality of these reactions is thus enigmatic. Here, we present a minimal mathematical model which can explain the directionality and regulation of both 'forward' and 'reverse' reactions. In this model, the substrates of the 'forbidden' reactions (between attL and attR in the absence of RDF, attP and attB in the presence of RDF) are trapped as inactive protein-DNA complexes, ensuring that these 'forbidden' reactions are extremely slow. The model is in good agreement with the observed in vitro kinetics of recombination by varphiC31 integrase, and defines core features of the system necessary and sufficient for directionality.

Pourcel, C., Midoux, C., Hauck, Y., Vergnaud, G., and Latino, L. Large Preferred Region for Packaging of Bacterial DNA by phiC725A, a Novel Pseudomonas aeruginosa F116-Like Bacteriophage. PLoS.One. 2017; 12(1):e0169684; PM: 28060939

ABSTRACT: Bacteriophage vB_PaeP_PAO1_phiC725A (short name phiC725A) was isolated following mitomycin C induction of C7-25, a clinical Pseudomonas aeruginosa strain carrying phiC725A as a prophage. The phiC725A genome sequence shows similarity to F116, a P. aeruginosa podovirus capable of generalized transduction. Likewise, phiC725A is a podovirus with long tail fibers. PhiC725A was able to lysogenize two additional P. aeruginosa strains in which it was maintained both as a prophage and in an episomal state. Investigation by deep sequencing showed that bacterial DNA carried inside phage particles originated predominantly from a 700-800kb region, immediately flanking the attL prophage insertion site, whether the phages were induced from a lysogen or recovered after infection. This indicates that during productive replication, recombination of phage genomes with the bacterial chromosome at the att site occurs occasionally, allowing packaging of adjacent bacterial DNA.

Pramono, K., Kuwahara, H., Itoh, T., Toyoda, A., Yamada, A., and Hongoh, Y. Discovery and Complete Genome Sequence of a Bacteriophage from an Obligate Intracellular Symbiont of a Cellulolytic Protist in the Termite Gut. Microbes.Environ. 3-17-2017; PM: 28321010

ABSTRACT: Termites depend nutritionally on their gut microbes, and protistan, bacterial, and archaeal gut communities have been extensively studied. However, limited information is available on viruses in the termite gut. We herein report the complete genome sequence (99,517 bp) of a phage obtained during a genome analysis of "Candidatus Azobacteroides pseudotrichonymphae" phylotype ProJPt-1, which is an obligate intracellular symbiont of the cellulolytic protist Pseudotrichonympha sp. in the gut of the termite Prorhinotermes japonicus. The genome of the phage, designated ProJPt-Bp1, was circular or circularly permuted, and was not integrated into the two circular chromosomes or five circular plasmids composing the host ProJPt-1 genome. The phage was putatively affiliated with the order Caudovirales based on sequence similarities with several phage-related genes; however, most of the 52 protein-coding sequences had no significant homology to sequences in the databases. The phage genome contained a tRNA-Gln (CAG) gene, which showed the highest sequence

similarity to the tRNA-Gln (CAA) gene of the host "Ca. A. pseudotrichonymphae" phylotype ProJPt-1. Since the host genome lacked a tRNA-Gln (CAG) gene, the phage tRNA gene may compensate for differences in codon usage bias between the phage and host genomes. The phage genome also contained a non-coding region with high nucleotide sequence similarity to a region in one of the host plasmids. No other phage-related sequences were found in the host ProJPt-1 genome. To the best of our knowledge, this is the first report of a phage from an obligate, mutualistic endosymbiont permanently associated with eukaryotic cells.

Pretorius, I. S. Synthetic genome engineering forging new frontiers for wine yeast. Crit Rev.Biotechnol. 2017; 37(1):112-136; PM: 27535766

ABSTRACT: Over the past 15 years, the seismic shifts caused by the convergence of biomolecular, chemical, physical, mathematical, and computational sciences alongside cutting-edge developments in information technology and engineering have erupted into a new field of scientific endeavor dubbed Synthetic Biology. Recent rapid advances in high-throughput DNA sequencing and DNA synthesis techniques are enabling the design and construction of new biological parts (genes), devices (gene networks) and modules (biosynthetic pathways), and the redesign of biological systems (cells and organisms) for useful purposes. In 2014, the budding yeast Saccharomyces cerevisiae became the first eukaryotic cell to be equipped with a fully functional synthetic chromosome. This was achieved following the synthesis of the first viral (poliovirus in 2002 and bacteriophage Phi-X174 in 2003) and bacterial (Mycoplasma genitalium in 2008 and Mycoplasma mycoides in 2010) genomes, and less than two decades after revealing the full genome sequence of a laboratory (S288c in 1996) and wine (AWRI1631 in 2008) yeast strain. A large international project - the Synthetic Yeast Genome (Sc2.0) Project - is now underway to synthesize all 16 chromosomes (approximately 12 Mb carrying approximately 6000 genes) of the sequenced S288c laboratory strain by 2018. If successful, S. cerevisiae will become the first eukaryote to cross the horizon of in silico design of complex cells through de novo synthesis, reshuffling, and editing of genomes. In the meantime, yeasts are being used as cell factories for the semi-synthetic production of high-value compounds, such as the potent antimalarial artemisinin, and food ingredients, such as resveratrol, vanillin, stevia, nootkatone, and saffron. As a continuum of previously genetically engineered industrially important yeast strains, precision genome engineering is bound to also impact the study and development of wine yeast strains supercharged with synthetic DNA. The first taste of what the future holds is the de novo production of the raspberry ketone aroma compound, 4-[4-hydroxyphenyl]butan-2-one, in a wine yeast strain (AWRI1631), which was recently achieved via metabolic pathway engineering and synthetic enzyme fusion. A peek over the horizon is revealing that the future of "Wine Yeast 2.0" is already here. Therefore, this article seeks to help prepare the wine industry - an industry rich in history and tradition on the one hand, and innovation on the other - for the inevitable intersection of the ancient art practiced by winemakers and the inventive science of pioneering "synthetic genomicists". It would be prudent to proactively engage all stakeholders - researchers, industry practitioners, policymakers, regulators, commentators, and consumers - in a meaningful dialog about the potential challenges and opportunities emanating from Synthetic Biology. To capitalize on the new vistas of synthetic yeast genomics, this paper presents wine yeast research in a fresh context, raises important questions and proposes new directions.

Prokhorov, N. S., Riccio, C., Zdorovenko, E. L., Shneider, M. M., Browning, C., Knirel, Y. A., Leiman, P. G., and Letarov, A. V. Function of bacteriophage G7C esterase tailspike in host cell adsorption. Mol.Microbiol. 5-17-2017; PM: 28513100

ABSTRACT: Bacteriophages recognize and bind to their hosts with the help of receptor-binding proteins (RBPs) that emanate from the phage particle in the form of fibers or tailspikes. RBPs show a great variability in their shapes, sizes, and location on the particle. Some RBPs are known to depolymerize surface polysaccharides of the host while others show no enzymatic activity. Here we report that both RBPs of podovirus.

Qin, K., Ji, X., Zhang, C., Ding, Y., Kuang, A., Zhang, S., Zhang, Q., Lin, L., and Wei, Y. Isolation and characterization of wetland VSW-3, a novel lytic cold-active bacteriophage of Pseudomonas fluorescens. Can.J.Microbiol. 2017; 63(2):110-118; PM: 28001438

ABSTRACT: Wetlands are often called the "kidneys of the Earth" and contribute substantially to environmental improvement. Pseudomonas fluorescens is a major contaminant of milk products and causes the spoilage of refrigerated foods and fresh poultry. In this study, we isolated and characterized a lytic cold-active bacteriophage named VSW-3 together with P. fluorescens SW-3 cells from the Napahai wetland in China. Electron microscopy showed that VSW-3 had an icosahedral head (56 nm) and a tapering tail (20 nm x 12 nm) and a genome size of approximate 40 kb. On the basis of the top-scoring hits in the BLASTP analysis, VSW-3 showed a high degree of module similarity to the Pseudomonas phages Andromeda and Bf7. The latent and burst periods were 45 and 20 min, respectively, with an average burst size of 90 phage particles per infected cell. The pH and thermal stability of VSW-3 were also explored. The optimal pH was found to be 7.0 and the activity decreased rapidly when the temperature exceeded 60 degrees C. VSW-3 is a cold-active bacteriophage, hence, it is important to research its ability to prevent product contamination caused by P. fluorescens and to characterize its relationship with its host P. fluorescens in the future.

Quigley, B. J. Z., Brown, S. P., Leggett, H. C., Scanlan, P. D., and Buckling, A. Within-host interference competition can prevent invasion of rare parasites. Parasitology. 5-15-2017; 1-6; PM: 28502267

ABSTRACT: Competition between parasite species or genotypes can play an important role in the establishment of parasites in new host populations. Here, we investigate a mechanism by which a rare parasite is unable to establish itself in a host population if a common resident parasite is already present (a 'priority effect'). We develop a simple epidemiological model and show that a rare parasite genotype is unable to invade if coinfecting parasite genotypes inhibit each other's transmission more than expected from simple resource partitioning. This is because a rare parasite is more likely to be in multiply-infected hosts than the common genotype, and hence more likely to pay the cost of reduced transmission. Experiments competing interfering clones of bacteriophage infecting a bacterium support the model prediction that the clones are unable to invade each other from rare. We briefly discuss the implications of these results for host-parasite ecology and (co)evolution.

Quinn, C. M. and Polenova, T. Structural biology of supramolecular assemblies by magic-angle spinning NMR spectroscopy. Q.Rev.Biophys. 2017; 50:e1; PM: 28093096

ABSTRACT: In recent years, exciting developments in instrument technology and experimental methodology have advanced the field of magic-angle spinning (MAS) nuclear magnetic resonance (NMR) to new heights. Contemporary MAS NMR yields atomic-level insights into structure and dynamics of an astounding range of biological systems, many of which cannot be studied by other methods. With the advent of fast MAS, proton detection, and novel pulse sequences, large supramolecular assemblies, such as cytoskeletal proteins and intact viruses, are now accessible for detailed analysis. In this review, we will discuss the current MAS NMR methodologies that enable characterization of complex biomolecular systems and will present examples of applications to several classes of assemblies comprising bacterial and mammalian cytoskeleton as well as human immunodeficiency virus 1 and bacteriophage viruses. The body of work reviewed herein is representative of the recent advancements in the field, with respect to the complexity of the systems studied, the quality of the data, and the significance to the biology.

Quistad, S. D., Grasis, J. A., Barr, J. J., and Rohwer, F. L. Viruses and the origin of microbiome selection and immunity. ISME.J. 2017; 11(4):835-840; PM: 27983723

ABSTRACT: The last common metazoan ancestor (LCMA) emerged over half a billion years ago. These complex metazoans provided newly available niche space for viruses and microbes. Modern day contemporaries, such as cnidarians, suggest that the LCMA consisted of two cell layers: a basal endoderm and a mucus-secreting ectoderm, which formed a surface mucus layer (SML). Here we propose a model for the origin of metazoan immunity based on external and internal microbial selection mechanisms. In this model, the SML concentrated bacteria and their associated viruses (phage) through physical dynamics (that is, the slower flow fields near a diffusive boundary layer), which selected for mucin-binding capabilities. The concentration of phage within the SML provided the LCMA with an external microbial selective described by the bacteriophage adherence to mucus (BAM) model. In the BAM model, phage adhere to mucus protecting the metazoan host against invading, potentially pathogenic bacteria. The same fluid dynamics that concentrated phage and bacteria in the SML also concentrated eukaryotic viruses. As eukaryotic viruses competed for host intracellular niche space, those viruses that provided the LCMA with immune protection were maintained. If a resident virus became pathogenic or if a non-beneficial infection occurred, we propose that tumor necrosis factor (TNF)-mediated programmed cell death, as well as other apoptosis mechanisms, were utilized to remove virally infected cells. The ubiquity of the mucosal environment across metazoan phyla suggest that both BAM and TNF-induced apoptosis emerged during the Precambrian era and continue to drive the evolution of metazoan immunity.

Rahbarnia, L., Farajnia, S., Babaei, H., Majidi, J., Veisi, K., Ahmadzadeh, V., and Akbari, B. Evolution of phage display technology: from discovery to application. J.Drug Target. 2017; 25(3):216-224; PM: 27819143

ABSTRACT: Phage display technology as a selection-based system is an attractive method for evolution of new biological drugs. Unique ability of phage libraries for displaying proteins on bacteriophage surfaces enable them to make a major contribution in diverse fields of researches related to the diagnosis and therapy of diseases. One of the great challenges facing researchers is the modification of phage

display technology and the development of new applications. This article reviews the molecular basis of phage display library, and summarizes the novel and specific applications of this technique in the field of biological drugs development including therapeutic antibodies, peptides, vaccines, and catalytic antibodies.

Rajagopalan, R. and Kroos, L. The dev Operon Regulates the Timing of Sporulation during Myxococcus xanthus Development. J.Bacteriol. 5-15-2017; 199(10); PM: 28264995

ABSTRACT: Myxococcus xanthus undergoes multicellular development when starved. Thousands of rod-shaped cells coordinate their movements and aggregate into mounds in which cells differentiate into spores. Mutations in the dev operon impair development. The dev operon encompasses a clustered regularly interspaced short palindromic repeat-associated (CRISPR-Cas) system. Null mutations in devI, a small gene at the beginning of the dev operon, suppress the developmental defects caused by null mutations in the downstream devR and devS genes but failed to suppress defects caused by a small in-frame deletion in devT We provide evidence that the original mutant has a second-site mutation. We show that devT null mutants exhibit developmental defects indistinguishable from devR and devS null mutants, and a null mutation in devI suppresses the defects of a devT null mutation. The similarity of DevTRS proteins to components of the CRISPR-associated complex for antiviral defense (Cascade), together with our molecular characterization of dev mutants, support a model in which DevTRS form a Cascade-like subcomplex that negatively autoregulates dev transcript accumulation and prevents DevI overproduction that would strongly inhibit sporulation. Our results also suggest that DevI transiently inhibits sporulation when regulated normally. The mechanism of transient inhibition may involve MrpC, a key transcription factor, whose translation appears to be weakly inhibited by DevI. Finally, our characterization of a devI devS mutant indicates that very little exo transcript is required for sporulation, which is surprising since Exo proteins help form the polysaccharide spore coat.IMPORTANCE CRISPR-Cas systems typically function as adaptive immune systems in bacteria. The dev CRISPR-Cas system of M. xanthus has been proposed to prevent bacteriophage infection during development, but how dev controls sporulation has been elusive. Recent evidence supported a model in which DevR and DevS prevent overproduction of DevI, a predicted 40-residue inhibitor of sporulation. We provide genetic evidence that DevT functions together with DevR and DevS to prevent DevI overproduction. We also show that spores form about 6 h earlier in mutants lacking devI than in the wild type. Only a minority of natural isolates appear to have a functional dev promoter and devI, suggesting that a functional dev CRISPR-Cas system evolved recently in niches where delayed sporulation and/or protection from bacteriophage infection proved advantageous.

Rattanakul, S. and Oguma, K. Analysis of Hydroxyl Radicals and Inactivation Mechanisms of Bacteriophage MS2 in Response to a Simultaneous Application of UV and Chlorine. Environ.Sci.Technol. 1-3-2017; 51(1):455-462; PM: 27997138

ABSTRACT: The simultaneous application of UV and chlorine (expressed as UV/Cl2) as a water treatment method may be a good disinfection option for UV-resistant microorganisms, such as human adenoviruses (HAdVs). In this study, we developed two approaches using UV/Cl2: one to quantitate the OH* radicals based on the degradation of the probe compound para-chlorobenzoic acid (pCBA) and the other to use bacteriophage MS2 to understand the virus inactivation mechanisms in response to UV,

chlorine and UV/Cl2 disinfection using reverse-transcription quantitative polymerase chain reaction (RT-qPCR), attachment and genome penetration assays. The results revealed that OH* radicals were produced at a concentration of 2.70 x 10-14 M in the UV/Cl2 treatment with a practical chlorine dose of 1 mg/L and with a minimum UV254 fluence of approximately 10 mJ/cm2, whereas UV or chlorine alone did not produce OH* radicals. In the UV/Cl2 treatment, synergistic effects on viral genome damage were observed, but were not directly due to OH* radicals. The ability of MS2 to penetrate the genome of the host bacteria was impaired, but its ability to attach to the host was not affected by the treatment. We concluded that the major cause of virus inactivation in response to UV/Cl2 was the damage to the viral genome caused by combination actions of chlorine species and OH* radicals.

Rauch, B. J., Silvis, M. R., Hultquist, J. F., Waters, C. S., McGregor, M. J., Krogan, N. J., and Bondy-Denomy, J. Inhibition of CRISPR-Cas9 with Bacteriophage Proteins. Cell. 1-12-2017; 168(1-2):150-158; PM: 28041849

ABSTRACT: Bacterial CRISPR-Cas systems utilize sequence-specific RNA-guided nucleases to defend against bacteriophage infection. As a countermeasure, numerous phages are known that produce proteins to block the function of class 1 CRISPR-Cas systems. However, currently no proteins are known to inhibit the widely used class 2 CRISPR-Cas9 system. To find these inhibitors, we searched cas9-containing bacterial genomes for the co-existence of a CRISPR spacer and its target, a potential indicator for CRISPR inhibition. This analysis led to the discovery of four unique type II-A CRISPR-Cas9 inhibitor proteins encoded by Listeria monocytogenes prophages. More than half of L. monocytogenes strains with cas9 contain at least one prophage-encoded inhibitor, suggesting widespread CRISPR-Cas9 inactivation. Two of these inhibitors also blocked the widely used Streptococcus pyogenes Cas9 when assayed in Escherichia coli and human cells. These natural Cas9-specific "anti-CRISPRs" present tools that can be used to regulate the genome engineering activities of CRISPR-Cas9.

Rees, J. C. and Barr, J. R. Detection of methicillin-resistant Staphylococcus aureus using phage amplification combined with matrix-assisted laser desorption/ionization mass spectrometry. Anal.Bioanal.Chem. 2017; 409(5):1379-1386; PM: 27866257

ABSTRACT: Antibiotic resistance continues to contribute significantly to morbidity and mortality across the world. Developing new tests for antibiotic-resistant bacteria is a core action to combat resistant infections. We describe a method that uses phage amplification detection (PAD) combined with matrix-assisted laser desorption/ionization mass spectrometry (MALDI-MS) to rapidly identify Staphylococcus aureus and determine phenotypic susceptibility to cefoxitin. Samples tested for S. aureus are incubated together with bacteriophage in the presence and absence of cefoxitin and subjected to rapid trypsin digestion followed by MALDI-MS analysis. Tryptic peptides derived from amplified phage proteins can be detected by MALDI-MS, as validated by time-of-flight (TOF)/TOF analysis of each peptide combined with database searching. Methicillin-resistant S. aureus show significant phage amplification in the presence of cefoxitin, while methicillin-sensitive S. aureus show no phage amplification relative to a no-antibiotic control. We also show that PAD methodology can be implemented on an FDA-approved commercial MALDI-MS bacterial identification system to identify S. aureus and determine antibiotic susceptibility. The novelty of this assay includes the use of phage-

derived tryptic peptides as detected by MALDI-MS to monitor the results of PAD on an instrument common to many modern microbiology laboratories.

Reindel, R. and Fiore, C. R. Phage Therapy: Considerations and Challenges for Development. Clin.Infect.Dis. 6-1-2017; 64(11):1589-1590; PM: 28329182

No Abstract Available.

Ren, Q., Wang, C., Jin, M., Lan, J., Ye, T., Hui, K., Tan, J., Wang, Z., Wyckoff, G. J., Wang, W., and Han, G. Z. Co-option of bacteriophage lysozyme genes by bivalve genomes. Open.Biol. 2017; 7(1); PM: 28100665

ABSTRACT: Eukaryotes have occasionally acquired genetic material through horizontal gene transfer (HGT). However, little is known about the evolutionary and functional significance of such acquisitions. Lysozymes are ubiquitous enzymes that degrade bacterial cell walls. Here, we provide evidence that two subclasses of bivalves (Heterodonta and Palaeoheterodonta) acquired a lysozyme gene via HGT, building on earlier findings. Phylogenetic analyses place the bivalve lysozyme genes within the clade of bacteriophage lysozyme genes, indicating that the bivalves acquired the phage-type lysozyme genes from bacteriophages, either directly or through intermediate hosts. These bivalve lysozyme genes underwent dramatic structural changes after their co-option, including intron gain and fusion with other genes. Moreover, evidence suggests that recurrent gene duplication occurred in the bivalve lysozyme genes. Finally, we show the co-opted lysozymes exhibit a capacity for antibacterial action, potentially augmenting the immune function of related bivalves. This represents an intriguing evolutionary strategy in the eukaryote-microbe arms race, in which the genetic materials of bacteriophages are co-opted by eukaryotes, and then used by eukaryotes to combat bacteria, using a shared weapon against a common enemy.

Richter, L., Bielec, K., Lesniewski, A., Los, M., Paczesny, J., and Holyst, R. Dense layer of bacteriophages ordered in alternating electric field and immobilized by surface chemical modification as sensing element for bacteria detection. ACS Appl.Mater.Interfaces. 5-19-2017; PM: 28523910

ABSTRACT: Faster and more sensitive environmental monitoring should be developed to face the worldwide problem of bacterial infections. To remedy this issue we demonstrate bacteria sensing element, which utilizes dense and ordered layers of bacteriophages specific for given bacteria strain. We combine 1) chemical modification of the surface to increase the surface coverage of bacteriophages 2) with alternating electric field to greatly increase the number of properly oriented bacteriophages at the surface. Usually in sensing elements a random orientation of bacteriophages results in steric hindrances, which cause that no more than few percent of all receptors is available. Increased number of properly ordered phages results in optimal performance of phage receptors, what manifests in up to 64-fold increase of sensitivity and limit of detection as low as 100 CFU mL-1. Our sensing elements can be applied for selective, sensitive and fast (15 min) bacteria detection. Well studied pair T4 bacteriophage - Escherichia coli was used as a model, however the method could be adapted to prepare bacteriophage-based sensors for detection of variety of bacterial strains.

Riedel, T., Wittmann, J., Bunk, B., Schober, I., Sproer, C., Gronow, S., and Overmann, J. A Clostridioides difficile bacteriophage genome encodes functional binary toxin-associated genes. J.Biotechnol. 5-20-2017; 250:23-28; PM: 28216103

ABSTRACT: Pathogenic clostridia typically produce toxins as virulence factors which cause severe diseases in both humans and animals. Whereas many clostridia like e.g., Clostridium perfringens, Clostridium botulinum or Clostridium tetani were shown to contain toxin-encoding plasmids, only toxin genes located on the chromosome were detected in Clostridioides difficile so far. In this study, we determined, annotated, and analyzed the complete genome of the bacteriophage phiSemix9P1 using single-molecule real-time sequencing technology (SMRT). To our knowledge, this represents the first C. difficile-associated bacteriophage genome that carries a complete functional binary toxin locus in its genome.

Rino, J., de Jesus, A. C., and Carmo-Fonseca, M. Quantitative Image Analysis of Single-Molecule mRNA Dynamics in Living Cells. Methods Mol.Biol. 2017; 1563:229-242; PM: 28324612

ABSTRACT: Single mRNA molecules can be imaged in living cells by a method that consists in genetically inserting binding sites for a bacteriophage protein in the gene of interest. The resulting reporter transgene is then integrated in the genome of cells that express the phage protein fused to a fluorescent tag. Upon transcription, binding of the fluorescent protein to its target sequence makes the RNA visible. With this approach it is possible to track, in real time, the life cycle of a precursor mRNA at the site of transcription in the nucleus and transport of mature mRNA to the cytoplasm. In order to measure the fluorescence associated with individual RNA molecules over time, we developed a semi-automated quantitative image analysis tool termed STaQTool. We describe in detail the implementation and application of the STaQTool software package, which is a generic tool able to process large 4D datasets allowing quantitative studies of different steps in gene expression.

Roszniowski, B., Latka, A., Maciejewska, B., Vandenheuvel, D., Olszak, T., Briers, Y., Holt, G. S., Valvano, M. A., Lavigne, R., Smith, D. L., and Drulis-Kawa, Z. The temperate Burkholderia phage AP3 of the Peduovirinae shows efficient antimicrobial activity against B. cenocepacia of the IIIA lineage. Appl.Microbiol.Biotechnol. 2017; 101(3):1203-1216; PM: 27770178

ABSTRACT: Burkholderia phage AP3 (vB_BceM_AP3) is a temperate virus of the Myoviridae and the Peduovirinae subfamily (P2likevirus genus). This phage specifically infects multidrug-resistant clinical Burkholderia cenocepacia lineage IIIA strains commonly isolated from cystic fibrosis patients. AP3 exhibits high pairwise nucleotide identity (61.7 %) to Burkholderia phage KS5, specific to the same B. cenocepacia host, and has 46.7-49.5 % identity to phages infecting other species of Burkholderia. The lysis cassette of these related phages has a similar organization (putative antiholin, putative holin, endolysin, and spanins) and shows 29-98 % homology between specific lysis genes, in contrast to Enterobacteria phage P2, the hallmark phage of this genus. The AP3 and KS5 lysis genes have conserved locations and high amino acid sequence similarity. The AP3 bacteriophage particles remain infective up to 5 h at pH 4-10 and are stable at 60 degrees C for 30 min, but are sensitive to chloroform, with no remaining infective particles after 24 h of treatment. AP3 lysogeny can occur by stable genomic integration and by pseudo-lysogeny. The lysogenic bacterial mutants did not exhibit any significant changes in virulence compared to wild-type host strain when tested in the Galleria

mellonella moth wax model. Moreover, AP3 treatment of larvae infected with B. cenocepacia revealed a significant increase ($P < 0.0001$) in larvae survival in comparison to AP3-untreated infected larvae. AP3 showed robust lytic activity, as evidenced by its broad host range, the absence of increased virulence in lysogenic isolates, the lack of bacterial gene disruption conditioned by bacterial tRNA downstream integration site, and the absence of detected toxin sequences. These data suggest that the AP3 phage is a promising potent agent against bacteria belonging to the most common B. cenocepacia IIIA lineage strains.

rredondo-Hernandez, L. J., az-Avalos, C., Lopez-Vidal, Y., Castillo-Rojas, G., and Mazari-Hiriart, M. FRNA Bacteriophages as Viral Indicators of Faecal Contamination in Mexican Tropical Aquatic Systems. PLoS.One. 2017; 12(1):e0170399; PM: 28114378

ABSTRACT: A particular challenge to water safety in populous intertropical regions is the lack of reliable faecal indicators to detect microbiological contamination of water, while the numerical relationships of specific viral indicators remain largely unexplored. The aim of this study was to investigate the numerical relationships of FRNA-bacteriophage genotypes, adenovirus 41, and human adenoviruses (HADV) in Mexican surface water systems to assess sewage contamination. We studied the presence of HADV, HADV41 and FRNA bacteriophage genotypes in water samples and quantified by qPCR and RT-qPCR. Virus and water quality indicator variances, as analyzed by principal component analysis and partial least squared regression, followed along the major percentiles of water faecal enterococci. FRNA bacteriophages adequately deciphered viral and point source water contamination. The strongest correlation for HADV was with FRNA bacteriophage type II, in water samples higher than the 50th percentiles of faecal enterococci, thus indicating urban pollution. FRNA bacteriophage genotypes I and III virus indicator performances were assisted by their associations with electrical conductivity and faecal enterococci. In combination, our methods are useful for inferring water quality degradation caused by sewage contamination. The methods used have potential for determining source contamination in water and, specifically, the presence of enteric viruses where clean and contaminated water have mixed.

Rumnieks, J. and Tars, K. Crystal Structure of the Maturation Protein from Bacteriophage Qbeta. J.Mol.Biol. 3-10-2017; 429(5):688-696; PM: 28111107

ABSTRACT: Virions of the single-stranded RNA bacteriophages contain a single copy of the maturation protein, which is bound to the phage genome and is required for the infectivity of the particles. The maturation protein mediates the adsorption of the virion to bacterial pili and the subsequent release and penetration of the genome into the host cell. Here, we report a crystal structure of the maturation protein from bacteriophage Qbeta. The protein has a bent, highly asymmetric shape and spans 110A in length. Apart from small local substructures, the overall fold of the maturation protein does not resemble that of other known proteins. The protein is organized in two distinct regions, an alpha-helical part with a four-helix core, and a beta stranded part that contains a seven-stranded sheet in the central part and a five-stranded sheet at the tip of the protein. The Qbeta maturation protein has two distinct, positively charged areas at opposite sides of the alpha-helical part, which are involved in genomic RNA binding. The maturation protein binds to each of the surrounding coat protein dimers in the capsid differently, and the interaction is considerably weaker compared to coat protein interdimer contacts. The coat protein- or RNA-binding residues are not preserved among different

ssRNA phage maturation proteins; instead, the distal end of the alpha-helical part is the most evolutionarily conserved, suggesting the importance of this region for maintaining the functionality of the protein.

Sabouri, S., Sepehrizadeh, Z., mirpour-Rostami, S., and Skurnik, M. A minireview on the in vitro and in vivo experiments with anti-Escherichia coli O157:H7 phages as potential biocontrol and phage therapy agents. Int.J.Food Microbiol. 2-21-2017; 243:52-57; PM: 27978506

ABSTRACT: Phage therapy is an old method of combating bacterial pathogens that has recently been taken into consideration due to the alarming spread of antibiotic resistance. Escherichia coli O157:H7 is a foodborne pathogen that causes hemorrhagic colitis and life-threatening Hemolytic Uremic Syndrome (HUS). There are several studies on isolation of specific phages against E. coli O157:H7 and more than 60 specific phages have been published so far. Although in vitro experiments have been successful in elimination or reduction of E. coli O157:H7numbers, in vivo experiments have not been as promising. This may be due to escape of bacteria to locations where phages have difficulties to enter or due to the adverse conditions in the gastrointestinal tract that affect phage viability and proliferation. To get around the latter obstacle, an alternative phage delivery method such as polymer microencapsulation should be tried. While the present time results are not very encouraging the work should be continued as more efficient phage treatment regimens might be found in future.

Salles, B. C., Costa, L. E., Alves, P. T., Dias, A. C., Vaz, E. R., Menezes-Souza, D., Ramos, F. F., Duarte, M. C., Roatt, B. M., Chavez-Fumagalli, M. A., Tavares, C. A., Goncalves, D. U., Rocha, R. L., Goulart, L. R., and Coelho, E. A. Leishmania infantum mimotopes and a phage-ELISA assay as tools for a sensitive and specific serodiagnosis of human visceral leishmaniasis. Diagn.Microbiol.Infect.Dis. 2017; 87(3):219-225; PM: 27939286

ABSTRACT: Serological methods used to diagnose visceral leishmaniasis (VL) are considered minimally invasive, but they present problems related with their sensitivity and/or specificity. In this study, a subtractive selection using the phage display technology against antibodies from healthy subjects living in endemic and non-endemic areas of disease, as well as from Chagas disease patients and those developing active VL, was developed. The aim of this study was to select bacteriophage-fused epitopes to be used in the serodiagnosis of human VL. Eight phage clones were selected after the bio-panning rounds, and their reactivity was evaluated in a phage-ELISA assay against a human serological panel. A wild-type clone and the recombinant K39-based immunochromatographic test were used as controls. In the results, it was shown that all clones showed an excellent performance to serologically identify VL patients, demonstrating the feasibility of the isolated phages for developing a specific and sensitive serodiagnosis of human VL.

Santiago-Rodriguez, T. M., Ly, M., Pride, D. T., and Toranzos, G. A. Draft Genome Sequence of an Enterococcus faecalis ATCC 19433 Siphovirus Isolated from Raw Domestic Sewage. Genome Announc. 1-19-2017; 5(3); PM: 28104647

ABSTRACT: We previously isolated and characterized an Enterococcus faecalis ATCC 19433 siphovirus from raw domestic sewage as a viral indicator of human fecal pollution. Here, we report the draft genome sequence of this bacteriophage.

Santos-Perez, I., Oksanen, H. M., Bamford, D. H., Goni, F. M., Reguera, D., and Abrescia, N. G. Membrane-assisted viral DNA ejection. Biochim.Biophys.Acta. 2017; 1861(3):664-672; PM: 27993658

ABSTRACT: Genome packaging and delivery are fundamental steps in the replication cycle of all viruses. Icosahedral viruses with linear double-stranded DNA (dsDNA) usually package their genome into a preformed, rigid procapsid using the power generated by a virus-encoded packaging ATPase. The pressure and stored energy due to this confinement of DNA at a high density is assumed to drive the initial stages of genome ejection. Membrane-containing icosahedral viruses, such as bacteriophage PRD1, present an additional architectural complexity by enclosing their genome within an internal membrane vesicle. Upon adsorption to a host cell, the PRD1 membrane remodels into a proteo-lipidic tube that provides a conduit for passage of the ejected linear dsDNA through the cell envelope. Based on volume analyses of PRD1 membrane vesicles captured by cryo-electron tomography and modeling of the elastic properties of the vesicle, we propose that the internal membrane makes a crucial and active contribution during infection by maintaining the driving force for DNA ejection and countering the internal turgor pressure of the host. These novel functions extend the role of the PRD1 viral membrane beyond tube formation or the mere physical confinement of the genome. The presence and assistance of an internal membrane might constitute a biological advantage that extends also to other viruses that package their linear dsDNA to high density within an internal vesicle.

Sarker, S. A., Berger, B., Deng, Y., Kieser, S., Foata, F., Moine, D., Descombes, P., Sultana, S., Huq, S., Bardhan, P. K., Vuillet, V., Praplan, F., and Brussow, H. Oral application of Escherichia coli bacteriophage: safety tests in healthy and diarrheal children from Bangladesh. Environ.Microbiol. 2017; 19(1):237-250; PM: 27750388

ABSTRACT: A T4-like coliphage cocktail was given with different oral doses to healthy Bangladeshi children in a placebo-controlled randomized phase I safety trial. Fecal phage detection was oral dose dependent suggesting passive gut transit of coliphages through the gut. No adverse effects of phage application were seen clinically and by clinical chemistry. Similar results were obtained for a commercial phage preparation (Coliproteus from Microgen/Russia). By 16S rRNA gene sequencing, only a low degree of fecal microbiota conservation was seen in healthy children from Bangladesh who were sampled over a time interval of 7 days suggesting a substantial temporal fluctuation of the fecal microbiota composition. Microbiota variability was not associated with the age of the children or the presence of phage in the stool. Stool microbiota composition of Bangladeshi children resembled that found in children of other regions of the world. Marked variability in fecal microbiota composition was also seen in 71 pediatric diarrhea patients receiving only oral rehydration therapy and in 38 patients receiving coliphage preparations or placebo when sampled 1.2 or 4 days apart respectively. Temporal stability of the gut microbiota should be assessed in case-control studies involving children before associating fecal microbiota composition with health or disease phenotypes.

Scanlan, P. D. Bacteria-Bacteriophage Coevolution in the Human Gut: Implications for Microbial Diversity and Functionality. Trends Microbiol. 3-22-2017; PM: 28342597

ABSTRACT: Antagonistic coevolution (AC) between bacteria and bacteriophages plays

a key role in driving and maintaining microbial diversity. Consequently, AC is predicted to affect all levels of biological organisation, from the individual to ecosystem scales. Nonetheless, we know nothing about bacteria-bacteriophage AC in perhaps the most important and clinically relevant microbial ecosystem known to humankind - the human gut microbiome. In this opinion piece I review current research on bacteria-phage AC in in vitro and natural populations of microbes. I then examine the evidence and discuss the potential role of AC in driving observed patterns of intra- and interindividual variation in the gut microbiome together with detailing the potential functional consequences of such AC-driven microbial variation for human health and disease.

Scanlan, P. D., Bischofberger, A. M., and Hall, A. R. Modification of Escherichia coli-bacteriophage interactions by surfactants and antibiotics in vitro. FEMS Microbiol.Ecol. 2017; 93(1); PM: 27737900

ABSTRACT: Although experiments indicate that the abiotic environment plays an important role in bacterial interactions with their parasitic viruses (bacteriophages or phages), it is not yet clear how exposure to compounds present in nature alters the impact of phages on bacterial growth and evolution. To address this question, we exposed Escherichia coli K12 MG1655, in combination with three lytic phages, to various substances that natural and clinical microbial populations are likely to encounter: bile salts (present in mammalian gastrointestinal tracts), sodium dodecyl sulfate (SDS, a common surfactant in cleaning and hygiene products) and four antibiotics (present at variable concentrations in natural and clinical environments). Our results show that bile salts and SDS can reduce the detrimental effect of phages on bacterial growth. In some cases these compounds completely mitigated any negative effects of phages on bacterial growth and consequently bacteria did not evolve resistance to phages in these conditions. The proportional effects of phages were unaffected by antibiotics in most combinations, excepting three cases of phage-drug synergy. These results suggest that accounting for interactions between phages and environmental factors such as surfactants and antibiotics will improve understanding of both bacterial growth and resistance evolution to phages in vivo and in nature.

Scanlan, P. D., Hall, A. R., and Buckling, A. Parasite genetic distance and local adaptation in co-evolving bacteria-bacteriophage populations. Mol.Ecol. 2017; 26(7):1747-1755; PM: 27775190

ABSTRACT: Antagonistic co-evolution between hosts and parasites can lead to local adaptation (LA) such that parasite fitness is greatest in sympatric hosts (or vice versa). The magnitude of LA typically increases with geographical distance, which is assumed to be because genetic (and hence phenotypic) distance increases with geographical distance. Here, we explicitly test the relationships between parasite genetic and phenotypic distance and LA using isolates of co-evolved viral parasites (lytic bacteriophage varphi2) and the host bacterium Pseudomonas fluorescens SBW25. We find positive relationships between parasite genotype and infectivity phenotype, but the strength of the relationship was greater when infectivity was defined by the identity of hosts that could be infected rather than the actual number of hosts infected (host range), and when measurements were compared within rather than among populations. Crucially, we find a monotonic relationship between LA and genetic distance across phage isolates from different populations, although in contrast to many geographical studies, parasite LA decreased with genetic distance. These results can be

explained by the fact that bacteria can rapidly adapt to phage infectivity mutations, but that evolved resistance has a degree of specificity to the local phage population. Our results show that antagonistic co-evolution alone can result in predictable links between genetic distance and host-parasite local adaptation.

Schuch, R., Khan, B. K., Raz, A., Rotolo, J. A., and Wittekind, M. Bacteriophage Lysin CF-301: a Potent Anti-Staphylococcal Biofilm Agent. Antimicrob.Agents Chemother. 5-1-2017; PM: 28461319

ABSTRACT: Biofilms pose a unique therapeutic challenge because of the antibiotic tolerance of constituent bacteria. Treatments for biofilm-based infections represent a major unmet medical need, requiring novel agents to eradicate mature biofilms. Our objective was to evaluate bacteriophage lysin CF-301 as a new agent to target Staphylococcus aureus biofilms. We used minimum biofilm eradicating concentration (MBEC) assays on ninety-five S. aureus strains to obtain a MBEC90 value of </=0.25 mug/ml for CF-301. Mature biofilms of coagulase-negative staphylococci, Streptococcus pyogenes, and Streptococcus agalactiae were also sensitive to disruption, with MBEC90 values ranging from 0.25-8 mug/ml. The potency of CF-301 was demonstrated against S. aureus biofilms formed on polystyrene, glass, surgical mesh, and catheters. In catheters, CF-301 removed all biofilm within 1 hour and killed all released bacteria by 6 hours. Mixed-species biofilms, formed by S. aureus and S. epidermidis on several surfaces, were removed by CF-301, as were S. aureus biofilms either enriched for small colony variants (SCVs) or grown in human synovial fluid. The antibacterial activity of CF-301 was further demonstrated against S. aureus persister cells in exponential and stationary phase populations. Finally, the anti-biofilm activity of CF-301 was greatly improved in combinations with the cell wall hydrolase lysostaphin when tested against a range of S. aureus strains. In all, the data shows CF-301 is highly effective at disrupting biofilms and killing biofilm bacteria, and, as such, may be an efficient new agent for treating staphylococcal infections with a biofilm component.

Secor, P. R., Michaels, L. A., Smigiel, K. S., Rohani, M. G., Jennings, L. K., Hisert, K. B., Arrigoni, A., Braun, K. R., Birkland, T. P., Lai, Y., Hallstrand, T. S., Bollyky, P. L., Singh, P. K., and Parks, W. C. Filamentous Bacteriophage Produced by Pseudomonas aeruginosa Alters the Inflammatory Response and Promotes Noninvasive Infection In Vivo. Infect.Immun. 2017; 85(1); PM: 27795361

ABSTRACT: Pseudomonas aeruginosa is an important opportunistic human pathogen that lives in biofilm-like cell aggregates at sites of chronic infection, such as those that occur in the lungs of patients with cystic fibrosis and nonhealing ulcers. During growth in a biofilm, P. aeruginosa dramatically increases the production of filamentous Pf bacteriophage (Pf phage). Previous work indicated that when in vivo Pf phage production was inhibited, P. aeruginosa was less virulent. However, it is not clear how the production of abundant quantities of Pf phage similar to those produced by biofilms under in vitro conditions affects pathogenesis. Here, using a murine pneumonia model, we show that the production of biofilm-relevant amounts of Pf phage prevents the dissemination of P. aeruginosa from the lung. Furthermore, filamentous phage promoted bacterial adhesion to mucin and inhibited bacterial invasion of airway epithelial cultures, suggesting that Pf phage traps P. aeruginosa within the lung. The in vivo production of Pf phage was also associated with reduced lung injury, reduced neutrophil recruitment, and lower cytokine levels. Additionally, when producing Pf phage, P. aeruginosa was less prone to phagocytosis by macrophages than bacteria not producing Pf phage. Collectively,

these data suggest that filamentous Pf phage alters the progression of the inflammatory response and promotes phenotypes typically associated with chronic infection.

Sedgeman, C. A., Su, Y., and Guengerich, F. P. Formation of S-[2-(N6-Deoxyadenosinyl)ethyl]glutathione in DNA and Replication Past the Adduct by Translesion DNA Polymerases. Chem.Res.Toxicol. 5-15-2017; 30(5):1188-1196; PM: 28395138

ABSTRACT: 1,2-Dibromoethane (DBE, ethylene dibromide) is a potent carcinogen due at least in part to its DNA cross-linking effects. DBE cross-links glutathione (GSH) to DNA, notably to sites on 2'-deoxyadenosine and 2'-deoxyguanosine (Cmarik , J. L. , et al. (1991) J. Biol. Chem. 267 , 6.

Senevirathne, A., Ghosh, K., Roh, E., and Kim, K. P. Complete genome sequence analysis of a novel Staphylococcus phage StAP1 and proposal of a new species in the genus Silviavirus. Arch.Virol. 3-21-2017; PM: 28324178

ABSTRACT: Bacteriophage StAP1 was isolated from a soil sample infecting Staphylococcus aureus and S. xylosus. Its genome was found to be 135,502 base pairs (bp) long with 30.00 mol% G+C content and 192 open reading frames. While no tRNA encoding genes were identified, 7 mobile elements were found to interrupt five StAP1 open reading frames. Comparative genomic and proteomic analysis consistently supports the establishment of a new species in the genus Silviavirus.

Sergeyev, I. V., Itin, B., Rogawski, R., Day, L. A., and McDermott, A. E. Efficient assignment and NMR analysis of an intact virus using sequential side-chain correlations and DNP sensitization. Proc.Natl.Acad.Sci.U.S.A. 5-16-2017; 114(20):5171-5176; PM: 28461483

ABSTRACT: An experimental strategy has been developed to increase the efficiency of dynamic nuclear polarization (DNP) in solid-state NMR studies. The method makes assignments simpler, faster, and more reliable via sequential correlations of both side-chain and Calpha resonances. The approach is particularly suited to complex biomolecules and systems with significant chemical-shift degeneracy. It was designed to overcome the spectral congestion and line broadening that occur due to sample freezing at the cryogenic temperatures required for DNP. Nonuniform sampling (NUS) is incorporated to achieve time-efficient collection of multidimensional data. Additionally, fast (25 kHz) magic-angle spinning (MAS) provides optimal sensitivity and resolution. Data collected in <1 wk produced a virtually complete de novo assignment of the coat protein of Pf1 virus. The peak positions and linewidths for samples near 100 K are perturbed relative to those near 273 K. These temperature-induced perturbations are strongly correlated with hydration surfaces.

Serwer, P. and Wright, E. T. Testing a proposed paradigm shift in analysis of phage DNA packaging. Bacteriophage. 2016; 6(4):e1268664; PM: 28090387

ABSTRACT: We argue that a paradigm shift is needed in the analysis of phage DNA packaging. We then test a prediction of the following paradigm shift-engendering hypothesis. The motor of phage DNA packaging has two cycles: (1) the well-known

packaging ATPase-driven (type 1) cycle and (2) a proposed back-up, shell expansion/contraction-driven (type 2) cycle that reverses type 1 cycle stalls by expelling accidentally packaged non-DNA molecules. We test the prediction that increasing the cellular concentration of all macromolecules will cause packaging-active capsids to divert to states of hyper-expansion and contraction. We use a directed evolution-derived, 3-site phage T3 mutant, adapted to propagation in concentrated bacterial cytoplasm. We find this prediction correct while discovering novel T3 capsids previously obscure.

Shafique, M., Alvi, I. A., Abbas, Z., and Ur, Rehman S. Assessment of biofilm removal capacity of a broad host range bacteriophage JHP against Pseudomonas aeruginosa. APMIS. 4-18-2017; PM: 28418081

ABSTRACT: Pseudomonas aeruginosa is an efficient biofilm-dwelling microbial pathogen, associated with nosocomial infections. These biofilm-associated infections are resistant to antibiotics and immune defenses, therefore pose major problem against their treatment. This scenario demands alternative therapeutic regimens, and bacteriophage therapy is one among potential strategies for clinical management of multiple drug resistance. In this investigation, the efficacy of a bacteriophage, JHP, is evaluated to eradicate P. aeruginosa biofilms. Growth kinetics of P. aeruginosa biofilm revealed that the highest cell density biofilm (1.5 x 1016 CFU/mL) was established within the polystyrene microtiter plate at 72 h post inoculation. Pseudomonas aeruginosa biofilms of different ages, treated with JHP (0.6 MOI) for different post-infection durations, reduced biomass from 2 to 4.5 logs (60-90%). JHP treatment before biofilm development reduced the bacterial load up to 9 logs (>95% bacterial load reduction) as compared with untreated control, which highlights its potential to prevent biofilm formation in indwelling medical devices. Combinations of JHP with other phages or antibiotics could be an efficient alternative for P. aeruginosa biofilm removal in clinical and industrial settings.

Shah, Punatar R., Martin, M. J., Wyatt, H. D., Chan, Y. W., and West, S. C. Resolution of single and double Holliday junction recombination intermediates by GEN1. Proc.Natl.Acad.Sci.U.S.A. 1-17-2017; 114(3):443-450; PM: 28049850

ABSTRACT: Genetic recombination provides an important mechanism for the repair of DNA double-strand breaks. Homologous pairing and strand exchange lead to the formation of DNA intermediates, in which sister chromatids or homologous chromosomes are covalently linked by four-way Holliday junctions (HJs). Depending on the type of recombination reaction that takes place, intermediates may have single or double HJs, and their resolution is essential for proper chromosome segregation. In mitotic cells, double HJs are primarily dissolved by the BLM helicase-TopoisomeraseIIIalpha-RMI1-RMI2 (BTR) complex, whereas single HJs (and double HJs that have escaped the attention of BTR) are resolved by structure-selective endonucleases known as HJ resolvases. These enzymes are ubiquitous in nature, because they are present in bacteriophage, bacteria, archaea, and simple and complex eukaryotes. The human HJ resolvase GEN1 is a member of the XPG/Rad2 family of 5'-flap endonucleases. Biochemical studies of GEN1 revealed that it cleaves synthetic DNA substrates containing a single HJ by a mechanism similar to that shown by the prototypic HJ resolvase, Escherichia coli RuvC protein, but it is unclear whether these substrates fully recapitulate the properties of recombination intermediates that arise within a physiological context. Here, we show that GEN1 efficiently cleaves both single and double HJs contained within large recombination

intermediates. Moreover, we find that GEN1 exhibits a weak sequence preference for incision between two G residues that reside in a T-rich region of DNA. These results contrast with those obtained with RuvC, which exhibits a strict requirement for the consensus sequence 5'-A/TTTG/C-3'.

Shang, Y., Wang, M., Xiao, G., Wang, X., Hou, D., Pan, K., Liu, S., Li, J., Wang, J., Arif, B. M., Vlak, J. M., Chen, X., Wang, H., Deng, F., and Hu, Z. Construction and Rescue of a Functional Synthetic Baculovirus. ACS Synth.Biol. 4-6-2017; PM: 28383905

ABSTRACT: Synthetic viruses provide a powerful platform to delve deeper into the nature and function of viruses as well as to engineer viruses with novel properties. So far, most synthetic viruses have been RNA viruses (<30 kb) and small DNA viruses, such as bacteriophage phiX174. Baculoviruses contain a large circular dsDNA genome of 80-180 kb and have been used as biocontrol agents and protein expression vectors. Here, we report on the first synthesis of a baculovirus based on the type species Autographa californica nucleopolyhedrovirus, AcMNPV, by a combination of PCR and transformation-associated recombination in yeast. The synthetic genome, designated AcMNPV-WIV-Syn1, is 145299 bp comprising the complete genome of AcMNPV except for the hr4a locus that was replaced with an approximately 11.5 kb cassette of bacterial and yeast artificial chromosomal elements and an egfp gene. Sf9 insect cells were transfected with AcMNPV-WIV-Syn1 DNA and progeny virus was examined by electron microscopy, and assayed in one-step growth curves and oral infectivity. The results conclusively showed that the rescued virus AcMNPV-WIV-Syn1 had structural and biological properties comparable to the parental virus. We validated a proof of concept that a bona fide baculovirus can be synthesized. The new platform allows manipulation at any or multiple loci and will facilitate future studies such as identifying the minimal baculovirus genome and construction of better expression vectors. This is the largest DNA virus synthesized so far, and its success is likely to be the impetus to stimulate the fields of other large DNA viruses such as herpesviruses and poxviruses.

Shankar, V., Gouda, M., Moncivaiz, J., Gordon, A., Reo, N. V., Hussein, L., and Paliy, O. Differences in Gut Metabolites and Microbial Composition and Functions between Egyptian and U.S. Children Are Consistent with Their Diets. mSystems. 2017; 2(1); PM: 28191503

ABSTRACT: Previous studies indicated that populations consuming a Mediterranean diet rich in fiber, vegetables, and fruits have a significantly lower risk of cardiovascular and metabolic diseases than populations of industrialized societies consuming diets enriched in processed carbohydrates, animal proteins, and fats. To explore the potential contributions of gut microbiota to the observed diet-related metabolic effects, we conducted an integrative analysis of distal gut microbiota composition and functions and intestinal metabolites in Egyptian and U.S. teenagers. All Egyptian gut microbial communities belonged to the Prevotella enterotype, whereas all but one of the U.S. samples were of the Bacteroides enterotype. The intestinal environment of Egyptians was characterized by higher levels of short-chain fatty acids, a higher prevalence of microbial polysaccharide degradation-encoding genes, and a higher proportion of several polysaccharide-degrading genera. Egyptian gut microbiota also appeared to be under heavier bacteriophage pressure. In contrast, the gut environment of U.S. children was rich in amino acids and lipid metabolism-associated compounds; contained more microbial genes encoding protein degradation, vitamin biosynthesis,

and iron acquisition pathways; and was enriched in several protein- and starch-degrading genera. Levels of 1-methylhistamine, a biomarker of allergic response, were elevated in U.S. guts, as were the abundances of members of Faecalibacterium and Akkermansia, two genera with recognized anti-inflammatory effects. The revealed corroborating differences in fecal microbiota structure and functions and metabolite profiles between Egyptian and U.S. teenagers are consistent with the nutrient variation between Mediterranean and Western diets. IMPORTANCE The human gastrointestinal microbiota functions as an important mediator of diet for host metabolism. To evaluate how consumed diets influence the gut environment, we carried out simultaneous interrogations of distal gut microbiota and metabolites in samples from healthy children in Egypt and the United States. While Egyptian children consumed a Mediterranean diet rich in plant foods, U.S. children consumed a Western diet high in animal protein, fats, and highly processed carbohydrates. Consistent with the consumed diets, Egyptian gut samples were enriched in polysaccharide-degrading microbes and end products of polysaccharide fermentation and U.S. gut samples were enriched in proteolytic microbes and end products of protein and fat metabolism. Thus, the intestinal microbiota might be selected on the basis of the diets that we consume, which can open opportunities to affect gut health through modulation of gut microbiota with dietary supplementations.

Shao, Q., Trinh, J. T., McIntosh, C. S., Christenson, B., Balazsi, G., and Zeng, L. Lysis-lysogeny coexistence: prophage integration during lytic development. Microbiologyopen. 2017; 6(1); PM: 27530202

ABSTRACT: The infection of Escherichia coli cells by bacteriophage lambda results in bifurcated means of propagation, where the phage decides between the lytic and lysogenic pathways. Although traditionally thought to be mutually exclusive, increasing evidence suggests that this lysis-lysogeny decision is more complex than once believed, but exploring its intricacies requires an improved resolution of study. Here, with a newly developed fluorescent reporter system labeling single phage and E. coli DNAs, these two distinct pathways can be visualized by following the DNA movements in vivo. Surprisingly, we frequently observed an interesting "lyso-lysis" phenomenon in lytic cells, where phage integrates its DNA into the host, a characteristic event of the lysogenic pathway, followed by cell lysis. Furthermore, the frequency of lyso-lysis increases with the number of infecting phages, and specifically, with CII activity. Moreover, in lytic cells, the integration site attB on the E. coli genome migrates toward the polar region over time, leading to more spatial overlap with the phage DNA and frequent colocalization/collision of attB and phage DNA, possibly contributing to a higher chance for DNA integration.

Sharaf, A., Mercati, F., Elmaghraby, I., Elbaz, R. M., and Marei, E. M. Functional and comparative genome analysis of novel virulent actinophages belonging to Streptomyces flavovirens. BMC.Microbiol. 3-3-2017; 17(1):51; PM: 28257628

ABSTRACT: BACKGROUND: Next Generation Sequencing (NGS) technologies provide exciting possibilities for whole genome sequencing of a plethora of organisms including bacterial strains and phages, with many possible applications in research and diagnostics. No Streptomyces flavovirens phages have been sequenced to date; there is therefore a lack in available information about S. flavovirens phage genomics. We report biological and physiochemical features and use NGS to provide the complete annotated genomes for two new strains (Sf1 and Sf3) of the virulent phage Streptomyces flavovirens, isolated from Egyptian soil samples. *RESULTS*: The S. flavovirens phages (Sf1

and Sf3) examined in this study show higher adsorption rates (82 and 85%, respectively) than other actinophages, indicating a strong specificity to their host, and latent periods (15 and 30 min.), followed by rise periods of 45 and 30 min. As expected for actinophages, their burst sizes were 1.95 and 2.49 virions per mL. Both phages were stable and, as reported in previous experiments, showed a significant increase in their activity after sodium chloride (NaCl) and magnesium chloride (MgCl2.6H2O) treatments, whereas after zinc chloride (ZnCl2) application both phages showed a significant decrease in infection. The sequenced phage genomes are parts of a singleton cluster with sizes of 43,150 bp and 60,934 bp, respectively. Bioinformatics analyses and functional characterizations enabled the assignment of possible functions to 19 and 28 putative identified ORFs, which included phage structural proteins, lysis components and metabolic proteins. Thirty phams were identified in both phages, 10 (33.3%) of them with known function, which can be used in cluster prediction. Comparative genomic analysis revealed significant homology between the two phages, showing the highest hits among Sf1, Sf3 and the closest Streptomyces phage (VWB phages) in a specific 13Kb region. However, the phylogenetic analysis using the Major Capsid Protein (MCP) sequences highlighted that the isolated phages belong to the BG Streptomyces phage group but are clearly separated, representing a novel sub-cluster. *CONCLUSION*: The results of this study provide the first physiological and genomic information for S. flavovirens phages and will be useful for pharmaceutical industries based on S. flavovirens and future phage evolution studies.

Sharma, M., Dashiell, G., Handy, E. T., East, C., Reynnells, R., White, C., Nyarko, E., Micallef, S., Hashem, F., and Millner, P. D. Survival of Salmonella Newport on Whole and Fresh-Cut Cucumbers Treated with Lytic Bacteriophages. J.Food Prot. 2017; 80(4):668-673; PM: 28294684

ABSTRACT: Salmonella enterica associated with consumption of cucumbers (Cucumis sativus) has led to foodborne outbreaks in the United States. Whole and fresh-cut cucumbers are susceptible to S. enterica contamination during growing, harvesting, and postharvest handling. The application of lytic bacteriophages specific for S. enterica was evaluated to reduce Salmonella populations on cucumbers. Unwaxed cucumbers ('Lisboa' variety, or mini-cucumbers purchased at retail) were inoculated with Salmonella Newport (5 log CFU per cucumber) and were sprayed with 3.2 mL of phosphate-buffered saline (control) or 10 log PFU/ml of SalmoFresh, a Salmonella-specific bacteriophage preparation (phage), to deliver 4.76 x 107 PFU/cm2. Cucumbers were stored at 10 or 22 degrees C for 7 days. Inoculated mini-cucumbers were sliced with a sterile knife to investigate Salmonella transfer to mesocarp, and cut pieces were stored at 4 degrees C for 2 days. Populations (log CFU per cucumber) of Salmonella Newport on phage-treated whole cucumbers were significantly ($P < 0.05$) smaller (2.44 +/- 0.94) than on control-treated cucumbers (4.27 +/- 0.37) on day 0. Populations on phage-treated cucumbers stored at 10 degrees C were 1.72 +/- 0.77 and 1.56 +/- 0.46, which were significantly lower than those on control-treated cucumbers (3.20 +/- 0.48 and 2.33 +/- 0.25) on days 1 and 4, respectively. Between days 0 and 1, populations on control-treated cucumbers stored at 10 and 22 degrees C declined by 1.07 and 2.47 log CFU per cucumber, respectively. At 22 degrees C, Salmonella Newport populations declined by 2.37 log CFU per cucumber between days 0 and 1. Phage application to whole cucumbers before slicing did not reduce the transfer of Salmonella Newport to fresh-cut slices. Lytic phage application may be a potential intervention to reduce Salmonella populations on whole cucumbers.

Sharma, S., Chatterjee, S., Datta, S., Prasad, R., Dubey, D., Prasad, R. K., and Vairale, M. G. Bacteriophages and its applications: an overview. Folia Microbiol.(Praha). 2017; 62(1):17-55; PM: 27718043

ABSTRACT: Bacteriophages (or phages), the most abundant viral entity of the planet, are omni-present in all the ecosystems. On the basis of their unique characteristics and anti-bacterial property, phages are being freshly evaluated taxonomically. Phages replicate inside the host either by lytic or lysogenic mode after infecting and using the cellular machinery of a bacterium. Since their discovery by Twort and d'Herelle in the early 1900s, phage became an important agent for combating pathogenic bacteria in clinical treatments and its related research gained momentum. However, due to recent emergence of bacterial resistance on antibiotics, applications of phage (phage therapy) become an inevitable option of research. Phage particles become popular as a biotechnological tool and treatment of pathogenic bacteria in a range of applied areas. However, there are few concerns over the application of phage-based solutions. This review deals with the updated phage taxonomy (ICTV 2015 Release and subsequent revision) and phage biology and the recent development of its application in the areas of biotechnology, biosensor, therapeutic medicine, food preservation, aquaculture diseases, pollution remediation, and wastewater treatment and issues related with limitations of phage-based remedy.

Sharma, U. and Paul, V. D. Bacteriophage lysins as antibacterials. Crit Care. 5-3-2017; 21(1):99; PM: 28468638

No Abstract Available.

Shlezinger, M., Khalifa, L., Houri-Haddad, Y., Coppenhagen-Glazer, S., Resch, G., Que, Y. A., Beyth, S., Dorfman, E., Hazan, R., and Beyth, N. Phage Therapy: A New Horizon in the Antibacterial Treatment of Oral Pathogens. Curr.Top.Med.Chem. 2017; 17(10):1199-1211; PM: 27770768

ABSTRACT: Dental diseases are perhaps the most prevalent infection-related diseases in humans. Biofilm is involved in almost every infectious disease compromising oral health, notably caries, periodontal disease, gingivitis, endodontic infections and peri-implantitis. Current therapies of biofilm-derived oral infections lack sensitivity; they are not species-specific and kill pathogenic species as well as commensal species, which are protective against the formation of pathogenic biofilms. Moreover, antibiotics have a limited effect on biofilm and are almost unused in oral diseases. A promising alternative approach is bacteriophage (phage) therapy. Phages play a key role in the natural balance in a predator-prey relationship with bacteria and thus have the potential to be efficient anti-bacterial agents. Phages are highly efficient against biofilm, strain specific and easy to isolate and manipulate. Thus, like in many other medicinal fields, phage therapy offers new horizons to dentistry, both therapeutics and research. The present review presents the etiology of common oral diseases, characterization of the infection and the treatment challenges of phage therapy in dentistry. Recent findings and development in the use of phages for prevention, control, and treatment of oral infections as well as possibilities of engineering the oral microbiome are discussed.

Shu, B. and Gong, P. The uncoupling of catalysis and translocation in the viral RNA-dependent RNA polymerase. RNA.Biol. 3-1-2017; 1-6; PM: 28277928

ABSTRACT: The nucleotide addition cycle of nucleic acid polymerases includes 2 major events: the pre-chemistry active site closure leading to the addition of one nucleotide to the product chain; the post-chemistry translocation step moving the polymerase active site one position downstream on its template. In viral RNA-dependent RNA polymerases (RdRPs), structural and biochemical evidences suggest that these 2 events are not tightly coupled, unlike the situation observed in A-family polymerases such as the bacteriophage T7 RNA polymerase. Recently, an RdRP translocation intermediate crystal structure of enterovirus 71 shed light on how translocation may be controlled by elements within RdRP catalytic motifs, and a series of poliovirus apo RdRP crystal structures explicitly suggest that a motif B loop may assist the movement of the template strand in late stages of transcription. Implications of RdRP catalysis-translocation uncoupling and the remaining challenges to further elucidate RdRP translocation mechanism are also discussed.

Singh, M. I., Ganesh, B., and Jain, V. On the domains of T4 phage sliding clamp gp45: An intermolecular crosstalk governs structural stability and biological activity. Biochim.Biophys.Acta. 2017; 1861(1 Pt A):3300-3310; PM: 27554844

ABSTRACT: BACKGROUND: DNA polymerase processivity factors are ubiquitously present in all living organisms. Notwithstanding their high significance, the molecular details of clamps pertaining to the factors contributing to their stability are presently lacking. The bacteriophage T4 sliding clamp gp45 forms a homotrimer that besides being involved in DNA replication, moonlights as a transcription factor. Here we have carried out a detailed characterization of gp45 to understand the role of monomer-monomer interface interactions in stability and functioning of the protein. *METHODS*: We generated several gp45 mutants harboring either Ala or Pro substitutions at the interface residues and performed a detailed investigation using biochemical and biophysical methods including circular dichroism, fluorescence anisotropy and quenching, differential scanning calorimetry, blue-native PAGE, cross-linking, size exclusion chromatography, and dynamic light scattering. We also carried out both transcription and DNA replication to understand the properties of the wild-type and the mutant proteins. *RESULTS*: One specific mutation S88P leads not only to monomerization, but also results in an unstable molecule. Most interestingly, mutating either Q125 or K164 in the gp45 C-terminal domain negatively affects the stability of the N-terminal domain. We also report that these residues upon mutation to alanine make gp45 inactive for late promoter transcription, whereas strand-displacement DNA replication ability remains unaltered. *CONCLUSIONS AND GENERAL SIGNIFICANCE*: The results suggest that the two domains of gp45 demonstrate an "inter-monomer" crosstalk that stabilizes the trimer. We also conclude that the residue-specific interactions at the interface allow the protein to function distinctly as replication and transcription factors.

Skaradzinska, A., Sliwka, P., Kuzminska-Bajor, M., Skaradzinski, G., Rzasa, A., Friese, A., Roschanski, N., Murugaiyan, J., and Roesler, U. H. The Efficacy of Isolated Bacteriophages from Pig Farms against ESBL/AmpC-Producing Escherichia coli from Pig and Turkey Farms. Front Microbiol. 2017; 8:530; PM: 28405193

ABSTRACT: Extended-spectrum beta-lactamases (ESBLs) and AmpC beta-lactamases are

plasmid (but also chromosomally) encoded enzymes found in Enterobacteriaceae, determining resistance to a variety of important antibiotics including penicillins, cephalosporins, and monobactams. In recent decades, the prevalence of ESBL/AmpC-producing bacteria has increased rapidly across the world. Here, we evaluate the potential use of bacteriophages in terms of a reduction of antibiotic-resistant bacteria in healthy animals. The aim of our studies was to isolate bacteriophages capable of destroying ESBL/AmpC-producing Escherichia coli isolated from livestock habitats. The efficacy of isolated phages against ESBL/AmpC E. coli strains varies, but creation of a phage cocktail with broad activity spectrum is possible. This may indicate that the role of phages may not be limited to phage therapy, but bacterial viruses may also be applied against spread of bacteria with antibiotic resistance genes in the environment. We also addressed the hypothesis, that phages, effective for therapeutic purposes may be isolated from distant places and even from different environments other than the actual location of the targeted bacteria. This may be beneficial for practical purposes, as the construction of effective phage preparations does not require access to disease outbreaks.

Smeal, S. W., Schmitt, M. A., Pereira, R. R., Prasad, A., and Fisk, J. D. Simulation of the M13 life cycle I: Assembly of a genetically-structured deterministic chemical kinetic simulation. Virology. 2017; 500:259-274; PM: 27644585

ABSTRACT: To expand the quantitative, systems level understanding and foster the expansion of the biotechnological applications of the filamentous bacteriophage M13, we have unified the accumulated quantitative information on M13 biology into a genetically-structured, experimentally-based computational simulation of the entire phage life cycle. The deterministic chemical kinetic simulation explicitly includes the molecular details of DNA replication, mRNA transcription, protein translation and particle assembly, as well as the competing protein-protein and protein-nucleic acid interactions that control the timing and extent of phage production. The simulation reproduces the holistic behavior of M13, closely matching experimentally reported values of the intracellular levels of phage species and the timing of events in the M13 life cycle. The computational model provides a quantitative description of phage biology, highlights gaps in the present understanding of M13, and offers a framework for exploring alternative mechanisms of regulation in the context of the complete M13 life cycle.

Smeal, S. W., Schmitt, M. A., Pereira, R. R., Prasad, A., and Fisk, J. D. Simulation of the M13 life cycle II: Investigation of the control mechanisms of M13 infection and establishment of the carrier state. Virology. 2017; 500:275-284; PM: 27569186

ABSTRACT: Bacteriophage M13 is a true parasite of bacteria, able to co-opt the infected cell and control the production of progeny across many cellular generations. Here, our genetically-structured simulation of M13 is applied to quantitatively dissect the interplay between the host cellular environment and the controlling interactions governing the phage life cycle during the initial establishment of infection and across multiple cell generations. Multiple simulations suggest that phage-encoded feedback interactions constrain the utilization of host DNA polymerase, RNA polymerase and ribosomes. The simulation reveals the importance of p5 translational attenuation in controlling the production of phage double-stranded DNA and suggests an underappreciated role for p5 translational self-attenuation in resource allocation. The control elements active in a single generation are sufficient to reproduce the experimentally-observed

multigenerational curing of the phage infection. Understanding the subtleties of regulation will be important for maximally exploiting M13 particles as scaffolds for nanoscale devices.

Soffer, N., Woolston, J., Li, M., Das, C., and Sulakvelidze, A. Bacteriophage preparation lytic for Shigella significantly reduces Shigella sonnei contamination in various foods. PLoS.One. 2017; 12(3):e0175256; PM: 28362863

ABSTRACT: ShigaShield is a phage preparation composed of five lytic bacteriophages that specifically target pathogenic Shigella species found in contaminated waters and foods. In this study, we examined the efficacy of various doses (9x105-9x107 PFU/g) of ShigaShield in removing experimentally added Shigella on deli meat, smoked salmon, pre-cooked chicken, lettuce, melon and yogurt. The highest dose (2x107 or 9x107 PFU/g) of ShigaShield applied to each food type resulted in at least 1 log (90%) reduction of Shigella in all the food types. There was significant (P<0.01) reduction in the Shigella levels in all phage treated foods compared to controls, except for the lowest phage dose (9x105 PFU/g) on melon where reduction was only ca. 45% (0.25 log). The genomes of each component phage in the cocktail were fully sequenced and analyzed, and they were found not to contain any "undesirable genes" including those listed in the US Code for Federal Regulations (40 CFR Ch1). Our data suggest that ShigaShield (and similar phage preparations with potent lytic activity against Shigella spp.) may offer a safe and effective approach for reducing the levels of Shigella in various foods that may be contaminated with the bacterium.

Sorensen, K. M., Meldgaard, T., Melchjorsen, C. J., Fridriksdottir, A. J., Pedersen, H., Petersen, O. W., and Kristensen, P. Upregulation of Mrps18a in breast cancer identified by selecting phage antibody libraries on breast tissue sections. BMC.Cancer. 1-5-2017; 17(1):19; PM: 28056857

ABSTRACT: BACKGROUND: One of the hallmarks of cancer is an altered energy metabolism, and here, mitochondria play a central role. Previous studies have indicated that some mitochondrial ribosomal proteins change their expression patterns upon transformation. *METHOD*: In this study, we have used the selection of recombinant antibody libraries displayed on the surface of filamentous bacteriophage as a proteomics discovery tool for the identification of breast cancer biomarkers. A small subpopulation of breast cells expressing both cytokeratin 19 and cytokeratin 14 was targeted using a novel selection procedure. *RESULTS*: We identified the mitochondrial ribosomal protein s18a (Mrps18a) as a protein which is upregulated in breast cancer. However, Mrps18a was not homogeneously upregulated in all cancer cells, suggesting the existence of sub-populations within the tumor. The upregulation was not confined to cytokeratin 19 and cytokeratin 14 double positive cells. *CONCLUSION*: This study illustrates how phage display can be applied towards the discovery of proteins which exhibit changes in their expression patterns. We identified the mitochondrial protein Mrps18a as being upregulated in human breast cancer cells compared to normal breast cells.

Sorensen, M. C., Gencay, Y. E., and Brondsted, L. Methods for Initial Characterization of Campylobacter jejuni Bacteriophages. Methods Mol.Biol. 2017; 1512:91-105; PM: 27885601

ABSTRACT: Here we describe an initial characterization of Campylobacter jejuni bacteriophages by host range analysis, genome size determination by pulsed-field gel electrophoresis, and receptor-type identification by screening mutants for phage sensitivity.

Spiering, M. M., Hanoian, P., Gannavaram, S., and Benkovic, S. J. RNA primer-primase complexes serve as the signal for polymerase recycling and Okazaki fragment initiation in T4 phage DNA replication. Proc.Natl.Acad.Sci.U.S.A. 5-15-2017; PM: 28507156

ABSTRACT: The opposite strand polarity of duplex DNA necessitates that the leading strand is replicated continuously whereas the lagging strand is replicated in discrete segments known as Okazaki fragments. The lagging-strand polymerase sometimes recycles to begin the synthesis of a new Okazaki fragment before finishing the previous fragment, creating a gap between the Okazaki fragments. The mechanism and signal that initiate this behavior-that is, the signaling mechanism-have not been definitively identified. We examined the role of RNA primer-primase complexes left on the lagging ssDNA from primer synthesis in initiating early lagging-strand polymerase recycling. We show for the T4 bacteriophage DNA replication system that primer-primase complexes have a residence time similar to the timescale of Okazaki fragment synthesis and the ability to block a holoenzyme synthesizing DNA and stimulate the dissociation of the holoenzyme to trigger polymerase recycling. The collision with primer-primase complexes triggering the early termination of Okazaki fragment synthesis has distinct advantages over those previously proposed because this signal requires no transmission to the lagging-strand polymerase through protein or DNA interactions, the mechanism for rapid dissociation of the holoenzyme is always collision, and no unique characteristics need to be assigned to either identical polymerase in the replisome. We have modeled repeated cycles of Okazaki fragment initiation using a collision with a completed Okazaki fragment or primer-primase complexes as the recycling mechanism. The results reproduce experimental data, providing insights into events related to Okazaki fragment initiation and the overall functioning of DNA replisomes.

Stanborough, T., Fegan, N., Powell, S. M., Tamplin, M., and Chandry, P. S. Insight into the Genome of Brochothrix thermosphacta, a Problematic Meat Spoilage Bacterium. Appl.Environ.Microbiol. 3-1-2017; 83(5); PM: 27986732

ABSTRACT: Brochothrix thermosphacta is a dominant but poorly studied meat spoilage organism. It is a close relative of the foodborne pathogen Listeria monocytogenes, and Brochothrix constitutes the second genus in the Listeriaceae family. Here, the genomes of 12 B. thermosphacta strains were sequenced, assembled into draft genomes, characterized, and compared with the genomes of Brochothrix campestris and L. monocytogenes Phenotypic properties including biogenic amine production and antibiotic and heavy metal susceptibilities were tested. Comparative genomic analyses revealed a high degree of similarity among the B. thermosphacta strains, with bacteriophage genes constituting a significant proportion of the accessory genome. Genes for the production of the malodorous compounds acetate, acetoin, butanediol, and fatty acids were found, as were stress response regulatory genes, which likely play important roles in the spoilage process. Amino acid decarboxylases were not identified in the genomes, and phenotypic testing confirmed their absence. Orthologs of Listeria virulence proteins involved in virulence regulation, intracellular survival, and surface

protein anchoring were found; however, key virulence genes were absent. Analysis of antibiotic susceptibility showed that strains were sensitive to the four tested antibiotics, except for one tetracycline-resistant isolate with plasmid-mediated tetracycline resistance genes. Strains tolerated higher levels of copper and cobalt than of cadmium although not at concentrations high enough to categorize the strains as being resistant. This study provides insight into the Brochothrix genome, links previous phenotypic data and data provided here to the gene inventory, and identifies genes that may contribute to the persistence of this organism in the food chain.IMPORTANCE Despite increasing knowledge and advances in food preservation techniques, microbial spoilage of foods causes substantial losses, with negative social and economic consequences. To better control the contamination and microbial spoilage of foods, fundamental knowledge of the biology of key spoilage bacteria is crucial. As a common meat spoilage organism, B. thermosphacta contributes substantially to spoilage-associated losses. Nonetheless, this organism and particularly its genome remain largely unstudied. This study contributes to improving our knowledge of the Brochothrix genus. Spoilage-relevant pathways and genes that may play a role in the survival of this organism in a food processing environment were identified, linking previous phenotypic data and data provided here to the gene inventory of Brochothrix and establishing parallels to and differences from the closely related foodborne pathogen L. monocytogenes.

Stanczak-Mrozek, K. I., Laing, K. G., and Lindsay, J. A. Resistance gene transfer: induction of transducing phage by sub-inhibitory concentrations of antimicrobials is not correlated to induction of lytic phage. J.Antimicrob.Chemother. 6-1-2017; 72(6):1624-1631; PM: 28369562

ABSTRACT: Objectives: Horizontal gene transfer of antimicrobial resistance (AMR) genes between clinical isolates via transduction is poorly understood. MRSA are opportunistic pathogens resistant to all classes of antimicrobial agents but currently no strains are fully drug resistant. AMR gene transfer between Staphylococcus aureus isolates is predominantly due to generalized transduction via endogenous bacteriophage, and recent studies have suggested transfer is elevated during host colonization. The aim was to investigate whether exposure to sub-MIC concentrations of antimicrobials triggers bacteriophage induction and/or increased efficiency of AMR gene transfer. Methods: Isolates from MRSA carriers were exposed to nine antimicrobials and supernatants were compared for lytic phage particles and ability to transfer an AMR gene. A new technology, droplet digital PCR, was used to measure the concentration of genes in phage particles. Results: All antibiotics tested induced lytic phage and AMR gene transduction, although the ratio of transducing particles to lytic particles differed substantially for each antibiotic. Mupirocin induced the highest ratio of transducing versus lytic particles. Gentamicin and novobiocin reduced UV-induced AMR transduction. The genes carried in phage particles correlated with AMR transfer or lytic particle activity, suggesting antimicrobials influence which DNA sequences are packaged into phage particles. Conclusions: Sub-inhibitory antibiotics induce AMR gene transfer between clinical MRSA, while combination therapy with an inhibiting antibiotic could potentially alter AMR gene packaging into phage particles, reducing AMR transfer. In a continually evolving environment, pathogens have an advantage if they can transfer DNA while lowering the risk of lytic death.

Stoffels, L., Taunt, H. N., Charalambous, B., and Purton, S. Synthesis of bacteriophage lytic proteins against Streptococcus pneumoniae in the chloroplast of Chlamydomonas reinhardtii. Plant Biotechnol.J. 2-3-2017; PM: 28160380

ABSTRACT: There is a pressing need to develop novel antibacterial agents given the widespread antibiotic resistance among pathogenic bacteria and the low specificity of the drugs available. Endolysins are antibacterial proteins that are produced by bacteriophage-infected cells to digest the bacterial cell wall for phage progeny release at the end of the lytic cycle. These highly efficient enzymes show a considerable degree of specificity for the target bacterium of the phage. Furthermore, the emergence of resistance against endolysins appears to be rare as the enzymes have evolved to target molecules in the cell wall that are essential for bacterial viability. Taken together, these factors make recombinant endolysins promising novel antibacterial agents. The chloroplast of the green unicellular alga Chlamydomonas reinhardtii represents an attractive platform for production of therapeutic proteins in general, not least due to the availability of established techniques for foreign gene expression, a lack of endotoxins or potentially infectious agents in the algal host, and low cost of cultivation. The chloroplast is particularly well suited to the production of endolysins as it mimics the native bacterial expression environment of these proteins while being devoid of their cell wall target. In this study, the endolysins Cpl-1 and Pal, specific to the major human pathogen Streptococcus pneumoniae, were produced in the C. reinhardtii chloroplast. The antibacterial activity of cell lysates and the isolated endolysins was demonstrated against different serotypes of S. pneumoniae, including clinical isolates and total recombinant protein yield was quantified at ~1.3 mg/g algal dry weight.

Stratton, C. W. Phages, Fitness, Virulence, and Synergy: A Novel Approach for the Therapy of Infections Caused by Pseudomonas aeruginosa. J.Infect.Dis. 3-1-2017; 215(5):668-670; PM: 28007923

No Abstract Available.

Strotskaya, A., Savitskaya, E., Metlitskaya, A., Morozova, N., Datsenko, K. A., Semenova, E., and Severinov, K. The action of Escherichia coli CRISPR-Cas system on lytic bacteriophages with different lifestyles and development strategies. Nucleic Acids Res. 2-28-2017; 45(4):1946-1957; PM: 28130424

ABSTRACT: CRISPR-Cas systems provide prokaryotes with adaptive defense against bacteriophage infections. Given an enormous variety of strategies used by phages to overcome their hosts, one can expect that the efficiency of protective action of CRISPR-Cas systems against different viruses should vary. Here, we created a collection of Escherichia coli strains with type I-E CRISPR-Cas system targeting various positions in the genomes of bacteriophages lambda, T5, T7, T4 and R1-37 and investigated the ability of these strains to resist the infection and acquire additional CRISPR spacers from the infecting phage. We find that the efficiency of CRISPR-Cas targeting by the host is determined by phage life style, the positions of the targeted protospacer within the genome, and the state of phage DNA. The results also suggest that during infection by lytic phages that are susceptible to CRISPR interference, CRISPR-Cas does not act as a true immunity system that saves the infected cell but rather enforces an abortive infection pathway leading to infected cell death with no phage progeny release.

Summers, W. C. Felix Hubert d'Herelle (1873-1949): History of a scientific mind. Bacteriophage. 2016; 6(4):e1270090; PM: 28090388

ABSTRACT: The discovery of bacteriophage one century ago by the French-Canadian Felix d'Herelle set off controversies as to the nature of bacteriophage as well as over the priority and credit for this discovery. The background and life of d'Herelle reveals a complex, self-taught outsider in science who was strongly influenced by his admiration of Louis Pasteur, but also his attachment to the philosophical positions of early 17th century philosophers, especially Francis Bacon. D'Herelle left substantial unpublished writings on his philosophical musings toward the end of his life.

Sun, B. and Wang, M. D. Single-Molecule Optical-Trapping Techniques to Study Molecular Mechanisms of a Replisome. Methods Enzymol. 2017; 582:55-84; PM: 28062045

ABSTRACT: The replisome is a multiprotein molecular machinery responsible for the replication of DNA. It is composed of several specialized proteins each with dedicated enzymatic activities, and in particular, helicase unwinds double-stranded DNA and DNA polymerase catalyzes the synthesis of DNA. Understanding how a replisome functions in the process of DNA replication requires methods to dissect the mechanisms of individual proteins and of multiproteins acting in concert. Single-molecule optical-trapping techniques have proved to be a powerful approach, offering the unique ability to observe and manipulate biomolecules at the single-molecule level and providing insights into the mechanisms of molecular motors and their interactions and coordination in a complex. Here, we describe a practical guide to applying these techniques to study the dynamics of individual proteins in the bacteriophage T7 replisome, as well as the coordination among them. We also summarize major findings from these studies, including nucleotide-specific helicase slippage and new lesion bypass pathway in T7 replication.

Sun, Y., Sun, Y., and Zhao, R. Establishment of MicroRNA delivery system by PP7 bacteriophage-like particles carrying cell-penetrating peptide. J.Biosci.Bioeng. 4-22-2017; PM: 28442387

ABSTRACT: MicroRNAs have great therapeutic potential in cancer and other diseases. However, their instability and low in vivo delivery efficiency limits their application. Recombinant PP7 bacteriophage-based virus-like particles (VLPs) could protect microRNAs against rapid degradation by RNase by packaging specific exogenous pre-microRNAs using the pac site. Insertion of a cell-penetrating peptide (CPP) into the AB-loop of VLPs could significantly improve the delivery efficiency of microRNAs into mammalian cells. Unlike other microRNA delivery methods (viral or non-viral vectors), recombinant PP7 VLPs carrying a CPP and microRNA could be efficiently expressed in Escherichia coli using the one-plasmid double expression system. Here we showed that PP7 VLPs carrying a CPP penetrated hepatoma SK-HEP-1 cells and delivered the pre-microRNA-23b, which was processed into a mature product within 24 h; a concentration of 10 nM was sufficient for the inhibition of hepatoma cell migration via the downregulation of liver-intestine cadherin expression. Furthermore, PP7 VLPs carrying a CPP and a pre-microRNA were not infectious, replicative, or cytotoxic. Therefore, recombinant PP7 VLPs can be used for simultaneous and targeted delivery of both microRNAs and peptides because of their ability to package specific exogenous RNA using the pac site and to display peptides.

Sun, Z., El, Omari K., Sun, X., Ilca, S. L., Kotecha, A., Stuart, D. I., Poranen, M. M., and Huiskonen, J. T. Double-stranded RNA virus outer shell assembly by bona fide domain-swapping. Nat.Commun. 3-13-2017; 8:14814; PM: 28287099

ABSTRACT: Correct outer protein shell assembly is a prerequisite for virion infectivity in many multi-shelled dsRNA viruses. In the prototypic dsRNA bacteriophage phi6, the assembly reaction is promoted by calcium ions but its biomechanics remain poorly understood. Here, we describe the near-atomic resolution structure of the phi6 double-shelled particle. The outer T=13 shell protein P8 consists of two alpha-helical domains joined by a linker, which allows the trimer to adopt either a closed or an open conformation. The trimers in an open conformation swap domains with each other. Our observations allow us to propose a mechanistic model for calcium concentration regulated outer shell assembly. Furthermore, the structure provides a prime exemplar of bona fide domain-swapping. This leads us to extend the theory of domain-swapping from the level of monomeric subunits and multimers to closed spherical shells, and to hypothesize a mechanism by which closed protein shells may arise in evolution.

Syngouna, V. I. and Chrysikopoulos, C. V. Inactivation of MS2 bacteriophage by titanium dioxide nanoparticles in the presence of quartz sand with and without ambient light. J.Colloid Interface Sci. 7-1-2017; 497:117-125; PM: 28282563

ABSTRACT: Virus inactivation by nanoparticles (NPs) is hypothesized to affect virus fate and transport in the subsurface. This study examines the interactions of viruses with titanium dioxide (TiO2) anatase NPs, which is a good disinfectant with unique physiochemical properties. The bacteriophage MS2 was used as a model virus. A series of batch experiments of MS2 inactivation by TiO2 NPs were conducted at room temperature (25 degrees C), in the presence and absence of quartz sand, with and without ambient light. Three sets of experiments were performed in phosphate buffered saline solution (PBS) and one in distilled deionized water (ddH2O). The virus inactivation experimental data were satisfactorily fitted with a pseudo-first order expression with a time dependent rate coefficient. Quartz sand was shown to affect MS2 inactivation by TiO2 NPs both in the presence and absence of ambient light, because, under the experimental conditions of this study, the quartz sand offers a protection to the attached MS2 against inactivation. Moreover, it was shown that low TiO2 concentration (10mg/L) affected only slightly MS2 inactivation with and without ambient light. Furthermore, PBS hindered MS2 inactivation by TiO2 NPs.

Szafranski, S. P., Winkel, A., and Stiesch, M. The use of bacteriophages to biocontrol oral biofilms. J.Biotechnol. 5-20-2017; 250:29-44; PM: 28108235

ABSTRACT: Infections induced by oral biofilms include caries, as well as periodontal, and peri-implant disease, and may influence quality of life, systemic health, and expenditure. As bacterial biofilms are highly resistant and resilient to conventional antibacterial therapy, it has been difficult to combat these infections. An innovative alternative to the biocontrol of oral biofilms could be to use bacteriophages or phages, the viruses of bacteria, which are specific, non-toxic, self-proliferating, and can penetrate into biofilms. Phages for Actinomyces naeslundii, Aggregatibacter actinomycetemcomitans, Enterococcus faecalis, Fusobacterium nucleatum, Lactobacillus spp., Neisseria spp., Streptococcus spp., and Veillonella spp. have been isolated and characterised. Recombinant phage enzymes (lysins) have been shown to lyse A. naeslundii and

Streptococcus spp. However, only a tiny fraction of available phages and their lysins have been explored so far. The unique properties of phages and their lysins make them promising but challenging antimicrobials. The genetics and biology of phages have to be further explored in order to determine the most effective way of applying them. Studying the effect of phages and lysins on multispecies biofilms should pave the way for microbiota engineering and microbiota-based therapy.

Szermer-Olearnik, B., Drab, M., Makosa, M., Zembala, M., Barbasz, J., Dabrowska, K., and Boratynski, J. Aggregation/dispersion transitions of T4 phage triggered by environmental ion availability. J.Nanobiotechnology. 4-24-2017; 15(1):32; PM: 28438164

ABSTRACT: BACKGROUND: Bacteriophage survives in at least two extremes of ionic environments: bacterial host (high ionic-cytosol) and that of soil (low ionic-environmental water). The impact of ionic composition in the micro- and macro-environments has not so far been addressed in phage biology. *RESULTS*: Here, we discovered a novel mechanism of aggregation/disaggregation transitions by phage virions. When normal sodium levels in phage media (150 mM) were lowered to 10 mM, advanced imaging by scanning electron microscopy, atomic force microscopy and dynamic light scattering all revealed formation of viral packages, each containing 20-100 virions. When ionic strength was returned from low to high, the aggregated state of phage reversed to a dispersed state, and the change in ionic strength did not substantially affect infectivity of the phage. By providing the direct evidence, that lowering of the sodium ion below the threshold of 20 mM causes rapid aggregation of phage while returning Na+ concentration to the values above this threshold causes dispersion of phage, we identified a biophysical mechanism of phage aggregation. *CONCLUSIONS*: Our results implicate operation of group behavior in phage and suggest a new kind of quorum sensing among its virions that is mediated by ions. Loss of ionic strength may act as a trigger in an evolutionary mechanism to improve the survival of bacteriophage by stimulating aggregation of phage when outside a bacterial host. Reversal of phage aggregation is also a promising breakthrough in biotechnological applications, since we demonstrated here the ability to retain viable virion aggregates on standard micro-filters.

Tan, H. L., Wang, P., and Li, W. [Advance on genome research of Yersinia pestis bacteriophage]. Zhonghua Liu Xing.Bing.Xue.Za Zhi. 4-10-2017; 38(4):561-564; PM: 28468083

ABSTRACT: Completion of the genome sequences on Yersinia pestis bacteriophage offered unprecedented opportunity for researchers to carry out related genomic studies. This review was based on the genomic sequences and provided a genomic perspective in describing the essential features of genome on Yersinia pestis bacteriophage. Based on the comparative genomics, genetic evolutionary relationship was discussed. Description of functions from the gene prediction and protein annotation provided evidence for further related studies.

Tao, P., Li, Q., Shivachandra, S. B., and Rao, V. B. Bacteriophage T4 as a Nanoparticle Platform to Display and Deliver Pathogen Antigens: Construction of an Effective Anthrax Vaccine. Methods Mol.Biol. 2017; 1581:255-267; PM: 28374254

ABSTRACT: Protein-based subunit vaccines represent a safer alternative to the whole pathogen in vaccine development. However, limitations of physiological instability and

low immunogenicity of such vaccines demand an efficient delivery system to stimulate robust immune responses. The bacteriophage T4 capsid-based antigen delivery system can robustly elicit both humoral and cellular immune responses without any adjuvant. Therefore, it offers a strong promise as a novel antigen delivery system. Currently Bacillus anthracis, the causative agent of anthrax, is a serious biothreat agent and no FDA-approved anthrax vaccine is available for mass vaccination. Here, we describe a potential anthrax vaccine using a T4 capsid platform to display and deliver the 83 kDa protective antigen, PA, a key component of the anthrax toxin. This T4 vaccine platform might serve as a universal antigen delivery system that can be adapted to develop vaccines against any infectious disease.

Tapia-Moreno, A., Juarez-Moreno, K., Gonzalez-Davis, O., Cadena-Nava, R. D., and Vazquez-Duhalt, R. Biocatalytic virus capsid as nanovehicle for enzymatic activation of Tamoxifen in tumor cells. Biotechnol.J. 4-3-2017; PM: 28371407

ABSTRACT: Most of the drugs used in chemotherapy should be activated by a transformation catalyzed by cytochrome P450 (CYP) enzymes. In this work, bacteriophage P22 virus-like particles (VLPs) containing CYP activity, immunologically inert and functionalized in order to be recognized by human cervix carcinoma cells and human breast adenocarcinoma cells were designed. The CYP was encapsulated inside the virus capsid obtained from the bacteriophage P22. CYP and coat protein were both heterologously expressed in E. coli. The VLPs with enzymatic activity were covered with polyethylene glycol that was functionalized in its distal end with folic acid in order to be recognized by folate receptors exhibited on tumor cells. The capacity of biocatalytic VLPs to be recognized and internalized into tumor cells is demonstrated. The VLP-treated cells showed enhanced capacity for the transformation of the pro-drug tamoxifen, which resulted in an increase of the cell sensitivity to this oncological drug. In this work, the potential use of biocatalytic VLPs vehicles as a delivery system of medical relevant enzymes is clearly demonstrated. In addition to cancer treatment, this technology also offers an interesting platform as nano-bioreactors for intracellular delivery of enzymatic activity for other diseases originated by the lack of enzymatic activity.

Templar, A., Schofield, D. M., and Nesbeth, D. N. Measuring E. coli and bacteriophage DNA in cell sonicates to evaluate the CAL1 reaction as a synthetic biology standard for qPCR. Biomol.Detect.Quantif. 2017; 11:21-30; PM: 28331815

ABSTRACT: We measured the impact of the presence of total Escherichia coli (E. coli) cellular material on the performance of the Linear Regression of Efficiency (LRE) method of absolute quantitative PCR (LRE qPCR), which features the putatively universal CAL1 calibration reaction, which we propose as a synthetic biology standard. We firstly used a qPCR reaction in which a sequence present in the lone genomic BirA locus is amplified. Amplification efficiency for this reaction, a key metric for many quantitative qPCR methods, was inhibited by cellular material from bioreactor cultivation to a greater extent than material from shake flask cultivation. We then compared LRE qPCR to the Standard Curve method of absolute qPCR (SC qPCR). LRE qPCR method matched the performance of the SC qPCR when used to measure 417-4.17 x 107 copies of the BirA target sequence present in a shake flask-derived cell sonicates sample, and for 97-9.7 x 105 copies in the equivalent bioreactor-derived sample. A plasmid-encoded T7 bacteriophage sequence was next used to compare the methods. In the presence of cell sonicates from samples of up to OD600 = 160, LRE qPCR outperformed SC qPCR in

the range of 1.54 x 108-1.54 x 1010 copies of the T7 target sequence and matched SC qPCR over 1.54 x 104-1.54 x 107 copies. These data suggest the CAL1 standard, combined with the LRE qPCR method, represents an attractive choice as a synthetic biology qPCR standard that performs well even when unpurified industrial samples are used as the source of template material.

Torres-Barcelo, C., Kaltz, O., Froissart, R., Gandon, S., Ginet, N., and Ansaldi, M. "French Phage Network"-Second Meeting Report. Viruses. 4-21-2017; 9(4); PM: 28430166

ABSTRACT: The study of bacteriophages (viruses of bacteria) includes a variety of approaches, such as structural biology, genetics, ecology, and evolution, with increasingly important implications for therapeutic and industrial uses. Researchers working with phages in France have recently established a network to facilitate the exchange on complementary approaches, but also to engage new collaborations. Here, we provide a summary of the topics presented during the second meeting of the French Phage Network that took place in Marseille in November 2016.

Trinh, J. T., Szekely, T., Shao, Q., Balazsi, G., and Zeng, L. Cell fate decisions emerge as phages cooperate or compete inside their host. Nat.Commun. 2-6-2017; 8:14341; PM: 28165024

ABSTRACT: The system of the bacterium Escherichia coli and its virus, bacteriophage lambda, is paradigmatic for gene regulation in cell-fate development, yet insight about its mechanisms and complexities are limited due to insufficient resolution of study. Here we develop a 4-colour fluorescence reporter system at the single-virus level, combined with computational models to unravel both the interactions between phages and how individual phages determine cellular fates. We find that phages cooperate during lysogenization, compete among each other during lysis, and that confusion between the two pathways occasionally occurs. Additionally, we observe that phage DNAs have fluctuating cellular arrival times and vie for resources to replicate, enabling the interplay during different developmental paths, where each phage genome may make an individual decision. These varied strategies could separate the selection for replication-optimizing beneficial mutations during lysis from sequence diversification during lysogeny, allowing rapid adaptation of phage populations for various environments.

Tripler, T. N., Teschke, C. M., and Alexandrescu, A. T. NMR assignments for the insertion domain of bacteriophage Sf6 coat protein. Biomol.NMR Assign. 2017; 11(1):35-38; PM: 27798771

ABSTRACT: The P22 bacteriophage group is a subgroup of the lambda phage supercluster, comprised of the three major sequence types Sf6, P22, and CUS-3, based on their capsid proteins. Our goal is to investigate the extent to which structure-function relationships are conserved for the viral coat proteins and I-domains in this subgroup. Sf6 is a phage that infects the human pathogen Shigella flexneri. The coat protein of Sf6 assembles into a procapsid, which further undergoes maturation during DNA packaging into an infectious virion. The Sf6 coat protein contains a genetically inserted domain, termed the I-domain, similar to the ones present in the P22 and CUS-3 coat proteins. Based on the P22 example, I-domains play important functional roles in capsid assembly, stability, viability, and size-determination. Here we report the 1H, 15N, and 13C chemical shift assignments for the I-domain of the Sf6 phage coat protein. Chemical shift-based secondary structure prediction and hydrogen-bond patterns from a long-range HNCO experiment indicate that the Sf6 I-domain adopts a 6-stranded beta-barrel fold like those

of P22 and CUS-3 but with important differences, including the absence of the D-loop that is critical for capsid assembly and the addition of a novel disordered loop region.

Tso, D., Peebles, C. L., Maurer, J. B., Duda, R. L., and Hendrix, R. W. On the catalytic mechanism of bacteriophage HK97 capsid crosslinking. Virology. 2017; 506:84-91; PM: 28359902

ABSTRACT: During maturation of the phage HK97 capsid, each of the 415 capsid subunits forms covalent bonds to neighboring subunits, stabilizing the capsid. Crosslinking is catalyzed not by a separate enzyme but by subunits of the assembled capsid in response to conformational rearrangements during maturation. This report investigates the catalytic mechanism. Earlier work established that the crosslinks are isopeptide (amide) bonds between side chains of a lysine on one subunit and an asparagine on another subunit, aided by a catalytic glutamate on a third subunit. The mature capsid structure suggests that the reaction may be facilitated by the arrival of a valine with the lysine to complete a hydrophobic pocket surrounding the glutamate, lysine and asparagine. We show that this valine has an essential role for efficient crosslinking, and that any of six other amino acids can successfully substitute for valine. Evidently none of the remaining 13 amino acids will work.

Tu, J., Park, T., Morado, D. R., Hughes, K. T., Molineux, I. J., and Liu, J. Dual host specificity of phage SP6 is facilitated by tailspike rotation. Virology. 2017; 507:206-215; PM: 28456019

ABSTRACT: Bacteriophage SP6 exhibits dual-host adsorption specificity. The SP6 tailspikes are recognized as important in host range determination but the mechanisms underlying dual host specificity are unknown. Cryo-electron tomography and sub-tomogram classification were used to analyze the SP6 virion with a particular focus on the interaction of tailspikes with host membranes. The SP6 tail is surrounded by six V-shaped structures that interconnect in forming a hand-over-hand hexameric garland. Each V-shaped structure consists of two trimeric tailspike proteins: gp46 and gp47, connected through the adaptor protein gp37. SP6 infection of Salmonella enterica serovars Typhimurium and Newport results in distinguishable changes in tailspike orientation, providing the first direct demonstration how tailspikes can confer dual host adsorption specificity. SP6 also infects S. Typhimurium strains lacking O antigen; in these infections tailspikes have no apparent specific role and the phage tail must therefore interact with a distinct host receptor to allow infection.

Turner, D., Wand, M. E., Briers, Y., Lavigne, R., Sutton, J. M., and Reynolds, D. M. Characterisation and genome sequence of the lytic Acinetobacter baumannii bacteriophage vB_AbaS_Loki. PLoS.One. 2017; 12(2):e0172303; PM: 28207864

ABSTRACT: Acinetobacter baumannii has emerged as an important nosocomial pathogen in healthcare and community settings. While over 100 of Acinetobacter phages have been described in the literature, relatively few have been sequenced. This work describes the characterisation and genome annotation of a new lytic Acinetobacter siphovirus, vB_AbaS_Loki, isolated from activated sewage sludge. Sequencing revealed that Loki encapsulates a 41,308 bp genome, encoding 51 predicted open reading frames. Loki is most closely related to Acinetobacter phage IME_AB3 and more distantly related to Burkholderia phage KL1, Paracoccus phage vB_PmaS_IMEP1 and Pseudomonas phages vB_Pae_Kakheti25, vB_PaeS_SCH_Ab26 and PA73. Loki is characterised by a narrow host range, among the 40 Acinetobacter isolates

tested, productive infection was only observed for the propagating host, A. baumannii ATCC 17978. Plaque formation was found to be dependent upon the presence of Ca2+ ions and adsorption to host cells was abolished upon incubation with a mutant of ATCC 17978 encoding a premature stop codon in lpxA. The complete genome sequence of vB_AbaS_Loki was deposited in the European Nucleotide Archive (ENA) under the accession number LN890663.

Umaraw, P., Prajapati, A., Verma, A. K., Pathak, V., and Singh, V. P. Control of campylobacter in poultry industry from farm to poultry processing unit: A review. Crit Rev.Food Sci.Nutr. 3-4-2017; 57(4):659-665; PM: 25898290

ABSTRACT: Campylobacter is an emerging zoonotic bacterial threat in the poultry industry. Most of the human cases of campylobacteriosis recorded have revealed their poultry origins. Various control measures have been employed both at the farm and processing levels to combat with it. The antibiotic treatment, phage therapy, competitive exclusion, and vaccination have been adapted at the farm level to reduce colonization of Campylobacter in poultry gut. While prevention of intestinal spillage, scheduled slaughter, logistic slaughter, chemical decontamination of carcasses are recommended to reduce contamination during processing. The postharvest interventions such as heat treatment, freezing, irradiation of contaminated carcass can effectively reduce Campylobacter contamination. Thus, integrated approaches are required to tackle infection of Campylobacter in humans.

Van Belleghem, J. D., Merabishvili, M., Vergauwen, B., Lavigne, R., and Vaneechoutte, M. A comparative study of different strategies for removal of endotoxins from bacteriophage preparations. J.Microbiol.Methods. 2017; 132:153-159; PM: 27913133

ABSTRACT: Bacterial endotoxins have high immunogenicity. Phage biology studies as well as therapeutic phage applications necessitate highly purified phage particles. In this study, we compared combinations of seven different endotoxin removal strategies and validated their endotoxin removal efficacy for five different phages (i.e. four Pseudomonas aeruginosa phages and one Staphylococcus aureus phage). These purification strategies included Endotrap HD column purification and/or CsCl density centrifugation in combination with Endotrap purification, followed by organic solvent (1-octanol), detergent (Triton X-100), enzymatic inactivation of the endotoxin using alkaline phosphatase and CIM monolytic anion exchange chromatography. We show that CsCl density purification of the P. aeruginosa phages, at an initial concentration of 1012-1013pfu/ml, led to the strongest reduction of endotoxins, with an endotoxin removal efficacy of up to 99%, whereas additional purification methods did not result in a complete removal of endotoxins from the phage preparations and only yielded an additional endotoxin removal efficacy of 23 to 99%, sometimes accompanied with strong losses in phage titer.

Van Tassell, M. L., Ibarra-Sanchez, L. A., Hoepker, G. P., and Miller, M. J. Hot topic: Antilisterial activity by endolysin PlyP100 in fresh cheese. J.Dairy Sci. 2017; 100(4):2482-2487; PM: 28161174

ABSTRACT: Our objective was to assess the antimicrobial efficacy of a Listeria bacteriophage endolysin that may address limitations of current antilisterial processes for

fresh cheeses. Listeria monocytogenes is highly problematic in the manufacture and processing of ready-to-eat foods due to its environmental persistence and its ability to grow under refrigerated storage. Special care must be taken to prevent listerial contamination during the production of fresh cheeses, as their delicate flavor and texture are incompatible with many of the antimicrobial processes and additives commonly used for other foods. Bacteriophage-derived cell wall hydrolytic enzymes, known as endolysins, comprise one possible intervention that may not suffer from the high strain specificity of their parent bacteriophages or the development of resistant strains. We recombinantly expressed endolysin PlyP100 and compared its lytic activity in vitro across several environmental parameters and target organisms, then incorporated it into a fresh cheese model challenged with a cocktail of L. monocytogenes. We show that PlyP100 demonstrates optimal activity under pH and salt concentrations consistent with a low-acid food matrix such as fresh cheese. Furthermore, we show that PlyP100 exhibits target specificity for gram-positive organisms with directly crosslinked peptidoglycan and displays considerable inhibitory activity against L. monocytogenes in fresh cheese for at least 4 wk under refrigerated storage. As PlyP100 demonstrates considerable promise for preventing the propagation of L. monocytogenes in fresh cheeses, this novel preservation method could help safeguard consumer health and the market expansion of an otherwise high-risk food with few other viable preservatives.

Verbree, C. T., Datwyler, S. M., Meile, S., Eichenseher, F., Donovan, D. M., Loessner, M. J., and Schmelcher, M. Identification of Peptidoglycan Hydrolase Constructs with Synergistic Staphylolytic Activity in Cow's Milk. Appl.Environ.Microbiol. 4-1-2017; 83(7); PM: 28159785

ABSTRACT: Peptidoglycan hydrolases (PGHs) have been suggested as novel therapeutics for the treatment of bovine mastitis. However, activity in the presence of cow's milk is an important requirement for drugs administered into the bovine udder. We have screened a library of >170 recombinant PGHs, including engineered bacteriophage endolysins, for enzymes with activity against Staphylococcus aureus in milk, using a microtiter plate-based protocol. Nine suitable PGH constructs were identified by this approach and further compared in time-kill assays for their efficacy against S. aureus in heat-treated milk. The three most active enzymes (lysostaphin, Ami2638A, and CHAPK_CWT-LST) reduced S. aureus in milk to undetectable numbers within minutes at nanomolar concentrations. Due to their different peptidoglycan cleavage sites, these PGH constructs revealed synergistic activity in most combinations, as demonstrated by checkerboard assays, spot assays, and time-kill experiments. Furthermore, they proved active against a selection of staphylococcal mastitis isolates from different geographical regions when applied individually or in synergistic combination. The most effective PGH combination completely eradicated S. aureus from milk, with no more bacteria being detected within 24 h after addition of the enzymes, corresponding to a reduction of >9 log units compared to the control. Efficacy was also retained at different inoculum levels (3 versus 6 log CFU/ml) and when S. aureus was grown in milk as opposed to broth prior to the experiments. In raw cow's milk, CHAPK_CWT-LST showed reduced efficacy, whereas both Ami2638A and lysostaphin retained their activity, reducing bacterial numbers by >3.5 log units within 3 h.IMPORTANCE Staphylococci and S. aureus in particular are a major cause of bovine mastitis, an inflammation of the mammary gland in cows associated with high costs and risks for consumers of milk products. S. aureus-induced mastitis, commonly treated by intramammary infusion of antibiotics, is characterized by low cure rates and increasing antibiotic resistance in bacteria. Therefore, alternative treatment options are highly desirable. PGHs, including bacteriophage endolysins, rapidly and specifically kill selected pathogens by degrading

their cell wall and are refractory to resistance development, therefore holding promise as novel antibacterial agents. This study employed a screening approach to identify PGH constructs with high staphylolytic activity in cow's milk within a large collection of enzymes. Our results suggest that the most promising enzymes identified by this strategy hold potential as novel mastitis therapeutics and support their further characterization in animal models.

Vernhes, E., Renouard, M., Gilquin, B., Cuniasse, P., Durand, D., England, P., Hoos, S., Huet, A., Conway, J. F., Glukhov, A., Ksenzenko, V., Jacquet, E., Nhiri, N., Zinn-Justin, S., and Boulanger, P. Erratum: High affinity anchoring of the decoration protein pb10 onto the bacteriophage T5 capsid. Sci.Rep. 4-28-2017; 7:43977; PM: 28452362

No Abstract Available.

Vernhes, E., Renouard, M., Gilquin, B., Cuniasse, P., Durand, D., England, P., Hoos, S., Huet, A., Conway, J. F., Glukhov, A., Ksenzenko, V., Jacquet, E., Nhiri, N., Zinn-Justin, S., and Boulanger, P. High affinity anchoring of the decoration protein pb10 onto the bacteriophage T5 capsid. Sci.Rep. 2-6-2017; 7:41662; PM: 28165000

ABSTRACT: Bacteriophage capsids constitute icosahedral shells of exceptional stability that protect the viral genome. Many capsids display on their surface decoration proteins whose structure and function remain largely unknown. The decoration protein pb10 of phage T5 binds at the centre of the 120 hexamers formed by the major capsid protein. Here we determined the 3D structure of pb10 and investigated its capsid-binding properties using NMR, SAXS, cryoEM and SPR. Pb10 consists of an alpha-helical capsid-binding domain and an Ig-like domain exposed to the solvent. It binds to the T5 capsid with a remarkably high affinity and its binding kinetics is characterized by a very slow dissociation rate. We propose that the conformational exchange events observed in the capsid-binding domain enable rearrangements upon binding that contribute to the quasi-irreversibility of the pb10-capsid interaction. Moreover we show that pb10 binding is a highly cooperative process, which favours immediate rebinding of newly dissociated pb10 to the 120 hexamers of the capsid protein. In extreme conditions, pb10 protects the phage from releasing its genome. We conclude that pb10 may function to reinforce the capsid thus favouring phage survival in harsh environments.

Visweswaran, G. R., Kurek, D., Szeliga, M., Pastrana, F. R., Kuipers, O. P., Kok, J., and Buist, G. Expression of prophage-encoded endolysins contributes to autolysis of Lactococcus lactis. Appl.Microbiol.Biotechnol. 2017; 101(3):1099-1110; PM: 27660179

ABSTRACT: Analysis of autolysis of derivatives of Lactococcus lactis subsp. cremoris MG1363 and subsp. lactis IL1403, both lacking the major autolysin AcmA, showed that L. lactis IL1403 still lysed during growth while L. lactis MG1363 did not. Zymographic analysis revealed that a peptidoglycan hydrolase activity of around 30 kDa is present in cell extracts of L. lactis IL1403 that could not be detected in strain MG1363. A comparison of all genes encoding putative peptidoglycan hydrolases of IL1403 and MG1363 led to the assumption that one or more of the 99 % homologous 27.9-kDa endolysins encoded by the prophages bIL285, bIL286 and bIL309 could account for the autolysis phenotype of IL1403. Induced expression of the endolysins from bIL285, bIL286 or bIL309 in L. lactis MG1363 resulted in detectable lysis or lytic activity. Prophage deletion and insertion

derivatives of L. lactis IL1403 had a reduced cell lysis phenotype. RT-qPCR and zymogram analysis showed that each of these strains still expressed one or more of the three phage lysins. A homologous gene and an endolysin activity were also identified in the natural starter culture L. lactis subsp. cremoris strains E8, Wg2 and HP, and the lytic activity could be detected under growth conditions that were identical as those used for IL1403. The results presented here show that these endolysins of L. lactis are expressed during normal growth and contribute to autolysis without production of (lytic) phages. Screening for natural strains expressing homologous endolysins could help in the selection of strains with enhanced autolysis and, thus, cheese ripening properties.

Voros, Z., Csik, G., Herenyi, L., and Kellermayer, M. S. Stepwise reversible nanomechanical buckling in a viral capsid. Nanoscale. 1-19-2017; 9(3):1136-1143; PM: 28009879

ABSTRACT: Viruses are nanoscale infectious agents constructed of a proteinaceous capsid that protects the packaged genomic material. Nanoindentation experiments using atomic force microscopy have, in recent years, provided unprecedented insight into the elastic properties, structural stability and maturation-dependent mechanical changes in viruses. However, the dynamics of capsid behavior are still unresolved. Here we used high-resolution nanoindentation experiments on mature, DNA-filled T7 bacteriophage particles. The elastic regime of the nanoindentation force trace contained discrete, stepwise transitions that cause buckling of the T7 capsid with magnitudes that are integer multiples of approximately 0.6 nm. Remarkably, the transitions are reversible and contribute to the rapid consolidation of the capsid structure against a force during cantilever retraction. The stepwise transitions were present even following the removal of the genomic DNA by heat treatment, indicating that they are related to the structure and dynamics of the capsomeric proteins. Dynamic force spectroscopy experiments revealed that the thermally activated consolidation step is approximately 104 times faster than spontaneous buckling, suggesting that the capsid stability is under strong dynamic control. Capsid structural dynamics may play an important role in protecting the genomic material from harsh environmental impacts. The nanomechanics approach employed here may be used to investigate the structural dynamics of other viruses and nanoscale containers as well.

Wagner, N., Brinks, E., Samtlebe, M., Hinrichs, J., Atamer, Z., Kot, W., Franz, C. M., Neve, H., and Heller, K. J. Whey powders are a rich source and excellent storage matrix for dairy bacteriophages. Int.J.Food Microbiol. 1-16-2017; 241:308-317; PM: 27835774

ABSTRACT: Thirteen whey powders and 5 whey powder formulations were screened for the presence of dairy bacteriophages using a representative set of 8 acid-producing Lactococcus lactis and 5 Streptococcus thermophilus, and 8 flavour-producing Leuconostoc pseudomesenteroides and Leuconostoc mesenteroides strains. Lytic L. lactis phages were detected in all samples, while S. thermophilus and Leuconostoc phages were present in 50% or 40% of the samples, respectively. Maximal phage titers were 6x107 plaque-forming units (pfu)/g of whey powder for L. lactis phages, 1x107pfu/g for Leuconostoc phages and 1x105pfu/g for S. thermophilus phages. In total, 55 phages were isolated and characterized. Thirty one of the 33 lactococcal phages tested belonged to the wide-spread 936 phage group. In the course of this study, a PCR detection method for Leuconostoc phages (Ali et al., 2013) was adapted to new phage isolates. Furthermore, a remarkably high stability of phages in whey powder samples was documented during a long-term storage period of 4 years.

Wallen, J. R., Zhang, H., Weis, C., Cui, W., Foster, B. M., Ho, C. M., Hammel, M., Tainer, J. A., Gross, M. L., and Ellenberger, T. Hybrid Methods Reveal Multiple Flexibly Linked DNA Polymerases within the Bacteriophage T7 Replisome. Structure. 1-3-2017; 25(1):157-166; PM: 28052235

ABSTRACT: The physical organization of DNA enzymes at a replication fork enables efficient copying of two antiparallel DNA strands, yet dynamic protein interactions within the replication complex complicate replisome structural studies. We employed a combination of crystallographic, native mass spectrometry and small-angle X-ray scattering experiments to capture alternative structures of a model replication system encoded by bacteriophage T7. Two molecules of DNA polymerase bind the ring-shaped primase-helicase in a conserved orientation and provide structural insight into how the acidic C-terminal tail of the primase-helicase contacts the DNA polymerase to facilitate loading of the polymerase onto DNA. A third DNA polymerase binds the ring in an offset manner that may enable polymerase exchange during replication. Alternative polymerase binding modes are also detected by small-angle X-ray scattering with DNA substrates present. Our collective results unveil complex motions within T7 replisome higher-order structures that are underpinned by multivalent protein-protein interactions with functional implications.

Wang, C., Chen, Q., Zhang, C., Yang, J., Lu, Z., Lu, F., and Bie, X. Characterization of a broad host-spectrum virulent Salmonella bacteriophage fmb-p1 and its application on duck meat. Virus Res. 5-3-2017; 236:14-23; PM: 28478136

ABSTRACT: The aim of this study was to find a virulent bacteriophage for the biocontrol of Salmonella in duck meat. A broad host-spectrum virulent phage, fmb-p1, was isolated and purified from an duck farm, and its host range was determined to include S. Typhimurium, S. Enteritidis, S. Saintpaul, S. Agona, S. Miami, S. Anatum, S. Heidelberg and S. Paratyphi-C. Electron microscopy and genome sequencing showed that fmb-p1 belongs to the family Siphoviridae. The genome of fmb-p1 is composed of a 43,327-bp double-stranded DNA molecule with 60 open reading frames and a total G+C content of 46.09%. There are no deleterious sequences or genes encoding known harmful products in the phage fmb-p1 genome. Phage fmb-p1 was stable under different temperature (40-75 degrees C), pH (4-10) and NaCl solutions (1-11%). The phage treatment (9.9x109 PFU/cm2) caused a peak reduction in S. Typhimurium of 4.52 log CFU/cm2 in ready-to-eat (RTE) duck meat, whereas potassium sorbate treatment (PS, 2mg/cm2) resulted in a 0.05-0.12 log reduction. Compared to PS treatment, there was significant difference in the S. Typhimurium reduction ($P<0.05$) by phage treatment at both 4 degrees C and 25 degrees C. The results suggested that phage could be applied to reduce Salmonella, on commercial poultry products.

Wang, S., Guo, R., Guo, Y. L., Shao, L. L., Liu, Y., Wei, S. J., Liu, Y. J., and Liu, Q. Z. Biological effects of chlamydiaphage phiCPG1 capsid protein Vp1 on chlamydia trachomatis in vitro and in vivo. J.Huazhong.Univ Sci.Technolog.Med.Sci. 2017; 37(1):115-121; PM: 28224434

ABSTRACT: The researches on chlamydia in recent years show that chlamydia bacteriophage may be a potential and effective means to solve the clinical infection of chlamydia trachomatis (Ct). We investigated the biological effect of chlamydiaphage phiCPG1 capsid protein Vp1 on Ct both in McCoy cells and genital tract of mice.

Different concentrations of Vp1 were co-incubated with Ct E serotype strain in McCoy cells. Female BALB/c mice were used to establish Ct E strain-induced urogenital infection model. They were randomly divided into five groups and given different treatments on the fifth day after Ct inoculation. Animals in groups 1 and 2 were given 30 muL different concentrations of Vp1 in the genital tract respectively, those in group 3 were intramuscularly injected with 30 muL Vp1, those in the infected group did not receive any intervention, and those in the control group received 30 muL PBS in the genital tract. The vaginal discharge was collected to identify the live chlamydia by cell culture and gene fragment by real time PCR different days after infection. Inhibition rate of 100 mug/mL and 50 mug/mL Vp1 proteins against Ct E strain in the McCoy cell cultures was 91% and 79% respectively. The number of intracellular Ct inclusion in the McCoy cells co-cultured with vaginal discharge of group 1 and group 2 was less than in the infected group, and that in group 1 was less than in group 2, on the 7th day after Ct inoculation. Real-time PCR showed that chlamydia concentration of the vaginal discharge in group 2 was lower than in the infected group, and that in group 1 was lower than in group 2 on the 10th day. It was suggested that Vp1 capsid proteins had inhibitory effect on the proliferation of Ct serovar E strain in cell culture and mouse genital tract.

Wang, S., Zhou, Z., Zhao, Z., Zhang, H., Haque, F., and Guo, P. Channel of viral DNA packaging motor for real time kinetic analysis of peptide oxidation states. Biomaterials. 2017; 126:10-17; PM: 28237908

ABSTRACT: Nanopore technology has become a powerful tool in single molecule sensing, and protein nanopores appear to be more advantageous than synthetic counterparts with regards to channel amenability, structure homogeneity, and production reproducibility. However, the diameter of most of the well-studied protein nanopores is too small to allow the passage of protein or peptides that are typically in multiple nanometers scale. The portal channel from bacteriophage SPP1 has a large channel size that allows the translocation of peptides with higher ordered structures. Utilizing single channel conductance assay and optical single molecule imaging, we observed translocation of peptides and quantitatively analyzed the dynamics of peptide oligomeric states in real-time at single molecule level. The oxidative and the reduced states of peptides were clearly differentiated based on their characteristic electronic signatures. A similar Gibbs free energy (DeltaG0) was obtained when different concentrations of substrates were applied, suggesting that the use of SPP1 nanopore for real-time quantification of peptide oligomeric states is feasible. With the intrinsic nature of size and conjugation amenability, the SPP1 nanopore has the potential for development into a tool for the quantification of peptide and protein structures in real time.

Wang, S., Gu, J., Lv, M., Guo, Z., Yan, G., Yu, L., Du, C., Feng, X., Han, W., Sun, C., and Lei, L. The antibacterial activity of E. coli bacteriophage lysin lysep3 is enhanced by fusing the Bacillus amyloliquefaciens bacteriophage endolysin binding domain D8 to the C-terminal region. J.Microbiol. 2017; 55(5):403-408; PM: 28124780

ABSTRACT: Bacteriophage endolysin is one of the most promising antibiotic substitutes, but in Gram-negative bacteria, the outer membrane prevents the lysin from hydrolyzing peptidoglycans and blocks the development of lysin applications. The prime strategy for new antibiotic substitutes is allowing lysin to access the peptidoglycan from outside of the bacteria by reformation of the lysin. In this study, the novel Escherichia coli (E. coli) phage lyase lysep3, which lacks outside-in catalytic ability, was fused with the N-terminal

region of the Bacillus amyloliquefaciens lysin including its cell wall binding domain D8 through the best manner of protein fusion based on the predicted tertiary structure of lysep3-D8 to obtain an engineered lysin that can lyse bacteria from the outside. Our results showed that lysep3-D8 could lyse both Gramnegative and Gram-positive bacteria, whereas lysep3 and D8 have no impact on bacterial growth. The MIC of lysep3-D8 on E. coli CVCC1418 is 60 mug/ml; lysep3-D8 can inhibit the growth of bacteria up to 12 h at this concentration. The bactericidal spectrum of lysep3-D8 is broad, as it can lyse of all of 14 E. coli strains, 3 P. aeruginosa strains, 1 Acinetobacter baumannii strain, and 1 Streptococcus strain. Lysep3-D8 has sufficient bactericidal effects on the 14 E. coli strains tested at the concentration of 100 mug/ml. The cell wall binding domain of the engineered lysin can destroy the integrity of the outer membrane of bacteria, thus allowing the catalytic domain to reach its target, peptidoglycan, to lyse the bacteria. Lysep3-D8 can be used as a preservative in fodder to benefit the health of animals. The method we used here proved to be a successful exploration of the reformation of phage lysin.

Wang, X., Wei, Z., Li, M., Wang, X., Shan, A., Mei, X., Jousset, A., Shen, Q., Xu, Y., and Friman, V. P. Parasites and competitors suppress bacterial pathogen synergistically due to evolutionary trade-offs. Evolution. 2017; 71(3):733-746; PM: 27925169

ABSTRACT: Parasites and competitors are important for regulating pathogen densities and subsequent disease dynamics. It is, however, unclear to what extent this is driven by ecological and evolutionary processes. Here, we used experimental evolution to study the eco-evolutionary feedbacks among Ralstonia solanacearum bacterial pathogen, Ralstonia-specific phage parasite, and Bacillus amyloliquefaciens competitor bacterium in the laboratory and plant rhizosphere. We found that while the phage had a small effect on pathogen densities on its own, it considerably increased the R. solanacearum sensitivity to antibiotics produced by B. amyloliquefaciens. Instead of density effects, this synergy was due to phage-driven increase in phage resistance that led to trade-off with the resistance to B. amyloliquefaciens antibiotics. While no evidence was found for pathogen resistance evolution to B. amyloliquefaciens antibiotics, the fitness cost of adaptation (reduced growth) was highest when the pathogen had evolved in the presence of both parasite and competitor. Qualitatively similar patterns were found between laboratory and greenhouse experiments even though the evolution of phage resistance was considerably attenuated in the tomato rhizosphere. These results suggest that evolutionary trade-offs can impose strong constraints on disease dynamics and that combining phages and antibiotic-producing bacteria could be an efficient way to control agricultural pathogens.

Waters, E. M., Neill, D. R., Kaman, B., Sahota, J. S., Clokie, M. R., Winstanley, C., and Kadioglu, A. Phage therapy is highly effective against chronic lung infections with Pseudomonas aeruginosa. Thorax. 3-6-2017; PM: 28265031

ABSTRACT: With an increase in cases of multidrug-resistant Pseudomonas aeruginosa, alternative and adjunct treatments are needed, leading to renewed interest in bacteriophage therapy. There have been few clinically relevant studies of phage therapy against chronic lung infections. Using a novel murine model that uses a natural respiratory inhalation route of infection, we show that phage therapy is an effective treatment against chronic P. aeruginosa lung infections. We also show efficacy against P. aeruginosa in a biofilm-associated cystic fibrosis lung-like environment. These studies

demonstrate the potential for phage therapy in the treatment of established and recalcitrant chronic respiratory tract infections.

Watkins, S. C. and Putonti, C. The use of informativity in the development of robust viromics-based examinations. PeerJ. 2017; 5:e3281; PM: 28480148

ABSTRACT: Metagenomics-based studies have provided insight into many of the complex microbial communities responsible for maintaining life on this planet. Sequencing efforts often uncover novel genetic content; this is most evident for phage communities, in which upwards of 90% of all sequences exhibit no similarity to any sequence in current data repositories. For the small fraction that can be identified, the top BLAST hit is generally posited as being representative of a viral taxon present in the sample of origin. Homology-based classification, however, can be misleading as sequence repositories capture but a small fraction of phage diversity. Furthermore, lateral gene transfer is pervasive within phage communities. As such, the presence of a particular gene may not be indicative of the presence of a particular viral species. Rather, it is just that: an indication of the presence of a specific gene. To circumvent this limitation, we have developed a new method for the analysis of viral metagenomic datasets. BLAST hits are weighted, integrating the sequence identity and length of alignments as well as a taxonomic signal, such that each gene is evaluated with respect to its information content. Through this quantifiable metric, predictions of viral community structure can be made with confidence. As a proof-of-concept, the approach presented here was implemented and applied to seven freshwater viral metagenomes. While providing a robust method for evaluating viral metagenomic data, the tool is versatile and can easily be customized to investigations of any environment or biome.

Weiss, G. A. and Hennet, T. Mechanisms and consequences of intestinal dysbiosis. Cell Mol.Life Sci. 3-28-2017; PM: 28352996

ABSTRACT: The composition of the gut microbiota is in constant flow under the influence of factors such as the diet, ingested drugs, the intestinal mucosa, the immune system, and the microbiota itself. Natural variations in the gut microbiota can deteriorate to a state of dysbiosis when stress conditions rapidly decrease microbial diversity and promote the expansion of specific bacterial taxa. The mechanisms underlying intestinal dysbiosis often remain unclear given that combinations of natural variations and stress factors mediate cascades of destabilizing events. Oxidative stress, bacteriophages induction and the secretion of bacterial toxins can trigger rapid shifts among intestinal microbial groups thereby yielding dysbiosis. A multitude of diseases including inflammatory bowel diseases but also metabolic disorders such as obesity and diabetes type II are associated with intestinal dysbiosis. The characterization of the changes leading to intestinal dysbiosis and the identification of the microbial taxa contributing to pathological effects are essential prerequisites to better understand the impact of the microbiota on health and disease.

Wendling, C. C., Piecyk, A., Refardt, D., Chibani, C., Hertel, R., Liesegang, H., Bunk, B., Overmann, J., and Roth, O. Tripartite species interaction: eukaryotic hosts suffer more from phage susceptible than from phage resistant bacteria. BMC.Evol.Biol. 4-11-2017; 17(1):98; PM: 28399796

ABSTRACT: BACKGROUND: Evolutionary shifts in bacterial virulence are often associated with a third biological player, for instance temperate phages, that can act as hyperparasites. By integrating as prophages into the bacterial genome they can contribute accessory genes, which can enhance the fitness of their prokaryotic carrier (lysogenic conversion). Hyperparasitic influence in tripartite biotic interactions has so far been largely neglected in empirical host-parasite studies due to their inherent complexity. Here we experimentally address whether bacterial resistance to phages and bacterial harm to eukaryotic hosts is linked using a natural tri-partite system with bacteria of the genus Vibrio, temperate vibriophages and the pipefish Syngnathus typhle. We induced prophages from all bacterial isolates and constructed a three-fold replicated, fully reciprocal 75 x 75 phage-bacteria infection matrix. *RESULTS*: According to their resistance to phages, bacteria could be grouped into three distinct categories: highly susceptible (HS-bacteria), intermediate susceptible (IS-bacteria), and resistant (R-bacteria). We experimentally challenged pipefish with three selected bacterial isolates from each of the three categories and determined the amount of viable Vibrio counts from infected pipefish and the expression of pipefish immune genes. While the amount of viable Vibrio counts did not differ between bacterial groups, we observed a significant difference in relative gene expression between pipefish infected with phage susceptible and phage resistant bacteria. *CONCLUSION*: These findings suggest that bacteria with a phage-susceptible phenotype are more harmful against a eukaryotic host, and support the importance of hyperparasitism and the need for an integrative view across more than two levels when studying host-parasite evolution.

Wolfe, M. K., Gallandat, K., Daniels, K., Desmarais, A. M., Scheinman, P., and Lantagne, D. Handwashing and Ebola virus disease outbreaks: A randomized comparison of soap, hand sanitizer, and 0.05% chlorine solutions on the inactivation and removal of model organisms Phi6 and E. coli from hands and persistence in rinse water. PLoS.One. 2017; 12(2):e0172734; PM: 28231311

ABSTRACT: To prevent Ebola transmission, frequent handwashing is recommended in Ebola Treatment Units and communities. However, little is known about which handwashing protocol is most efficacious. We evaluated six handwashing protocols (soap and water, alcohol-based hand sanitizer (ABHS), and 0.05% sodium dichloroisocyanurate, high-test hypochlorite, and stabilized and non-stabilized sodium hypochlorite solutions) for 1) efficacy of handwashing on the removal and inactivation of non-pathogenic model organisms and, 2) persistence of organisms in rinse water. Model organisms E. coli and bacteriophage Phi6 were used to evaluate handwashing with and without organic load added to simulate bodily fluids. Hands were inoculated with test organisms, washed, and rinsed using a glove juice method to retrieve remaining organisms. Impact was estimated by comparing the log reduction in organisms after handwashing to the log reduction without handwashing. Rinse water was collected to test for persistence of organisms. Handwashing resulted in a 1.94-3.01 log reduction in E. coli concentration without, and 2.18-3.34 with, soil load; and a 2.44-3.06 log reduction in Phi6 without, and 2.71-3.69 with, soil load. HTH performed most consistently well, with significantly greater log reductions than other handwashing protocols in three models. However, the magnitude of handwashing efficacy differences was small, suggesting protocols are similarly efficacious. Rinse water demonstrated a 0.28-4.77 log reduction in remaining E. coli without, and 0.21-4.49 with, soil load and a 1.26-2.02 log reduction in Phi6 without, and 1.30-2.20 with, soil load. Chlorine resulted in significantly less persistence of E. coli in both conditions and Phi6 without soil load in rinse water ($p<0.001$). Thus,

chlorine-based methods may offer a benefit of reducing persistence in rinse water. We recommend responders use the most practical handwashing method to ensure hand hygiene in Ebola contexts, considering the potential benefit of chlorine-based methods in rinse water persistence.

Won, G., Hajam, I. A., and Lee, J. H. Improved lysis efficiency and immunogenicity of Salmonella ghosts mediated by co-expression of lambda phage holin-endolysin and X174 gene E. Sci.Rep. 3-23-2017; 7:45139; PM: 28332591

ABSTRACT: Bacterial ghosts (BGs) are empty cell envelopes derived from Gram-negative bacteria by bacteriophage X174 gene E mediated lysis. They represent a novel inactivated vaccine platform; however, the practical application of BGs for human vaccines seems to be limited due to the safety concerns on the presence of viable cells in BGs. Therefore, to improve the lysis efficiency of the gene E, we exploited the peptidoglycan hydrolyzing ability of the lambda phage holin-endolysins to expedite the process of current BG production system. In this report, we constructed a novel ghost plasmid encoding protein E and holin-endolysins in tandem. We observed that sequential expressions of the gene E and the holin-endolysins elicited rapid and highly efficient Salmonella lysis compared to the lysis mediated by gene E only. These lysed BGs displayed improved immunogenicity in mice compared to the gene E mediated BGs. Consequently, seventy percent of the mice immunized with these novel ghosts survived against a lethal challenge while all the mice vaccinated with gene E mediated ghosts died by day 9 post-infection. We conclude that this novel strategy has the potential to generate highly efficient inactivated candidate vaccines that could replace the currently available bacterial vaccines.

Wu, B., Wang, R., and Fane, A. G. The roles of bacteriophages in membrane-based water and wastewater treatment processes: A review. Water Res. 3-1-2017; 110:120-132; PM: 27998784

ABSTRACT: Membrane filtration processes have been widely applied in water and wastewater treatment for many decades. Concerns related to membrane treatment effectiveness, membrane lifespan, and membrane fouling control have been paid great attention. To achieve sustainable membrane operation with regards to low energy and maintenance cost, monitoring membrane performance and applying suitable membrane control strategies are required. As the most abundant species in water and wastewater, bacteriophages have shown great potential to be employed in membrane processes as (1) indicators to assess membrane performance considering their similar properties to human pathogenic waterborne viruses; (2) surrogate particles to monitor membrane integrity due to their nano-sized nature; and (3) biological agents to alleviate membrane fouling because of their antimicrobial properties. This study aims to provide a comprehensive review on the roles of bacteriophages in membrane-based water and wastewater treatment processes, with focuses on their uses for membrane performance examination, membrane integrity monitoring, and membrane biofouling control. The advantages, limitations, and influencing factors for bacteriophage-based applications are reported. Finally, the challenges and prospects of bacteriophage-based applications in membrane processes for water treatment are highlighted.

Xing, S., Pan, X., Sun, Q., Pei, G., An, X., Mi, Z., Huang, Y., Zhao, B., and Tong, Y. Complete Genome Sequence of a Novel Multidrug-Resistant Klebsiella pneumoniae Phage, vB_Kpn_IME260. Genome Announc. 5-11-2017; 5(19); PM: 28495757

ABSTRACT: Klebsiella pneumoniae is the most common clinically important opportunistic bacterial pathogen and its infection is often iatrogenic. Its drug resistance poses a grave threat to public health. The genomic data reported here comprise an important resource for research on phage therapy in the control of drug-resistant bacteria.

Xing, S., Ma, T., Zhang, X., Huang, Y., Mi, Z., Sun, Q., An, X., Fan, H., Wu, S., Wei, L., and Tong, Y. First complete genome sequence of a virulent bacteriophage infecting the opportunistic pathogen Serratia rubidaea. Arch.Virol. 3-6-2017; PM: 28265773

ABSTRACT: A Serratia rubidaea phage, vB_Sru IME250, was isolated from hospital sewage. The morphology suggested that phage vB_Sru IME250 should be classified as a member of the family Myoviridae. High-throughput sequencing revealed that the phage genome has 154,938 nucleotides and consists of 193 coding DNA sequences, 90 of which have putative functions. The genome of vB_Sru IME250 is a linear, double-stranded DNA with an average GC content of 40.04%. The phage has a relatively high similarity to Klebsiella phage 0507-KN2-1, with a genome coverage of 84%.

Xu, D., Jia, R., Li, Y., and Gu, T. Advances in the treatment of problematic industrial biofilms. World J.Microbiol.Biotechnol. 2017; 33(5):97; PM: 28409363

ABSTRACT: In nature, microorganisms tend to form biofilms that consist of extracellular polymeric substances with embedded sessile cells. Biofilms, especially mixed-culture synergistic biofilm consortia, are notoriously difficult to treat. They employ various defense mechanisms against attacks from antimicrobial agents. Problematic industrial biofilms cause biofouling as well as biocorrosion, also known as microbiologically influenced corrosion. Biocides are often used to treat biofilms together with scrubbing or pigging. Unfortunately, chemical treatments suppress vulnerable microbial species while allowing resistant species to take over. Repeated treatment cycles are typically needed in biofilm mitigation. This leads to biocide dosage escalation, causing environmental problems, higher costs and sometimes operational problems such as scale formation. New treatment methods are being developed such as enhanced biocide treatment and bacteriophage treatment. Special materials such as antibacterial stainless steels are also being created to combat biofilms. This review discussed some of the advances made in the fight against problematic industrial biofilms.

Xu, J. and Xiang, Y. Membrane penetration by bacterial viruses. J.Virol. 4-12-2017; PM: 28404851

ABSTRACT: The bacteriophage varphi29 infects gram-positive Bacillus subtilis with a short non-contractile tail. Recent studies have shown that the varphi29 tail protein gp9 forms a hexameric tube with six long loops of membrane-active peptides blocking in the tube at the distal end of the tail. The long loops exit upon genome release and form a membrane pore for passage of the genome. The membrane penetration mechanism of the varphi29 tail might be common among tailed bacteriophages.

Xu, R., Shieh, Y. C., and Stewart, D. S. Comparison of RNA extraction kits for the purification and detection of an enteric virus surrogate on green onions via RT-PCR. J.Virol.Methods. 2017; 239:61-68; PM: 27836658

ABSTRACT: Real-time reverse transcriptase-polymerase chain reaction (RT-PCR) offers a rapid and sensitive molecular method for detection of enteric viruses. Unfortunately, these assays are often hampered by the low virus titre found in foods and PCR inhibition due to matrix carryover during RNA extraction. Four commercial RNA extraction kits (Qiagen's QIAamp Viral RNA Mini and UltraSens Virus kits, MoBio UltraClean Tissue & Cells RNA Isolation kit, and Ambion MagMAX Viral RNA Isolation kit) were evaluated for their ability to extract and purify MS2 bacteriophage RNA, an enteric virus surrogate, from inoculated green onions, a food which has been associated with viral gastroenteritis outbreaks. Inoculated green onion wash concentrates and green onion pieces with and without Qiagen QIAshredder homogenization were assayed in the kit comparison. MS2 detection and PCR inhibition were evaluated using a duplex real-time RT-PCR for MS2 and an exogenous internal amplification control (IAC) assay. Without homogenization, MS2 inoculated at 40pfu/g was detected in at least 4 lots of green onion wash concentrates using the silica-membrane spin-column kits. Inhibition was a factor for the magnetic silica-based MagMAX kit, which resulted in detection of MS2 in 1 of 5. Addition of QIAshredder homogenization prior to extraction did not adversely affect the silica-membrane kit results but improved the MS2 detection by MagMAX to 5 of 5 lots. Use of a 1:10 dilution of primary RNA extracts also improved detection. The QIAamp Viral RNA Mini and MagMAX kits were further compared for detection of MS2 from green onion pieces inoculated at 20 and 5pfu/g. Using homogenization, the MagMAX kit detected 20pfu/g in only 1 of 2 green onion lots, whereas the QIAamp Viral RNA kit detected 2 of 2 lots at 5 pfu/g without homogenization.

Xu, R. G., Jenkins, H. T., Chechik, M., Blagova, E. V., Lopatina, A., Klimuk, E., Minakhin, L., Severinov, K., Greive, S. J., and Antson, A. A. Viral genome packaging terminase cleaves DNA using the canonical RuvC-like two-metal catalysis mechanism. Nucleic Acids Res. 4-7-2017; 45(6):3580-3590; PM: 28100693

ABSTRACT: Bacteriophages and large dsDNA viruses encode sophisticated machinery to translocate their DNA into a preformed empty capsid. An essential part of this machine, the large terminase protein, processes viral DNA into constituent units utilizing its nuclease activity. Crystal structures of the large terminase nuclease from the thermophilic bacteriophage G20c show that it is most similar to the RuvC family of the RNase H-like endonucleases. Like RuvC proteins, the nuclease requires either Mn2+, Mg2+ or Co2+ ions for activity, but is inactive with Zn2+ and Ca2+. High resolution crystal structures of complexes with different metals reveal that in the absence of DNA, only one catalytic metal ion is accommodated in the active site. Binding of the second metal ion may be facilitated by conformational variability, which enables the two catalytic aspartic acids to be brought closer to each other. Structural comparison indicates that in common with the RuvC family, the location of the two catalytic metals differs from other members of the RNase H family. In contrast to a recently proposed mechanism, the available data do not support binding of the two metals at an ultra-short interatomic distance. Thus we postulate that viral terminases cleave DNA by the canonical RuvC-like mechanism.

Yakushevich, L. On the mechanical analogue of DNA. J.Biol.Phys. 2017; 43(1):113-125; PM: 28039557

ABSTRACT: The creation of mechanical analogues of biological systems is known as a useful instrument that helps to understand better the dynamical mechanisms of the functioning of living organisms. Mechanical analogues of biomolecules are usually constructed for imitation of their internal mobility, which is one of the most important properties of the molecules. Among the different types of internal motions, angular oscillations of nitrous bases are of special interest because they make a substantial contribution to the base pairs opening that in turn is an important element of the process of the DNA-protein recognition. In this paper, we investigate the possibility to construct a mechanical analogue for imitation of angular oscillations of nitrous bases in inhomogeneous DNA. It is shown that the analogue has the form of a mechanical chain of non-identical pendulums that oscillate in the gravitational field of the Earth and coupled by identical springs. The masses and lengths of pendulums, as well as the distances between neighboring pendulums and the rigidity of springs are calculated. To illustrate the approach, we present the result of construction of the mechanical analogue of the fragment of the sequence of bacteriophage T7D.

Yamashita, M., Leyden, M. R., Adaniya, H., Cheung, M. P., Hirai, T., Qi, Y., and Shintake, T. Graphene specimen support technique for low voltage STEM imaging. Microscopy.(Oxf). 4-27-2017; 1-11; PM: 28453814

ABSTRACT: The scanning transmission electron microscopy (STEM) mode of today's field emission scanning electron microscopes enables sub-nanometer resolution imaging. Graphene is a single-atom thick, electrically conductive material, making it an excellent specimen support for the low voltage STEM imaging of nanometer-sized objects such as viruses. Here we present low voltage STEM images of bacteriophage T4 recorded on highly cleaned graphene films. The results show that ultrathin graphene support films markedly improve image signal at low accelerating voltages. Staining with a low atomic number methylamine vanadate stain combined with the graphene support film enables the clear visualization of the fine structure of the T4 tail by the low voltage STEM technique. Despite the advantages of graphene support films, difficulties are often encountered in placing hydrophilic biological samples on hydrophobic graphene electron microscopy grids. We employed a spin sedimentation sample loading method to overcome this problem.

Yan, C., Zhang, Y., Yang, H., Yu, J., and Wei, H. Combining phagomagnetic separation with immunoassay for specific, fast and sensitive detection of Staphylococcus aureus. Talanta. 8-1-2017; 170:291-297; PM: 28501172

ABSTRACT: A Staphylococcus aureus (S. aureus)-specific lytic bacteriophage P-S. aureus-9, isolated from an environmental water sample, was assembled on magnetic beads for capturing S. aureus from samples through magnetic separation. Horseradish Peroxidase (HRP) labeled immunoglobulin (IgG) antibodies were used to detect the captured S. aureus by reacting with protein A on S. aureus followed by colorimetric signals, which were generated from the catalytic reaction between HRP and the substrate 3,3',5,5'-Tetramethylbenzidine (TMB). Under optimal conditions, the calibration curve was linear from 1.0x104 to 1.0x106CFUmL-1. The limit of detection (LOD) for the assay was 2.47x103CFUmL-1 and 8.86x103CFUmL-1 of S. aureus in PBS and apple juice, respectively. Moreover, the whole assay revealed outstanding specificity towards S. aureus, without any interference of common pathogenic bacteria, and can be completed within 90min

without any pre-enrichment. As far as known, it was the first time to detect S. aureus based on the double site recognition of bacteriophage and mammal IgG. The novel approach has shown good potentials for a rapid, specific, cheap and simple detection of S. aureus in food samples.

Yang, H. and Patel, D. J. New CRISPR-Cas systems discovered. Cell Res. 2017; 27(3):313-31; PM: 28220773

ABSTRACT: In bacteria and archaea, CRISPR-Cas adaptive immune systems utilize RNA-guided endonucleases to defend against invasion by foreign nucleic acids of bacteriophage, virus and plasmid origin. In a recent paper published in Nature, Burstein et al. identified the first Cas9 protein in uncultivated archaea and two novel CRISPR-CasX and CRISPR-CasY systems in uncultivated bacteria by capitalizing on analysis of terabase-scale metagenomic datasets from natural uncultivated organisms.

Yang, L., Li, W., Jiang, G. Z., Zhang, W. H., Ding, H. Z., Liu, Y. H., Zeng, Z. L., and Jiang, H. X. Characterization of a P1-like bacteriophage carrying CTX-M-27 in Salmonella spp. resistant to third generation cephalosporins isolated from pork in China. Sci.Rep. 1-18-2017; 7:40710; PM: 28098241

ABSTRACT: The aim of this study was to elucidate the epidemiology of third generation cephalosporin resistant Samonella isolates from pork of a slaughterhouse in China and the features of transferable elements carrying blaCTX-M genes. One hundred and twenty-six (7.3%) Salmonella isolates were identified; S. Derby and S. Rissen were the most two prevalent serotypes. Among these isolates 20 (15.8%) were resistant to third generation cephalosporins and nine of them carried blaCTX-M-27. S1-PFGE and replicon typing of blaCTX-M-27-carrying plasmids showed that seven were untypeable plasmids of about 104 Kb and two were IncP plasmids of about 300 Kb. Complete sequence analysis of one PBRT-untypeable plasmid showed it was a P1-like bateriophage, named SJ46, which contained a non-phage-associated region with several mobile elements, including Tn1721, ISEcp1B and IS903D. The other six 104 Kb PBRT-untypeable blaCTX-M-27-carrying plasmids also harboured the same phage-insertion region of SJ46 suggesting that they were the same P1-like bacteriophage. PFGE profiles of the parental strains revealed both potential vertical and horizontal spread of this P1-like blaCTX-M-27-containing element. Additionally, the representative gene of the P1 family bacteriophage, repL, was detected in 19.0% (24/126) of the isolates. This study indicated a potential role of P1-family bacteriophage in capture and spread of antimicrobial resistance in pathogens.

Yang, L., Li, W., Jiang, G. Z., Zhang, W. H., Ding, H. Z., Liu, Y. H., Zeng, Z. L., and Jiang, H. X. Corrigendum: Characterization of a P1-like bacteriophage carrying CTX-M-27 in Salmonella spp. resistant to third generation cephalosporins isolated from pork in China. Sci.Rep. 4-26-2017; 7:46728; PM: 28443633

No Abstract Available.

Yeh, T. Y. Complete nucleotide sequence of a new filamentous phage, Xf109, which integrates its genome into the chromosomal DNA of Xanthomonas oryzae. Arch.Virol. 2017; 162(2):567-572; PM: 27743252

ABSTRACT: Unlike Ff-like coliphages, certain filamentous Inoviridae phages integrate their genomes into the host chromosome and enter a prophage state in their infectious cycle. This lysogenic life cycle was first reported for Xanthomonas citri Cf phage. However, except for the X. citri phages Cf and XacF1, complete genome sequence information about lysogenic Xanthomonas phages is not available to date. A proviral sequence of Xf109 phage was identified in the genome of Xanthomonas oryzae, the rice bacterial blight pathogen, and revived as infectious virions to lysogenize its host de novo. The genome of Xf109 phage is 7190 nucleotides in size and contains 12 predicted open reading frames in an organization similar to that of the Cf phage genome. Seven of the Xf109 proteins show significant sequence similarity to Cf and XacF1 phage proteins, while its ORF4 shares 92 % identity with the major coat protein of X. phage oryzae Xf. Integration of Xf109 phage DNA into the host genome is site-specific, and the attP/attB sequence contains the dif core sequence 5'-TATACATTATGCGAA-3', which is identical to that of Cf, XacF1, and Xanthomonas campestris phage varphiLf. To my knowledge, this is the first complete genome sequence of a filamentous bacteriophage that infects X. oryzae.

Yeh, Y., Purushothaman, P., Gupta, N., Ragnone, M., Verma, S. C., and de Mello, A. S. Bacteriophage application on red meats and poultry: Effects on Salmonella population in final ground products. Meat.Sci. 2017; 127:30-34; PM: 28110127

ABSTRACT: This research was conducted to study the effects of bacteriophage application during tumbling on Salmonella populations in ground meat and poultry. Red meat trim and poultry were inoculated with a Salmonella cocktail to result in a contamination level of 7logCFU/g in ground products. A commercial preparation containing bacteriophages S16 and Felix-O1a (FO1a) was applied during tumbling at 107 and 108PFU/ml. Samples were held at 4 degrees C for 6h and 18h (red meat) and 30min and 6h (poultry). Overall, bacteriophage application on trim reduced 1 and 0.8logCFU/g of Salmonella in ground beef and ground pork, respectively. For ground chicken and ground turkey, Salmonella was reduced by 1.1 and 0.9logCFU/g, respectively. This study shows that bacteriophage application during tumbling of red meat trim and poultry can provide additional Salmonella control in ground products.

Yuan, Y. and Gao, M. Jumbo Bacteriophages: An Overview. Front Microbiol. 2017; 8:403; PM: 28352259

ABSTRACT: Tailed bacteriophages with genomes larger than 200 kbp are classified as Jumbo phages, and are rarely isolated by conventional methods. These phages are designated "jumbo" owing to their most notable features of a large phage virion and large genome size. However, in addition to these, jumbo phages also exhibit several novel characteristics that have not been observed for phages with smaller genomes, which differentiate jumbo phages in terms of genome organization, virion structure, progeny propagation, and evolution. In this review, we summarize available reports on jumbo phages and discuss the differences between jumbo phages and small-genome phages. We also discuss data suggesting that jumbo phages might have evolved from phages with smaller genomes by acquiring additional functional genes, and that these additional genes reduce the dependence of the jumbo phages on the host bacteria.

Yung, M. C., Bourguet, F. A., Carpenter, T. S., and Coleman, M. A. Re-directing bacterial microcompartment systems to enhance recombinant expression of lysis protein E from bacteriophage varphiX174 in Escherichia coli. Microb.Cell Fact. 4-26-2017; 16(1):71; PM: 28446197

ABSTRACT: BACKGROUND: Recombinant expression of toxic proteins remains a challenging problem. One potential method to shield toxicity and thus improve expression of these proteins is to encapsulate them within protein compartments to sequester them away from their targets. Many bacteria naturally produce so-called bacterial microcompartments (BMCs) in which enzymes comprising a biosynthetic pathway are encapsulated in a proteinaeous shell, which is in part thought to shield the cells from the toxicity of reaction intermediates. As a proof-of-concept, we attempted to encapsulate toxic, lysis protein E (E) from bacteriophage varphiX174 inside recombinant BMCs to enhance its expression and achieve higher yields during downstream purification. *RESULTS*: E was fused with various N-terminal BMC targeting tags (PduP-, PduD-, and EutC-tags, 18-20 amino acids) and co-expressed with appropriate BMC shell proteins that associate with the tags and are required to form BMCs. Only BMC targeted E fusions, but not non-tagged E, could be successfully cloned, suggesting that the BMC tags reduce the toxicity of E. A PduP-tagged E system appeared to achieve the highest expression of E. Co-expression of Pdu BMC shell proteins with PduP-E increased its expression by 20-50%. Affinity purification of PduP-E via Ni-NTA in the presence of Empigen BB detergent yielded 270 microg of PduP-E per L of induced culture. Removal of the PduP-tag via proteolysis resulted in a final yield of 200 microg of E per L of induced culture, a nearly order of magnitude (~sevenfold) improvement compared to prior reports. *CONCLUSIONS*: These results demonstrate improved expression of varphiX174 lysis protein E via re-directed BMC systems and ultimately higher E purification yields. Similar strategies can be used to enhance expression of other toxic proteins in recombinant Escherichia coli systems.

Zambenedetti, M. R., Pavoni, D. P., Dallabona, A. C., Dominguez, A. C., Poersch, C. O., Fragoso, S. P., and Krieger, M. A. Internal control for real-time polymerase chain reaction based on MS2 bacteriophage for RNA viruses diagnostics. Mem.Inst.Oswaldo Cruz. 2017; 112(5):339-347; PM: 28403327

ABSTRACT: BACKGROUND: Real-time reverse transcription polymerase chain reaction (RT-PCR) is routinely used to detect viral infections. In Brazil, it is mandatory the use of nucleic acid tests to detect hepatitis C virus (HCV), hepatitis B virus and human immunodeficiency virus in blood banks because of the immunological window. The use of an internal control (IC) is necessary to differentiate the true negative results from those consequent from a failure in some step of the nucleic acid test. *OBJECTIVES*: The aim of this study was the construction of virus-modified particles, based on MS2 bacteriophage, to be used as IC for the diagnosis of RNA viruses. *METHODS*: The MS2 genome was cloned into the pET47b(+) plasmid, generating pET47b(+)-MS2. MS2-like particles were produced through the synthesis of MS2 RNA genome by T7 RNA polymerase. These particles were used as non-competitive IC in assays for RNA virus diagnostics. In addition, a competitive control for HCV diagnosis was developed by cloning a mutated HCV sequence into the MS2 replicase gene of pET47b(+)-MS2, which produces a non-propagating MS2 particle. The utility of MS2-like particles as IC was evaluated in a one-step format multiplex real-time RT-PCR for HCV detection. *FINDINGS*: We demonstrated that both competitive and non-competitive IC could be successfully used to monitor the HCV amplification

performance, including the extraction, reverse transcription, amplification and detection steps, without compromising the detection of samples with low target concentrations. In conclusion, MS2-like particles generated by this strategy proved to be useful IC for RNA virus diagnosis, with advantage that they are produced by a low cost protocol. An attractive feature of this system is that it allows the construction of a multicontrol by the insertion of sequences from more than one pathogen, increasing its applicability for diagnosing different RNA viruses.

Zarrouk, K., Piret, J., and Boivin, G. Herpesvirus DNA polymerases: Structures, functions and inhibitors. Virus Res. 1-30-2017; PM: 28153606

ABSTRACT: Human herpesviruses are large double-stranded DNA viruses belonging to the Herpesviridae family. These viruses have the ability to establish lifelong latency into the host and to periodically reactivate. Primary infections and reactivations of herpesviruses cause a large spectrum of diseases and may lead to severe complications in immunocompromised patients. The viral DNA polymerase is a key enzyme in the lytic phase of the infection by herpesviruses. This review focuses on the structures and functions of viral DNA polymerases of herpes simplex virus (HSV) and human cytomegalovirus (HCMV). DNA polymerases of HSV (UL30) and HCMV (UL54) belong to B family DNA polymerases with which they share seven regions of homology numbered I to VII as well as a delta-region C which is homologous to DNA polymerases delta. These DNA polymerases are multi-functional enzymes exhibiting polymerase, 3'-5' exonuclease proofreading and ribonuclease H activities. Furthermore, UL30 and UL54 DNA polymerases form a complex with UL42 and UL44 processivity factors, respectively. The mechanisms involved in their polymerisation activity have been elucidated based on structural analyses of the DNA polymerase of bacteriophage RB69 crystallized under different conformations, i.e. the enzyme alone or in complex with DNA and with both DNA and incoming nucleotide. All antiviral agents currently used for the prevention or treatment of HSV and HCMV infections target the viral DNA polymerases. However, long-term administration of these antivirals may lead to the emergence of drug-resistant isolates harboring mutations in genes encoding viral enzymes that phosphorylate drugs (i.e., nucleoside analogues) and/or DNA polymerases.

Zelasko, S., Gorski, A., and Dabrowska, K. Delivering phage therapy per os: benefits and barriers. Expert.Rev.Anti.Infect.Ther. 2017; 15(2):167-179; PM: 27885865

ABSTRACT: INTRODUCTION: Multidrug-resistant bacterial infections of the gastrointestinal tract pose a serious public health concern. High levels of antibiotic drug resistance, along with the potential for antibiotics to precipitate disease or alter the gut microbiome has prompted research into alternative treatment methods. Evidence suggests that bacteriophage therapy delivered per os may be well-suited to target such infections. Areas covered: Herein, we discuss the specific advantages and challenges of using orally administered phage therapy. Our literature review encompasses recent works using phages to target various clinically-relevant bacteria in vivo. We also provide insights into methods that aim to overcome the barriers to effective phage transit through the harsh gastrointestinal environment. Expert commentary: Evidence from a number of in vivo animal studies suggests that targeting bacterial infections using phages delivered orally holds potential. Efficacious oral phage therapy depends on the delivery of sufficient phage titers to the infection site, which may be hindered by the host's gastrointestinal tract and immune response.

Zhang, C., Zhang, Z., Li, J., Qin, K., Wei, Y., Zhang, Q., Lin, L., and Ji, X. Complete genome sequence of the lytic cold-active Pseudomonas fluorescens bacteriophage VSW-3 from Napahai plateau wetland. Virus Genes. 2017; 53(1):146-150; PM: 27796639

ABSTRACT: The lytic cold-active bacteriophage VSW-3, belonging to the Podoviridae family and infecting the host Pseudomonas fluorescens SW-3, was isolated from the Napahai plateau wetland in China. With the development of sequencing technology, the study of Pseudomonas genomic diversity has increased; however, knowledge of cold-active phages infecting Pseudomonas is limited. The newly sequenced phage VSW-3 was classified based on virion morphology by transmission electron microscope. Sequence analysis revealed that the genome size was 40,556 bp with an overall GC content of 57.54 % and 46 open reading frames. The genome was organized into several modules containing genes for packaging, structural proteins, replication/transcription, and phage lysis. The sequence contained 45 potential promoters, 3 transcription terminators, and yet no tRNAs. This is the first report of cold-active Pseudomonas fluorescens bacteriophage genome sequencing.

Zhang, L., Xu, D., Huang, Y., Zhu, X., Rui, M., Wan, T., Zheng, X., Shen, Y., Chen, X., Ma, K., and Gong, Y. Structural and functional characterization of deep-sea thermophilic bacteriophage GVE2 HNH endonuclease. Sci.Rep. 2-13-2017; 7:42542; PM: 28211904

ABSTRACT: HNH endonucleases in bacteriophages play a variety of roles in the phage lifecycle as key components of phage DNA packaging machines. The deep-sea thermophilic bacteriophage Geobacillus virus E2 (GVE2) encodes an HNH endonuclease (GVE2 HNHE). Here, the crystal structure of GVE2 HNHE is reported. This is the first structural study of a thermostable HNH endonuclease from a thermophilic bacteriophage. Structural comparison reveals that GVE2 HNHE possesses a typical betabetaalpha-metal fold and Zn-finger motif similar to those of HNH endonucleases from other bacteriophages, apart from containing an extra alpha-helix, suggesting conservation of these enzymes among bacteriophages. Biochemical analysis suggests that the alanine substitutions of the conserved residues (H93, N109 and H118) in the HNH motif of GVE2 HNHE abolished 94%, 60% and 83% of nicking activity, respectively. Compared to the wild type enzyme, the H93A mutant displayed almost the same conformation while the N108A and H118A mutants had different conformations. In addition, the wild type enzyme was more thermostable than the mutants. In the presence of Mn2+ or Zn2+, the wild type enzyme displayed distinct DNA nicking patterns. However, high Mn2+ concentrations were needed for the N109A and H118A mutants to nick DNA while Zn2+ inactivated their nicking activity.

Zhang, L. and Tripathi, A. Archaeal RNA ligase from thermoccocus kodakarensis for template dependent ligation. RNA.Biol. 1-2-2017; 14(1):36-44; PM: 27715457

ABSTRACT: Nicking-sealing RNA ligases play a significant biological role in host defense and cellular repair, and have become an important molecular tool in biomedical engineering. Due to the propensity for RNA to form secondary structures, RNA modifying enzymes with elevated optimum temperatures are highly desired. Current characterized double stranded RNA ligases, such as the bacteriophage T4 RNA ligase 2, while possessing good template dependency, are not active at elevated temperatures. The few characterized RNA ligases from thermophiles exhibit high template independency.

We synthesize and characterize here, KOD RNA ligase (KOD1Rnl), a thermostable and template dependent RNA ligase from the archaeon, Thermoccocus Kodakarensis. We disclose that a 13 time reduction in template independent ligation can be achieved with the addition of a single stranded DNase, such as RecJ. We also elucidate the effects of the presence of blood proteins on the activity of KOD1Rnl. Template dependent and thermostable RNA ligases, such as KOD RNA ligase, can be utilized in RNA detection, modification and sequencing.

Zhao, H., Li, K., Lynn, A. Y., Aron, K. E., Yu, G., Jiang, W., and Tang, L. Structure of a headful DNA-packaging bacterial virus at 2.9 A resolution by electron cryo-microscopy. Proc.Natl.Acad.Sci.U.S.A. 4-4-2017; 114(14):3601-3606; PM: 28320961

ABSTRACT: The enormous prevalence of tailed DNA bacteriophages on this planet is enabled by highly efficient self-assembly of hundreds of protein subunits into highly stable capsids. These capsids can stand with an internal pressure as high as approximately 50 atmospheres as a result of the phage DNA-packaging process. Here we report the complete atomic model of the headful DNA-packaging bacteriophage Sf6 at 2.9 A resolution determined by electron cryo-microscopy. The structure reveals the DNA-inflated, tensed state of a robust protein shell assembled via noncovalent interactions. Remarkable global conformational polymorphism of capsid proteins, a network formed by extended N arms, mortise-and-tenon-like intercapsomer joints, and abundant beta-sheet-like mainchain:mainchain intermolecular interactions, confers significant strength yet also flexibility required for capsid assembly and DNA packaging. Differential formations of the hexon and penton are mediated by a drastic alpha-helix-to-beta-strand structural transition. The assembly scheme revealed here may be common among tailed DNA phages and herpesviruses.

Zhao, X., Shen, M., Jiang, X., Shen, W., Zhong, Q., Yang, Y., Tan, Y., Agnello, M., He, X., Hu, F., and Le, S. Transcriptomic and Metabolomics Profiling of Phage-Host Interactions between Phage PaP1 and Pseudomonas aeruginosa. Front Microbiol. 2017; 8:548; PM: 28421049

ABSTRACT: The basic biology of bacteriophage-host interactions has attracted increasing attention due to a renewed interest in the therapeutic potential of bacteriophages. In addition, knowledge of the host pathways inhibited by phage may provide clues to novel drug targets. However, the effect of phage on bacterial gene expression and metabolism is still poorly understood. In this study, we tracked phage-host interactions by combining transcriptomic and metabolomic analyses in Pseudomonas aeruginosa infected with a lytic bacteriophage, PaP1. Compared with the uninfected host, 7.1% (399/5655) of the genes of the phage-infected host were differentially expressed genes (DEGs); of those, 354 DEGs were downregulated at the late infection phase. Many of the downregulated DEGs were found in amino acid and energy metabolism pathways. Using metabolomics approach, we then analyzed the changes in metabolite levels in the PaP1-infected host compared to un-infected controls. Thymidine was significantly increased in the host after PaP1 infection, results that were further supported by increased expression of a PaP1-encoded thymidylate synthase gene. Furthermore, the intracellular betaine concentration was drastically reduced, whereas choline increased, presumably due to downregulation of the choline-glycine betaine pathway. Interestingly, the choline-glycine betaine pathway is a potential antimicrobial target; previous studies have shown that betB inhibition results in the depletion of betaine and the accumulation of betaine aldehyde, the combination of which is toxic to P.

aeruginosa. These results present a detailed description of an example of phage-directed metabolism in P. aeruginosa. Both phage-encoded auxiliary metabolic genes and phage-directed host gene expression may contribute to the metabolic changes observed in the host.

Zheng, Y., Lorenzo, C., and Beal, P. A. DNA editing in DNA/RNA hybrids by adenosine deaminases that act on RNA. Nucleic Acids Res. 4-7-2017; 45(6):3369-3377; PM: 28132026

ABSTRACT: Adenosine deaminases that act on RNA (ADARs) carry out adenosine (A) to inosine (I) editing reactions with a known requirement for duplex RNA. Here, we show that ADARs also react with DNA/RNA hybrid duplexes. Hybrid substrates are deaminated efficiently by ADAR deaminase domains at dA-C mismatches and with E to Q mutations in the base flipping loop of the enzyme. For a long, perfectly matched hybrid, deamination is more efficient with full length ADAR2 than its isolated deaminase domain. Guide RNA strands for directed DNA editing by ADAR were used to target six different 2-deoxyadenosines in the M13 bacteriophage ssDNA genome. DNA editing efficiencies varied depending on the sequence context of the editing site consistent with known sequence preferences for ADARs. These observations suggest the reaction within DNA/RNA hybrids may be a natural function of human ADARs. In addition, this work sets the stage for development of a new class of genome editing tools based on directed deamination of 2-deoxyadenosines in DNA/RNA hybrids.

Zhou, J., Meng, L., Sun, C., Chen, S., Sun, F., Luo, P., and Zhao, Y. A new biochromatography model based on DNA origami assembled PPARgamma: construction and evaluation. Anal.Bioanal.Chem. 2017; 409(12):3059-3065 PM: 28289761

ABSTRACT: As drug targets, receptors have potential to screen drugs. Silica is an attractive support to immobilize receptors; however, the lack of biocompatibility makes it easier for receptors to lose bioactivity, which remains an obstacle to its widespread use. With the advantage of biocompatibility, DNA origami can be used as a biological carrier to improve the biocompatibility of silica and assemble receptors. In this study, a new biochromatography model based on DNA origami was constructed. A large quantity of M13ssDNA was used as a scaffold, leading to significant costs, so M13ssDNA was self-produced from the bacteriophage particles. This approach is demonstrated using the ligand binding domain of gamma isoform peroxisome proliferator-activated receptor (PPARgamma-LBD) as a research object. PPARgamma-LBD was assembled on DNA origami carrier and then coupled on the surface of silica. The products were packed into the column as stationary phase to construct the biochromatography with the ability to recognize drugs. Affinity and specificity of the biochromatography model were evaluated by HPLC. The final results showed that the biochromatography could recognize rosiglitazone specifically, which further proved that the model could screen chemical compositions interacted with PPARgamma. It was the first time to take advantage of DNA origami to assemble PPARgamma to construct biochromatography. The new biochromatography model has the advantages of being efficient, convenient, and high-throughput. This method affords a new way to rapidly and conveniently screen active ingredients from complex sample plant extracts and natural product-like libraries.

Zhou, Y., Marar, A., Kner, P., and Ramasamy, R. P. Charge-Directed Immobilization of Bacteriophage on Nanostructured Electrode for Whole-Cell Electrochemical Biosensors. Anal.Chem. 5-22-2017; PM: 28485143

ABSTRACT: A new type of carbon nanotube (CNT)-based impedimetric biosensing method has been developed for rapid and selective detection of live bacterial cells. A proof-of-concept study was conducted using T2 bacteriophage-based biosensors for electrochemical detection of Escherichia coli B. The T2 bacteriophage (virus) served as the biorecognition element, which was immobilized on polyethylenimine (PEI)-functionalized carbon nanotube transducer on glassy carbon electrode. Charge-directed, orientated immobilization of bacteriophage particles on carbon nanotubes was achieved through covalent linkage of phage capsid onto the carbon nanotubes. The presence of the immobilized phage on carbon nanotube-modified electrode was confirmed by fluorescence microscopy. Electrochemical impedance spectroscopy (EIS) was used to monitor the changes in the interfacial impedance due to the binding of E. coli B to T2 phage on the CNT-modified electrode. The detection was highly selective toward the B strain of E. coli as no signal was observed for the nonhost K strain of E. coli. The present achievable detection limit of the biosensor is 103 CFU/mL.

Zhou, Y., Zhang, H., Bao, H., Wang, X., and Wang, R. The lytic activity of recombinant phage lysin LysKDeltaamidase against staphylococcal strains associated with bovine and human infections in the Jiangsu province of China. Res.Vet.Sci. 2017; 111:113-119; PM: 28235706

ABSTRACT: We investigated the lytic activity of the bacteriophage endolysin (lysin) LysKDeltaamidase against live methicillin-resistant and-susceptible staphylococcal strains clinically isolated from bovine milk and humans from different origins of China. Antibiotic resistance patterns, multilocus sequence typing and SCCmec type of 137 staphylococcal strains isolated from bovine milk associated with bovine mastitis and human diseases were studied. A lytic enzyme, LysKDeltaamidase, was constructed by fusing the N-terminal 220 amino acids with the C-terminal 105 amino acids of staphylococcal phage lysin LysK. Herein, the antimicrobial activity of LysKDeltaamidase against 66 methicillin-resistant staphylococcal strains and 71 methicillin-susceptible staphylococcal strains isolated from bovine milk and from humans in China were studied. Our results show that the lysin displayed a broad lytic spectrum; in vitro treatment killed all 137 of the milk and clinical isolates of staphylococci strains tested, including MRSA, methicillin-susceptible S. aureus (MSSA), MR-Staphylococcus hominis ssp. homins, MR-Staphylococcus epidermidis and MR-Staphylococcus haemolyticus as evidenced by scanning electron microscopy, transmission electron microscopy, turbidity reduction assay and disruption of biofilms. The present results suggest that LysKDeltaamidase has the potential to be an alternative therapeutic agent against pathogenic methicillin-resistant and-susceptible staphylococcal strains isolated from China.

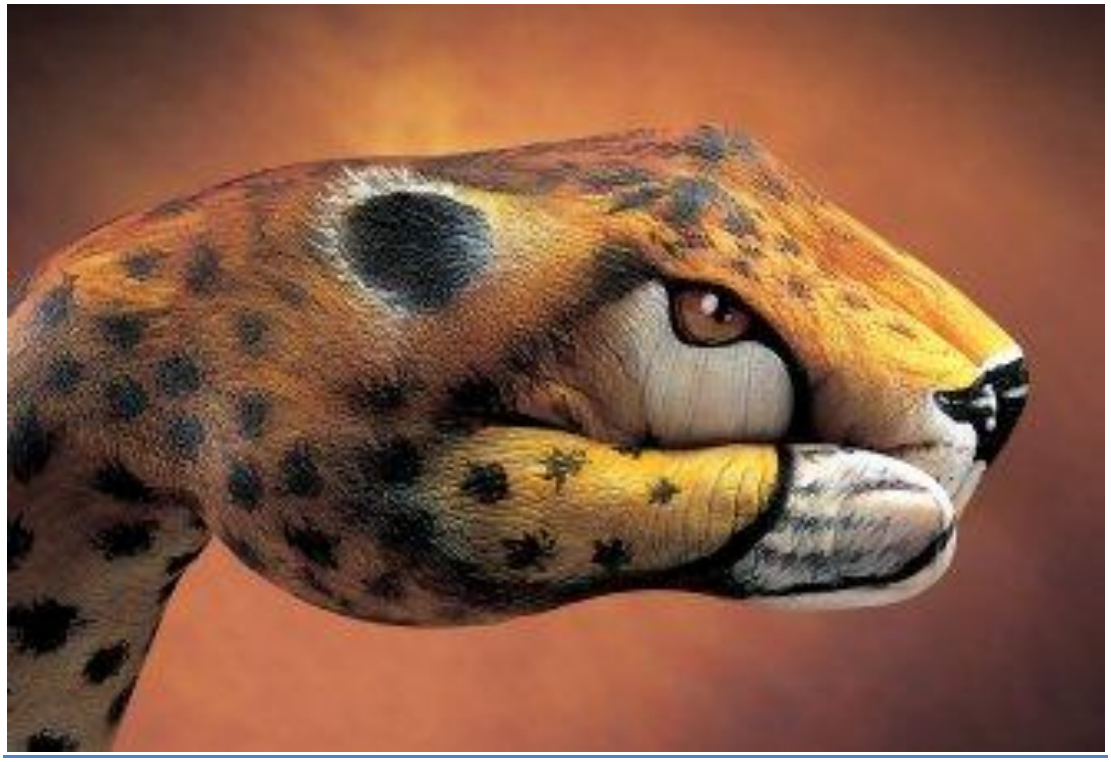
Zhou, Z., Bedwell, G. J., Li, R., Palchoudhury, S., Prevelige, P. E., Jr., and Gupta, A. Pathways for Gold Nucleation and Growth over Protein Cages. Langmuir. 5-18-2017; PM: 28514857

ABSTRACT: Proteins are widely utilized as templates in biomimetic synthesis of gold nanocrystals. However, the role of proteins in mediating the pathways for gold nucleation and growth is not well understood, in part because of the lack of spatial resolution in probing the complicated biomimetic mineralization process. Self-assembled protein cages, with larger size and symmetry, can facilitate in the visualization of both

biological and inorganic components. We have utilized bacteriophage P22 protein cages of ~ 60 nm diameter for investigating the nucleation and growth of gold nanocrystals. By adding a gold precursor into solution with pre-existing protein cages and a reducing agent, gold nuclei/prenucleation clusters form in solution, which then locate and attach to specific binding sites on protein cages, and further grow to form gold nanocrystals. In contrast, addition of the reducing agent into solution with incubated gold precursor and protein cages leads to formation of gold nuclei/prenucleation clusters both in solution and on the surface of protein cages that then grow into gold nanocrystals. Analyzing the results obtained via these alternate routes provide important insights into the pathways of protein-mediated biomimetic nucleation of gold that challenge the importance of incubation, which is widely utilized in the biotemplated synthesis of inorganic nanocrystals.

Zygiel, E. M., Noren, K. A., Adamkiewicz, M. A., Aprile, R. J., Bowditch, H. K., Carroll, C. L., Cerezo, M. A. S., Dagher, A. M., Hebert, C. R., Hebert, L. E., Mahame, G. M., Milne, S. C., Silvestri, K. M., Sutherland, S. E., Sylvia, A. M., Taveira, C. N., VanValkenburgh, D. J., Noren, C. J., and Hall, M. F. Various mutations compensate for a deleterious lacZalpha insert in the replication enhancer of M13 bacteriophage. PLoS.One. 2017; 12(4):e0176421;PM: 28445507

ABSTRACT: M13 and other members of the Ff class of filamentous bacteriophages have been extensively employed in myriad applications. The Ph.D. series of phage-displayed peptide libraries were constructed from the M13-based vector M13KE. As a direct descendent of M13mp19, M13KE contains the lacZalpha insert in the intergenic region between genes IV and II, where it interrupts the replication enhancer of the (+) strand origin. Phage carrying this 816-nucleotide insert are viable, but propagate in E. coli at a reduced rate compared to wild-type M13 phage, presumably due to a replication defect caused by the insert. We have previously reported thirteen compensatory mutations in the 5'-untranslated region of gene II, which encodes the replication initiator protein gIIp. Here we report several additional mutations in M13KE that restore a wild-type propagation rate. Several clones from constrained-loop variable peptide libraries were found to have ejected the majority of lacZalpha gene in order to reconstruct the replication enhancer, albeit with a small scar. In addition, new point mutations in the gene II 5'-untranslated region or the gene IV coding sequence have been spontaneously observed or synthetically engineered. Through phage propagation assays, we demonstrate that all these genetic modifications compensate for the replication defect in M13KE and restore the wild-type propagation rate. We discuss the mechanisms by which the insertion and ejection of the lacZalpha gene, as well as the mutations in the regulatory region of gene II, influence the efficiency of replication initiation at the (+) strand origin. We also examine the presence and relevance of fast-propagating mutants in phage-displayed peptide libraries.



Cheetah, Guido Daniele, used with permission from Guido Daniele

I. Probiotics & Bacteriotherapy

Determination of the optimal enrichment Artemia franciscana with a synbiotic combination of probiotics Pediococcus acidilactici and prebiotic fructooligosaccharide. Vet.Res.Forum. 2017; 8(1):49-54; PM: 28473897

ABSTRACT: In this study the optimal amount of enriching Artemia franciscana with a synbiotic combination of Pediococcus acidilactici and fructooligosaccharide (FOS(was investigated. The experiment was conducted in a completely randomized design in ten treatments: multi-level probiotics P. acidilactici (1x109, 1x108 and 1x 107 CFU per L) and multi-level enriched prebiotic FOS (1, 2 and 5) g per L of solution and control. To evaluate the enrichment of adult artemia with each treatment, sampling was performed at 2, 4 and 6 hr after initiation of enrichment. The results showed that a synbiotic containing a probiotic treatments P. acidilactici at 1 x 109 and 1 x 108 CFU per L had more bacteria than a synbiotic containing a probiotic treatment with 1 x 107 CFU per L ($p < 0.05$), but did not show significant difference between levels of 1 x 109 and 1 x 108 CFU per L ($p > 0.05$). The highest number of attached bacteria (6.78 +/- 0.03 log CFU g-1) to adult artemia was shown after 6 hr of enrichment that showed significant difference with 2 hr, but did not show significant difference with 4 hr time. In conclusion, the results of this study showed that adult artemia in a short time (about 4 hr) unlike nauplii artemia can retain a large amount of probiotic (1 x 108 CFU P. acidilactici per L and 5 g per L FOS prebiotic) on their own.

Abildgaard, A., Elfving, B., Hokland, M., Wegener, G., and Lund, S. Probiotic treatment reduces depressive-like behaviour in rats independently of diet. Psychoneuroendocrinology. 2017; 79:40-48; PM: 28259042

ABSTRACT: The gut microbiota has recently emerged as an important regulator of brain physiology and behaviour in animals, and ingestion of certain bacteria (probiotics) therefore appear to be a potential treatment for major depressive disorder (MDD). However, some conceptual and mechanistical aspects need further elucidation. We therefore aimed at investigating whether the habitual diet may interact with the effect of probiotics on depression-related behaviour and further examined some potentially involved mechanisms underlying the microbe-mediated behavioural effects. Forty male Sprague-Dawley rats were fed a control (CON) or high-fat diet (HFD) for ten weeks and treated with either a multi-species probiotic formulation or vehicle for the last five weeks. Independently of diet, probiotic treatment markedly reduced depressive-like behaviour in the forced swim test by 34% (95% CI: 22-44%). Furthermore, probiotic treatment skewed the cytokine production by stimulated blood mononuclear cells towards IFNgamma, IL2 and IL4 at the expense of TNFalpha and IL6. In addition, probiotics lowered hippocampal transcript levels of factors involved in HPA axis regulation (Crh-r1, Crh-r2 and Mr), whereas HFD increased these levels. A non-targeted plasma metabolomics analysis revealed that probiotics raised the level of indole-3-propionic acid, a potential neuroprotective agent. Our findings clearly support probiotics as a potential treatment strategy in MDD. Importantly, the efficacy was not attenuated by intake of a "Western pattern" diet associated with MDD. Mechanistically, the HPA axis, immune system and microbial tryptophan metabolism could be important in this context. Importantly, our study lend inspiration to clinical trials on probiotics in depressed patients.

Abildgaard, A., Elfving, B., Hokland, M., Lund, S., and Wegener, G. Probiotic treatment protects against the pro-depressant-like effect of high-fat diet in Flinders Sensitive Line rats. Brain Behav.Immun. 4-25-2017; PM: 28450222

ABSTRACT: Major depressive disorder (MDD) is highly associated with dysmetabolic conditions, such as obesity and diabetes mellitus type 2, and the gut microbiota may interact with both disease entities. We have previously shown that a high-fat diet (HFD) exacerbated depressive-like behaviour uniquely in Flinders Sensitive Line (FSL) rats that inherently present with an increased level of depressive-like behaviour compared with Flinders Resistant Line (FRL) rats. We therefore investigated whether multispecies probiotics possessed anti-depressant-like effect in FSL rats or protected against the pro-depressant-like effect of HFD. We also examined blood and cerebral T cell subsets as well as plasma cytokines. Lastly, we investigated the effect of HFD in outbred Sprague-Dawley (SD) rats to substantiate the association between depressive-like behaviour and any immunological measures affected by HFD. HFD exacerbated the depressive-like behaviour in FSL rats in the forced swim test, whereas SD rats remained unaffected. Probiotic treatment completely precluded the pro-depressant-like effect of HFD, but it did not affect FSL rats on control diet. Cerebral T lymphocyte CD4/8 ratios closely mirrored the behavioural changes, whereas the proportions of Treg and Th17 subsets were unaltered. No association between blood and brain CD4/8 ratios were evident; nor did plasma cytokine levels change as a consequence of HFD of probiotic treatment. Our findings suggest that MDD may hold a dysmetabolic component that responds to probiotic treatment. This finding has wide implications owing to the high metabolic comorbidity in MDD. Furthermore, the close association between depressive-like behaviour and cerebral T cell populations demonstrate lymphocyte-brain interactions as a promising future research area in the field of psychoneuroimmunology.

Abrahamsson, T. R., Wu, R. Y., and Sherman, P. M. Microbiota in Functional Gastrointestinal Disorders in Infancy: Implications for Management. Nestle.Nutr.Inst.Workshop Ser. 2017; 88:107-115; PM: 28346927

ABSTRACT: The complex and diverse intestinal microbiome is recognized as important in promoting human health. An altered gut microflora, referred to as dysbiosis, is increasingly recognized as having an etiologic role in a variety of conditions, including functional gastrointestinal disorders: colic in infants and irritable bowel syndrome in older children. Probiotics are defined as live microorganisms that, if ingested in sufficient amounts, restore microbial homeostasis and have a benefit on health. Randomized controlled trials indicate that probiotics can be effective in a variety of intestinal conditions, including colic and irritable bowel syndrome. Probiotics may promote gut microbial diversity, but timing of the intervention appears crucial. Strain-specific effects on colonization resistance, epithelial barrier integrity, modulation of signal transduction, impacts on innate and adaptive immune responses, and effects on visceral hyperalgesia likely explain the observed variability in various probiotic strains. In the future, probiotics are likely to be chosen for use in a defined clinical setting based on underlying mechanism(s) of action. The precise component of the probiotic agent mediating observed effects is the subject of current research. Unresolved issues relate to optimal dosages, timing of ingestion, single versus combination formulations, maintenance of viability in storage, and the merits of employing probiotic-derived products.

Adhikari, P. A., Cosby, D. E., Cox, N. A., Lee, J. H., and Kim, W. K. Effect of dietary bacteriophage supplementation on internal organs, fecal excretion, and ileal immune response in laying hens challenged by Salmonella Enteritidis. Poult.Sci. 4-26-2017; PM: 28453774

ABSTRACT: With the current researches on replacing antibiotics with different dietary interventions, bacteriophages (BP) are potential antimicrobial intervention because of their ability to affect specific bacteria. A study was conducted to evaluate the role of BP against Salmonella enterica serovar Enteritidis (SE) on SE internal organs colonization and ileum immune response in laying hens. Hens were challenged both orally and intracloacally with 108 cfu/mL cells of nalidixic acid resistant Salmonella Enteritidis (SENAR). Thirty-two Single Comb White Leghorns were randomly allocated to 4 dietary treatments: 1) unchallenged control (negative control; T1), 2) SENAR challenged control (positive control; T2), 3) SENAR challenged + 0.1% BP (T3), and 4) SENAR challenged + 0.2% BP (T4). The number of SENAR in the ceca was significantly reduced by 0.2% BP supplementation ($P < 0.05$) at 7 d post infection (dpi). The respective number of SENAR was reduced from 2.9 log cfu/gm in T2 and T3 to 2.0 log cfu/gm in T4. There was no significant effect of T3 on reduction of numbers of cecal SENAR. A significant reduction of SENAR was observed in the liver with gall bladder (LGB) from 0.75 in T2 to 0.18 log cfu/gm in T4. In the spleen, T4 significantly reduced ($P < 0.05$) SENAR to 0.56 log cfu/gm compared to T2 and T3 (0.94 log cfu/gm). There was no significant effect of T3 in reduction of prevalence of spleen SENAR. By supplementing 0.2% BP (T4), the SENAR in the ovary was reduced to 0 log cfu/gm. There was a significant reduction ($P < 0.05$) in fecal SENAR at 6 dpi by T4 (0.71 log cfu/gm) compared to the positive control (1.57 log cfu/gm). The expression of interferon (IFN)-Gamma, interleukin (IL)-6, and IL-10 was significantly increased in the ileum by SENAR challenge compared to the negative control. This study suggests that apart from commonly used prebiotics or probiotics, BP are pathogen-specific and can be used as one of the dietary strategies to reduce SE colonization and induce immune modulation in laying hens.

Adnan, M., Patel, M., and Hadi, S. Functional and health promoting inherent attributes of Enterococcus hirae F2 as a novel probiotic isolated from the digestive tract of the freshwater fish Catla catla. PeerJ. 2017; 5:e3085; PM: 28316889

ABSTRACT: BACKGROUND: Probiotic microorganisms are gaining global importance because of their use in the preparation of a nutraceutical or in the treatment of infections. As per the health industry demand, there is an urgent need for exploring new indigenous probiotic strains with its specific origin due to variation in gut microflora, different food habits and specific host-microbial interactions. The main objective of the present study was to isolate and identify a novel probiotic Enterococcus strain from the gut of Catla catla fish and evaluate its potentiality as a potent probiotic. *METHODS*: The whole study was designed with the isolation of novel lactic acid bacterial strain from the gut of Catla catla fish with their biochemical and molecular identifications. The potentiality of the isolated strain as a potent probiotic was carried out according to the parameters described in FAD/WHO guidelines for the evaluation of probiotics in food. *RESULTS*: The isolated strain was confirmed as Enterococcus hirae F2 on the basis of various biochemical and 16s rRNA gene sequencing methods. Enterococcus hirae F2 was able to survive under highly acidic and bile salt concentration with the ability for the production of lipase and Bsh enzyme. It was also able to survive under simulated gastrointestinal conditions with the inhibition ability of various pathogens. The antioxidant potentiality with the cell surface hydrophobicity and cell aggregation ability confirms its

potentiality as a potent probiotic. All the results detail the potency of Enterococcus hirae F2 as a novel probiotic for a safer use. *DISCUSSION*: The isolation of Enterococcus hirae with probiotic potential from the gut of fish is a new approach and done for the first time. However, the whole study concluded that the isolated strain might be used as a novel probiotic in the food industry for the production of new probiotic products which imparts health benefits to the host.

Aggarwal, A., Sarangi, A. N., Gaur, P., Shukla, A., and Aggarwal, R. Gut microbiome in children with enthesitis-related arthritis in a developing country and the effect of probiotic administration. Clin.Exp.Immunol. 2017; 187(3):480-489; PM: 27861762

ABSTRACT: In Asia, enthesitis-related arthritis (ERA) is the most frequent category of juvenile idiopathic arthritis. ERA has a strong association with human leucocyte antigen (HLA)-B27 and subclinical gut inflammation. In an HLA-B27 transgenic rat model, the presence of Bacteroides bacteria in the gut appears to cause spondyloarthropathy (SpA). Thus, we studied gut microbiota in children with ERA. Stool specimens from 33 patients with ERA and 14 age-matched healthy controls were studied; none had any gastrointestinal symptom, or had received a drug known to affect gut motility or microbiota in the preceding 6 weeks. From each specimen, a cDNA library for the V3 region of bacterial 16S rRNA was subjected to high-throughput, massively parallel sequencing. Relationship of the specimens was studied using principal co-ordinate analysis (PCoA), and abundances of various bacterial taxa and alpha diversity were compared between groups. In eight patients, a repeat faecal specimen was studied after 12 weeks of probiotic therapy. The 55 specimens yielded a median (range) of 397 315 (102 093-1 502 380) high-quality reads each. In PCoA, gut microbiota from ERA showed a wider dispersion than those from controls. In patients, families Bacteroidaceae and Enterobacteriaceae were more abundant and Prevotellaceae were less abundant than in controls. Also, genera Bacteroides, Entercoccus and Klebsiella were over-represented and genus Prevotella was under-represented in ERA patients. Probiotic therapy led to a non-significant increase in Prevotellaceae. Patients with ERA have a dysbiosis in the gut, with increased abundance of Bacteroides and reduction of Prevotella. Probiotic supplementation in a subset of patients did not reverse these changes significantly.

Ahktar, N. and Pathak, K. Probiotics as a Tool to Biosynthesize Metallic Nanoparticles: Research Reports and Patents Survey. Recent Pat Drug Deliv.Formul. 3-13-2017; PM: 28294074

ABSTRACT: BACKGROUND: Probiotics are the live microbes that exert beneficial effects on the health of the host cell and thus creating novel nanoformulations via probiotic bacteria have gained tremendous momentum recently. The probiotic bacteria are being employed in synthesizing or more specifically biosynthesizing several nanoparticles like metallic as well as non-metallic nanoparticles. Biosynthesis of metallic nanoparticles is currently focused of research nowadays due to several applications thereof. Research inputs have led to exploration of probiotic bacteria in biosynthesizing novel metallic nanoparticles. *OBJECTIVE*: The present review explores various research and patent reports on metallic nanoparticles biosynthesized using probiotic bacteria. *METHOD*: Through the sites, www.freepatentsonline.com and www.uspto.gov/patft, patents have been retrieved including US patents, EP and WIPO patents. *RESULTS*: Various reports and patents have revealed that probiotic bacteria can effectively produce metallic nanoparticles. These nanoparticles have found applications in cosmetics,

pharmaceutics, medicine and biotechnology. Areas of future research can include the exploration of formulation aspects of metallic nanoparticles of iron, zinc, tellurium and synthesis of these particles using yeast, fungi, plant extracts and several biomaterials. *CONCLUSION*: Use of probiotic bacteria in synthesizing metallic nanoparticles is an effective biosynthetic approach. However, the technique needs wider exploration for newer metallic/nonmetallic/metalloid NPs for therapeutic applications.

Ait, Seddik H., Bendali, F., Cudennec, B., and Drider, D. Anti-pathogenic and probiotic attributes of Lactobacillus salivarius and Lactobacillus plantarum strains isolated from feces of Algerian infants and adults. Res.Microbiol. 2017; 168(3):244-254; PM: 28093322

ABSTRACT: Sixty-seven (67) lactic acid bacteria (LAB) isolates belonging to Lactobacillus genus were isolated from human feces and tested for their auto-aggregation and cell surface hydrophobicity in order to establish their adhesion capabilities, a prerequisite for probiotic selection. Strains with the upmost auto-aggregation and cell surface hydrophobicity scores were identified by MALDI-TOF spectrometry and 16S rDNA sequencing as Lactobacillus plantarum (p25lb1 and p98lb1) and Lactobacillus salivarius (p85lb1 and p104lb1). These strains were also able to adhere to human epithelial colorectal adenocarcinoma Caco-2 cells, with percentages ranging from 4.68 to 9.59%. They displayed good survival under conditions mimicking the gastrointestinal environment and remarkably impeded adhesion and invasion of human Caco-2 by Listeria monocytogenes and Enteropathogenic Escherichia coli. It should also be noted that Lb. plantarum p98lb1 was able to reduce in vitro cholesterol concentration by about 32%, offering an additional health attribute.

Aitoro, R., Simeoli, R., Amoroso, A., Paparo, L., Nocerino, R., Pirozzi, C., di, Costanzo M., Meli, R., De, Caro C., Picariello, G., Mamone, G., Calignano, A., Nagler, C. R., and Berni, Canani R. Extensively hydrolyzed casein formula alone or with L. rhamnosus GG reduces beta-lactoglobulin sensitization in mice. Pediatr.Allergy Immunol. 2017; 28(3):230-237; PM: 27992668

ABSTRACT: BACKGROUND: Extensively hydrolyzed casein formula (EHCF) has been proposed for the prevention and is commonly used for the treatment of cow's milk allergy (CMA). The addition of the probiotic Lactobacillus rhamnosus GG (LGG) to EHCF may induce faster acquisition of tolerance to cow's milk. The mechanisms underlying this effect are largely unexplored. We investigated the effects of EHCF alone or in combination with LGG on beta-lactoglobulin (BLG) sensitization in mice. *METHODS*: Three-week-old C3H/HeOuJ mice were sensitized by oral administration of BLG using cholera toxin as adjuvant at weekly intervals for 5 weeks (sensitization period). Two experimental phases were conducted: (i) EHCF or EHCF+LGG given daily, starting 2 weeks before the sensitization period and then given daily for 5 weeks and (ii) EHCF or EHCF+LGG given daily for 4 weeks, starting 1 week after the sensitization period. Diet free of cow's milk protein was used as control. Acute allergic skin response, anaphylactic symptom score, body temperature, intestinal permeability, anti-BLG serum IgE, and interleukin (IL)-4, IL-5, IL-10, IL-13, IFN-gamma mRNA expression were analyzed. Peptide fractions of EHCF were characterized by reversed-phase (RP)-HPLC, MALDI-TOF mass spectrometry, and nano-HPLC/ESI-MS/MS. *RESULTS*: Extensively hydrolyzed casein formula administration before or after BLG-induced sensitization significantly reduced acute allergic skin reaction, anaphylactic symptom score, body temperature decrease, intestinal permeability increase, IL-4, IL-5, IL-13, and anti-BLG IgE production. EHCF

increased expression of IFN-gamma and IL-10. Many of these effects were significantly enhanced by LGG supplementation. The peptide panels were similar between the two study formulas and contained sequences that could have immunoregulatory activities. *CONCLUSIONS*: The data support dietary intervention with EHCF for CMA prevention and treatment through a favorable immunomodulatory action. The observed effects are significantly enhanced by LGG supplementation.

Akar, M., Eras, Z., Oncel, M. Y., Arayici, S., Guzoglu, N., Canpolat, F. E., Uras, N., and Oguz, S. S. Impact of oral probiotics on neurodevelopmental outcomes in preterm infants. J.Matern.Fetal Neonatal Med. 2017; 30(4):411-415; PM: 27045204

ABSTRACT: OBJECTIVE: The aim of the study was to evaluate the neurodevelopment outcomes of very low birth weight (VLBW) preterm infants supplemented with oral probiotics for the prevention of necrotizing enterocolitis (NEC). *METHODS*: A prospective follow-up study was performed in a cohort of VLBW preterm infants enrolled in a single center randomized controlled clinical trial to evaluate the efficacy of oral probiotics for the prevention of NEC. Cognitive and neuromotor developments were assessed by using the Bayley scales of infant development II. Sensory and neurological performance was evaluated by standard techniques. The primary outcome was neurodevelopmental impairment at 18-24 months' corrected age. *RESULTS*: A total of 400 infants completed the trial protocol. Of the 370 infants eligible for follow-up, 249 infants (124 in the probiotics group and 125 in the control group) were evaluated. There was no significant difference in any of the neurodevelopmental and sensory outcomes between the two groups. *CONCLUSION*: Oral probiotic given to VLBW infants to reduce the incidense and severity of NEC started with the first feed did not affect neuromotor, neurosensory and cognitive outcomes at 18-24 months' corrected age.

Al-Muzafar, H. M. and Amin, K. A. Probiotic mixture improves fatty liver disease by virtue of its action on lipid profiles, leptin, and inflammatory biomarkers. BMC.Complement Altern.Med. 1-13-2017; 17(1):43; PM: 28086768

ABSTRACT: BACKGROUND: A high fat diet has an essential role in the pathogenesis of non-alcoholic fatty liver disease (NAFLD). This condition is characterized by hepatic fat accumulation (steatosis) and is associated with obesity, diabetes, and fibrosis or cirrhosis of the liver. Probiotics may be useful in the treatment of steatosis. This study examined the effects of an ingested probiotic formulation on the lipid profiles, liver functions, leptin levels, and inflammatory marker levels of rats with NAFLD that had been induced via high fat and sucrose diet (HFSD). *METHODS*: Young male albino rats were randomly divided into three groups: a control group that was fed a standard diet; a second group that was fed a HFSD; and a third group that was given both a HFSD and ingestible probiotic mixtures. The groups were fed these diets for 16 weeks, and were then examined. *RESULTS*: HFSD-only rats showed hypertriglyceridemia, hypercholesterolemia, and elevated low density lipoprotein (LDL) levels, and their serum alanine transaminase (ALT) and bilirubin levels were significantly higher than those of the control group. Compared to rats on the standard diet, HFSD-only rats showed higher levels of tumor necrosis factor alpha (TNF-alpha) and interleukin 6 (IL-6), increased serum leptin levels, and increased resistin hormone levels in the adipose tissues. In the third group, the inclusion of the probiotic mixture seemed to ameliorate the effects of the HFSD diet. The NAFD + probiotics group showed improved lipid profiles, better leptin and resistin levels, and better TNF-alpha and IL-6 levels than the NAFD-only group. They also showed no signs of

NAFLD. *CONCLUSIONS*: The probiotic mixture showed promise as a treatment for NAFLD pathogenesis, and may improve HFSD-induced steatosis through its effects on leptin, resistin, inflammatory biomarkers, and hepatic function markers. We also established that gut microbiota-mediated regulation of lipid profiles was dependent on dietary lipids and carbohydrates.

Al-Rubaye, A. A., Ekesi, N. S., Zaki, S., Emami, N. K., Wideman, R. F., Jr., and Rhoads, D. D. Chondronecrosis with osteomyelitis in broilers: Further defining a bacterial challenge model using the wire flooring model. Poult.Sci. 2-1-2017; 96(2):332-340; PM: 27587724

ABSTRACT: Lameness in broiler chickens is a significant animal welfare and financial issue. Bacterial chondronecrosis with osteomyelitis (BCO) leading to lameness can be enhanced by rearing young broilers on wire flooring. Using the wire floor system, we identified Staphylococcus agnetis as the predominant isolate in BCO of the proximal tibiae and femora, and blood of lame broilers. Administration of S. agnetis isolates in water can induce lameness. We now report that the wire floor system increases bacterial translocation into the blood stream. We have also determined that approximately 105 CFU/mL is the minimum effective dose in the drinking water and that challenge at 10, 20, or 30 days of age produces similar incidences of lameness. BCO isolates of S. agnetis are much more effective than other Staphylococcus species and can overwhelm the protective effects of some commercial probiotics. Finally, we also demonstrated that the BCO lameness induced by administration of S. agnetis in the drinking water is transmissible to unchallenged broilers in the same pen.

Al, Khodor S. and Shatat, I. F. Gut microbiome and kidney disease: a bidirectional relationship. Pediatr.Nephrol. 2017; 32(6):921-931; PM: 27129691

ABSTRACT: Recent technological advances and efforts, including powerful metagenomic and metatranscriptomic analyses, have led to a tremendous growth in our understanding of microbial communities. Changes in microbial abundance or composition of human microbial communities impact human health or disease state. However, explorations into the mechanisms underlying host-microbe interactions in health and disease are still in their infancy. Although changes in the gut microbiota have been described in patients with kidney disease, the relationships between pathogenesis, mechanisms of disease progression, and the gut microbiome are still evolving. Here, we review changes in the host-microbiome symbiotic relationship in an attempt to explore the bidirectional relationship in which alterations in the microbiome affect kidney disease progression and how kidney disease may disrupt a balanced microbiome. We also discuss potential targeted interventions that may help re-establish this symbiosis and propose more effective ways to deploy traditional treatments in patients with kidney disease.

Albenzio, M., Santillo, A., Caroprese, M., Della, Malva A., and Marino, R. Bioactive Peptides in Animal Food Products. Foods. 5-9-2017; 6(5); PM: 28486398

ABSTRACT: Proteins of animal origin represent physiologically active components in the human diet; they exert a direct action or constitute a substrate for enzymatic hydrolysis upon food processing and consumption. Bioactive peptides may descend from the hydrolysis by digestive enzymes, enzymes endogenous to raw food materials, and

enzymes from microorganisms added during food processing. Milk proteins have different polymorphisms for each dairy species that influence the amount and the biochemical characteristics (e.g., amino acid chain, phosphorylation, and glycosylation) of the protein. Milk from other species alternative to cow has been exploited for their role in children with cow milk allergy and in some infant pathologies, such as epilepsy, by monitoring the immune status. Different mechanisms concur for bioactive peptides generation from meat and meat products, and their functionality and application as functional ingredients have proven effects on consumer health. Animal food proteins are currently the main source of a range of biologically-active peptides which have gained special interest because they may also influence numerous physiological responses in the organism. The addition of probiotics to animal food products represent a strategy for the increase of molecules with health and functional properties.

Alizadeh, M., Munyaka, P., Yitbarek, A., Echeverry, H., and Rodriguez-Lecompte, J. C. Maternal antibody decay and antibody-mediated immune responses in chicken pullets fed prebiotics and synbiotics. Poult.Sci. 1-1-2017; 96(1):58-64; PM: 27433011

ABSTRACT: Three experiments were conducted to evaluate the effect of yeast-derived carbohydrates (YDC), and a blend of probiotics and YDC (synbiotic, SNB) on serum IgG concentration, maternal-derived antibody (MDA) decay, and specific antibody-mediated immune response in chick pullets following immunization with T-cell dependent antigens. A total of 300 day-old pullet chicks were randomly assigned to 3 dietary treatments including: a basal diet (Control), and diets containing YDC, and SNB (Lactobacillus acidophilus, L. casei, Streptococcus faecium, and Bacillus subtilis, and YDC). In experiment one, on d 1 and wk 3, 4, 5, and 6, blood samples were collected and serum were analyzed by ELISA for total IgG (Y), and MDA against Newcastle disease virus (NDV) and infectious bursal disease virus (IBDV). The second experiment examined the specific antibody against infectious bronchitis virus (IBV) in pullet chicks following vaccination against IBV at d 1. Finally, in experiment 3, on d 21 and 28 posthatch, 10 birds per treatment were immunized intramuscularly with both sheep red blood cells (SRBC) and bovine serum albumin (BSA), and 11 after immunization serum samples were analyzed by hemagglutination assay for antibody response to SRBC, and by ELISA for serum IgM and IgG response to BSA. The results demonstrated that diet containing SNB increased serum IgG at wk 3 posthatch. However, the decay rate of MDA against NDV and IBDV were not affected by dietary treatments. Birds fed YDC showed higher specific antibody response against IBV in wk 4, while both diets containing YDC and SNB decreased antibody response to IBV in wk 6. In addition, specific antibody response against SRBC and BSA was not affected by diets. In conclusion, supplementation of diet with SNB improved humoral immunity by increasing IgG concentration in serum, and modulated the adaptive antibody-mediated immune response against IBV.

Alkasir, R., Li, J., Li, X., Jin, M., and Zhu, B. Human gut microbiota: the links with dementia development. Protein Cell. 2017; 8(2):90-102; PM: 27866330

ABSTRACT: Dementia is a comprehensive category of brain diseases that is great enough to affect a person's daily functioning. The most common type of dementia is Alzheimer's disease, which makes most of cases. New researches indicate that gastrointestinal tract microbiota are directly linked to dementia pathogenesis through triggering metabolic diseases and low-grade inflammation progress. A novel strategy is proposed for the

management of these disorders and as an adjuvant for psychiatric treatment of dementia and other related diseases through modulation of the microbiota (e.g. with the use of probiotics).

Alkaya, B., Laleman, I., Keceli, S., Ozcelik, O., Cenk, Haytac M., and Teughels, W. Clinical effects of probiotics containing Bacillus species on gingivitis: a pilot randomized controlled trial. J.Periodontal Res. 2017; 52(3):497-504; PM: 27859252

ABSTRACT: BACKGROUND AND OBJECTIVE: Lactobacillus spp. and bifidobacteria are the most frequently used probiotics in oral health research. However, although probiotic effects have been suggested for other genera, such as bacilli, no trials are available to describe the effect of bacilli probiotics on gingivitis in humans. The aim of the present study was to evaluate the clinical effects of a bacilli-containing toothpaste, a mouthrinse and a toothbrush cleaner versus a placebo in patients with generalized gingivitis. *MATERIAL AND METHODS*: In this double-blind placebo-controlled randomized clinical trial, nonsmoking, systemically healthy patients with generalized gingivitis were included. They used a placebo or an experimental probiotic Bacillus subtilis-, Bacillus megaterium- and Bacillus pumulus-containing toothpaste, mouthrinse and toothbrush cleaner for 8 wk. Primary outcome measures of interest were plaque and gingivitis index, and the secondary outcome measures were pocket probing depth and bleeding on probing. *RESULTS*: Twenty male and 20 female patients were randomized over the two groups. All participants could be included in the final analysis. Although plaque and gingivitis indices were significantly reduced after 8 wk, no intergroup differences could be found at any time point. Also, for the secondary outcome measure, intragroup but no intergroup differences could be detected. No harm or unintended effects were reported by the patients after using the study products. *CONCLUSIONS*: This study did not show any statistically significant differences between a placebo and a bacilli-containing toothpaste, mouthrinse and toothbrush cleaner on gingivitis parameters.

Allen, A. P., Clarke, G., Cryan, J. F., Quigley, E. M. M., and Dinan, T. G. Bifidobacterium infantis 35624 and other probiotics in the management of irritable bowel syndrome. Strain specificity, symptoms, and mechanisms. Curr.Med.Res.Opin. 5-19-2017; 1-3; PM: 28436237

No Abstract Available.

Alok, A., Singh, I. D., Singh, S., Kishore, M., Jha, P. C., and Iqubal, M. A. Probiotics: A New Era of Biotherapy. Adv.Biomed.Res. 2017; 6:31; PM: 28401078

ABSTRACT: Probiotics or health-beneficial bacteria have only recently been introduced in dentistry after years of successful use in mainly gastrointestinal disorders. The concept of bacteriotherapy was first introduced in the beginning of 20th century. They are administered in different quantities that allow for colon colonization. These products help in stimulating health promoting flora and also suppressing the pathologic colonization and disease spread. The use of probiotic plays an important aspect in dentistry too, ever since the oral infections occupied the prime spot among the other infections affecting the humans. Probiotics strengthen the immune system to combat allergies, stress, exposure to toxic substances, and other diseases. This review is an attempt to discuss briefly the role of probiotics in oral health.

Amaral, M. A., Guedes, G. H. B. F., Epifanio, M., Wagner, M. B., Jones, M. H., and Mattiello, R. Network meta-analysis of probiotics to prevent respiratory infections in children and adolescents. Pediatr.Pulmonol. 2017; 52(6):833-843; PM: 28052594

ABSTRACT: Probiotics have emerged as a promising intervention for the prevention of respiratory tract infections (RTIs) in children. Assess the effect of probiotics on prevention of RTIs in children and adolescents. MEDLINE, EMBASE, LILACS, SCIELO, CINAHL, SCOPUS, and Web of Science. Key words: "respiratory tract infections" AND probiotics. Randomized controlled trials RCT assessing the effect of probiotics on RTIs in children and adolescents were included. Two reviewers, working independently, to identify studies that met the eligibility criteria. Main and secondary outcomes were RTIs and adverse effects, respectively. Twenty-one trials with 6.603 participants were included. Pairwise meta-analysis suggested that Lactobacillus casei rhamnosus (LCA) was the only effective probiotic to the rate of RTIs compared to placebo (RR0.38; CrI 0.19-0.45). Network analysis showed that the LCA exhibited 54.7% probability of being classified in first, while the probability of Lactobacillus fermentum CECT5716 (LFC) being last in the ranking was 15.3%. LCA showed no better effect compared to other probiotic strains by indirect analysis. This systematic review found a lack of evidence to support the effect of probiotic on the incidence rate of respiratory infections in children and adolescents. Pediatr Pulmonol. 2017;52:833-843. (c) 2017 Wiley Periodicals, Inc.

Amat, S., Subramanian, S., Timsit, E., and Alexander, T. W. Probiotic bacteria inhibit the bovine respiratory pathogen Mannheimia haemolytica serotype 1 in vitro. Lett.Appl.Microbiol. 2017; 64(5):343-349; PM: 28178767

ABSTRACT: This study evaluated the potential of probiotic bacteria to inhibit growth and cell adhesion of the bovine respiratory pathogen Mannheimia haemoltyica serotype 1. The inhibitory effects of nine probiotic strains (Lactobacillus acidophilus, Lactobacillus casei, Lactobacillus helveticus, Lactobacillus plantarum, Lactobacillus rhamnosus, Lactococcus lactis, Streptococcus thermophilus and two Paenibacillus polymyxa strains) against M. haemolytica were evaluated using a spot-on-lawn method. Probiotic strains were then tested for their adherence to bovine bronchial epithelial (BBE) cells and the ability to displace and compete against M. haemolytica on BBE. Except for S. thermophilus, all probiotic strains inhibited the growth of M. haemolytica, with zones of inhibition ranging between 12 and 19 mm. Lactobacillus strains and Lactococcus lactis displayed greater ($P < 0.05$) BBE adhesion compared with M. heamolytica (8.3%) and other probiotics (<2.2%). Strains of P. polymyxa and L. acidophilus caused the greatest reduction in M. haemolytica adherence, through both displacement and competition, compared with other probiotics. The results of this study suggest that probiotics may have the potential to colonize the bovine respiratory tract, and exert antagonistic effects against M. haemolytica serotype 1. *SIGNIFICANCE AND IMPACT OF THE STUDY*: A common method to control bovine respiratory disease (BRD) in feedlots is through mass medication with antibiotics upon cattle entry (i.e. metaphylaxis). Increasingly, antimicrobial resistance in BRD bacterial pathogens has been observed in feedlots, which may have important implications for cattle health. In this study, probiotic strains were shown to adhere to bovine respiratory cells and inhibit the BRD pathogen M. haemolytica serotype 1 through competition and displacement. Probiotics may therefore offer a mitigation strategy to reduce BRD bacterial pathogens, in place of metaphylactic antimicrobials.

Anderson, J. L., Miles, C., and Tierney, A. C. Effect of probiotics on respiratory, gastrointestinal and nutritional outcomes in patients with cystic fibrosis: A systematic review. J.Cyst.Fibros. 2017; 16(2):186-197; PM: 27693010

ABSTRACT: BACKGROUND: An increasing body of research investigating the use of probiotics to improve health outcomes in patients with cystic fibrosis (CF) prompted the need to systematically assess and summarize the relevant literature. *METHODS*: An electronic search of five databases and three trial databases was conducted. Studies describing the administration of probiotics to patients with CF older than 2years, with a comparator group on respiratory, gastrointestinal and nutritional outcomes were included. *RESULTS*: Three pre-post studies and six randomised controlled trials met the inclusion criteria. Overall studies showed a positive effect of probiotics on reducing the number of pulmonary exacerbations and decreasing gastrointestinal inflammation. There was limited effect of probiotics on other outcomes and inadequate evidence for the effects of specific probiotic species and strains. *CONCLUSION*: The findings suggest that probiotics may improve respiratory and gastrointestinal outcomes in a stable CF clinic population with no reported evidence of harm. There is inadequate evidence at this time to recommend a specific species, strain or dose of probiotic as likely to be of significant benefit.

Andreev, D. N., Dicheva, D. T., and Maev, I. V. [Possibilities for optimization of eradication therapy for Helicobacter pylori infection in modern clinical practice]. Ter.Arkh. 2017; 89(2):84-90; PM: 28393827

ABSTRACT: A steady decline in the effectiveness of standard eradication therapy (ET) regimens for Helicobacter pylori infection necessitates a search for ways of their optimization, by enhancing the efficiency of treatment protocols and by improving their safety and tolerability. The review systematizes the data available in the literature on main accessible methods for optimizing ET regimens. Among the optimization methods that can considerably enhance the efficiency of ET regimens, one may identify their addition of a bismuth agent (by 10-20%), the use of rebamipide (by 11.9%), adjuvant therapy with probiotics (by 8.1-13%), or double-dose proton pump inhibitors (by 8%). Only adjuvant therapy with probiotics results in a significant decrease in the incidence of side effects from ET. In posteradication period, rebamipide should be used to potentiate gastric mucosal repair and to regress inflammatory processes.

Angelakis, E. Weight gain by gut microbiota manipulation in productive animals. Microb.Pathog. 2017; 106:162-170; PM: 27836763

ABSTRACT: Antibiotics, prebiotics and probiotics are widely used as growth promoters in agriculture. In the 1940s, use of Streptomyces aureofaciens probiotics resulted in weight gain in animals, which led to the discovery of chlortetracycline. Tetracyclines, macrolides, avoparcin and penicillins have been commonly used in livestock agriculture to promote growth through increased food intake, weight gain, and improved herd health. Prebiotic supplements including oligosaccharides, fructooligosaccharides, and galactosyl-lactose improve the growth performance of animals. Probiotics used in animal feed are mainly bacterial strains of Gram-positive bacteria and have been effectively used for weight gain in chickens, pigs, ruminants and in aquaculture. Antibiotics, prebiotics and probiotics all modify the gut microbiota and the effect of a probiotic

species on the digestive flora is probably determined by bacteriocin production. Regulations governing the introduction of novel probiotics and prebiotics vary by geographical region and bias is very common in industry-funded studies. Probiotic and prebiotic foods have been consumed for centuries, either as natural components of food, or as fermented foods and it is possible to cause the same weight gain effects in humans as in animals. This review presents the use of growth promoters in food-producing animals to influence food intake and weight gain.

Aoyagi, Y., Park, S., Matsubara, S., Honda, Y., Amamoto, R., Kushiro, A., Miyazaki, K., and Shephard, R. J. Habitual intake of fermented milk products containing Lactobacillus casei strain Shirota and a reduced risk of hypertension in older people. Benef.Microbes. 2-7-2017; 8(1):23-29; PM: 27903092

ABSTRACT: This study investigated relationships between the frequent intake of fermented milk products containing Lactobacillus casei strain Shirota (LcS) and the onset of hypertension (resting systemic pressure >/=140 mmHg [systolic]/>/=90 mmHg [diastolic], a doctor's diagnosis and/or antihypertensive medicine use) during a 5-year period in 352 communityliving Japanese aged 65 to 93 years (125 men and 227 women). Initially normotensive subjects were divided into two groups (n=254 and n=98) on the basis of their intake of fermented milk products (<3 or >/=3 times/week, respectively), as estimated during an interview by a certified nutritionist. The incidence of hypertension over the 5-year interval was significantly lower in those who took fermented milk products >/=3 rather than <3 times/week (6.1 vs 14.2%, P=0.037). A multivariate-adjusted proportional hazards model predicted that blood pressures were significantly more likely to remain normal over 5 years in subjects who took >/=3 fermented milk products rather than <3 times/ week (relative risk 0.398 [95% confidence interval 0.167-0.948], P=0.037). These results suggest that after adjustment for potential confounders, the risk of developing hypertension is substantially lower in elderly people who take fermented milk products containing LcS at least 3 times a week.

Arboleya, S., Martinez-Camblor, P., Solis, G., Suarez, M., Fernandez, N., de Los Reyes-Gavilan CG, and Gueimonde, M. Intestinal Microbiota and Weight-Gain in Preterm Neonates. Front Microbiol. 2017; 8:183; PM: 28228752

ABSTRACT: The involvement of the gut microbiota on weight-gain and its relationship with childhood undernutrition and growth has been reported. Thus, the gut microbiota constitutes a potential therapeutic target for preventing growth impairment. However, our knowledge in this area is limited. In this study we aimed at evaluating the relationship among early microbiota, growth, and development in preterm infants. To this end we assessed the levels of specific microorganisms by qPCR, and those of short chain fatty acids by mean of gas-chromatography, in feces from 63 preterm newborns and determined their weight-gain during the first months. The statistical analyses performed indicate an influence of the intestinal microbiota in weight-gain, with the levels of some microorganisms showing a significant association with the weight-gain of the infant. The levels of specific microbial groups during the first days of life were found to affect weight gain by the age of 1 month. Moreover, clustering of the infants on the basis of the microbiota composition at 1 month of age rendered groups which showed differences in weight z-scores. Our results suggest an association between the gut microbiota composition and weight-gain in preterm infants at early life and point out potential microbial targets for favoring growth and maturation in these infants.

Ardalan, M. and Vahed, S. Z. Gut microbiota and renal transplant outcome. Biomed.Pharmacother. 2017; 90:229-236; PM: 28363168

ABSTRACT: Gaining long-term graft function and patient survival remain a critical challenge following kidney transplantation. Genetic and environmental factors do not completely account for the individual's graft outcome. Recently, it is reported that gut microbial community (microbiota) is associated with complications in kidney allograft recipients, as well. Commensal microbiota plays a significant role in the immunomodulation of transplant recipient responses. Different factors can disrupt the reciprocal interaction between microbiota and the host immune responses and lead to infection and rejection complications in the organ recipient. In this review, we address the relation between microbiota and immune system along with their possible roles in renal graft outcome. We next highlight the beneficial effects of probiotics on the management of kidney diseases and solid organ transplantation. Finally, we reflect on the potential impacts of probiotics on host physiology. Hopefully, a deeper understanding of the function and composition of microbiota can help clinics develop strategies to restore the normal microbiota and facilitate the clinical management of grafts in the forthcoming future.

Arena, M. P., Capozzi, V., Spano, G., and Fiocco, D. The potential of lactic acid bacteria to colonize biotic and abiotic surfaces and the investigation of their interactions and mechanisms. Appl.Microbiol.Biotechnol. 2017; 101(7):2641-2657; PM: 28213732

ABSTRACT: Lactic acid bacteria (LAB) are a heterogeneous group of Gram-positive bacteria that comprise several species which have evolved in close association with humans (food and lifestyle). While their use to ferment food dates back to very ancient times, in the last decades, LAB have attracted much attention for their documented beneficial properties and for potential biomedical applications. Some LAB are commensal that colonize, stably or transiently, host mucosal surfaces, inlcuding the gut, where they may contribute to host health. In this review, we present and discuss the main factors enabling LAB adaptation to such lifestyle, including the gene reprogramming accompanying gut colonization, the specific bacterial components involved in adhesion and interaction with host, and how the gut niche has shaped the genome of intestine-adapted species. Moreover, the capacity of LAB to colonize abiotic surfaces by forming structured communities, i.e., biofilms, is briefly discussed, taking into account the main bacterial and environmental factors involved, particularly in relation to food-related environments. The vast spread of LAB surface-associated communities and the ability to control their occurrence hold great potentials for human health and food safety biotechnologies.

Arnold, J. W., Monteagudo-Mera, A., Altermann, E., Cadenas, M. B., Thompson, A. L., and zcarate-Peril, M. A. Genome Sequences of Potential Probiotic Lactobacillus rhamnosus Isolates from Human Infants. Genome Announc. 4-6-2017; 5(14); PM: 28385840

ABSTRACT: Probiotics provide health benefits to their hosts, including modulation of host immune response, inhibition of colonization by pathogens, modulation of the gut microbiota, and epithelial barrier enhancement. Here, we present the draft genome sequences of two newly isolated Lactobacillus rhamnosus strains of probiotic potential from healthy human infants.

Aroniadis, O. C., Drossman, D. A., and Simren, M. A Perspective on Brain-Gut Communication: The American Gastroenterology Association and American Psychosomatic Society Joint Symposium on Brain-gut Interactions and the Intestinal Microenvironment. Psychosom.Med. 1-17-2017; PM: 27922565

ABSTRACT: BACKGROUND: Alterations in brain-gut communication and the intestinal microenvironment have been implicated in a variety of medical and neuropsychiatric diseases. Three central areas require basic and clinical research: (1) how the intestinal microenvironment interacts with the host immune system, central nervous system and enteric nervous system; (2) the role of the intestinal microenvironment in the pathogenesis of medical and neuropsychiatric disease; (3) the effects of diet, prebiotics, probiotics and fecal microbiota transplantation on the intestinal microenvironment and the treatment of disease. *METHODS*: This review article is based on a symposium convened by the American Gastroenterology Association and American Psychosomatic Society to foster interest in the role of the intestinal microenvironment in brain-gut communication and pathogenesis of neuropsychiatric and biopsychosocial disorders. The aim was to define the stat-of-the-art of the current scientific knowledge base and to identify guidelines and future directions for new research in this area. *RESULTS*: This review provides a characterization of the intestinal microbial composition and function. We also provide evidence for the interactions between the intestinal microbiome, the host and the environment. The role of the intestinal microbiome in medical and neuropsychiatric diseases is reviewed as well as the treatment effects of manipulation of the intestinal microbiome. *CONCLUSIONS*: Based on this review, opportunities and challenges for conducting research in the field are described, leading to potential avenues for future research.

Aryantini, N. P., Yamasaki, E., Kurazono, H., Sujaya, I. N., Urashima, T., and Fukuda, K. In vitro safety assessments and antimicrobial activities of Lactobacillus rhamnosus strains isolated from a fermented mare's milk. Anim Sci.J. 2017; 88(3):517-525; PM: 27476815

ABSTRACT: Safety and probiotic characteristics such as antimicrobial activities of three Lactobacillus rhamnosus strains, FSMM15, FSMM22 and FSMM26, previously isolated as potential probiotics from fermented mare's milk were investigated. The three FSMM strains were susceptible to ampicillin, gentamycin, kanamycin, streptomycin, tetracycline and chloramphenicol, whereas they were resistant to erythromycin (minimal inhibitory concentration (MIC) = 4-8 microg/mL) and clindamycin (MIC = 4 microg/mL); bioconversion of bile salts, hemolytic activity and mucin degradation activity were negative; enzymatic activities of alpha-chymotrypsin and beta-glucosidase were detected, but those of alpha-galactosidase, beta-glucuronidase and N-acetyl-beta-glucosaminidase, were undetectable. Among the strains, strain FSMM15 was chosen as a safer probiotic candidate due mainly to the lack of plasminogen binding ability. Despite lower acid production of strain FSMM15 than others, its cell-free culture supernatant inhibited growths of Salmonella Typhimurium LT-2, Shigella sonnei, Listeria monocytogenes, and Escherichia coli O157 with comparable levels of ampicillin, suggesting a favorable aspect of strain FSMM15 as a probiotic strain.

Aryantini, N. P. D., Kondoh, D., Nishiyama, K., Yamamoto, Y., Mukai, T., Sujaya, I. N., Urashima, T., and Fukuda, K. Anchorless cell surface proteins function as laminin-binding adhesins in Lactobacillus rhamnosus FSMM22. FEMS Microbiol.Lett. 3-1-2017; 364(6); PM: 28333282

ABSTRACT: Anchorless cell surface proteins (CSPs) were extracted with 1 M lithium chloride solution from Lactobacillus rhamnosus FSMM22. Loss of the anchorless CSPs resulted in a 2-fold decrease in FSMM22 cells bound to a constitutive extracellular matrix glycoprotein, laminin, in vitro. DNA-binding protein HU, glyceraldehyde-3-phosphate dehydrogenase, lactate dehydrogenase and 30S ribosomal protein S19 (RpsS) were identified by mass spectrometry in the extract as laminin-binding adhesins. Among the four proteins, RpsS was immunohistochemically confirmed to exist on the cell surface. Our findings strongly suggest that anchorless CSPs can enhance bacterial adhesion to the host.

Asha, M. K., Debraj, D., Dethe, S., Bhaskar, A., Muruganantham, N., and Deepak, M. Effect of Flavonoid-Rich Extract of Glycyrrhiza glabra on Gut-Friendly Microorganisms, Commercial Probiotic Preparations, and Digestive Enzymes. J.Diet.Suppl. 5-4-2017; 14(3):323-333; PM: 27588327

ABSTRACT: Flavonoid-rich extract prepared from Glycyrrhiza glabra has been found to be beneficial in patients with functional dyspepsia and was reported to possess some gut health-promoting properties such as antioxidant, anti-inflammatory and anti-Helicobacter pylori activities. In the present study, the flavonoid-rich extract of Glycyrrhiza glabra was evaluated for its compatibility with probiotic strains (Lactobacillus casei, Lactobacillus fermentum, Lactobacillus plantarum, and Streptococcus thermophilus), commercial probiotic drinks, and digestive enzymes (pancreatic alpha-amylase, alpha-glucosidase, phytase, xylanase, and pancreatic lipase). Results of this study indicated that the flavonoid-rich extract of Glycyrrhiza glabra is compatible with the tested probiotic strains, probiotic drinks and digestive enzymes.

Atia, A., Gomma, A. I., Fliss, I., Beyssac, E., Garrait, G., and Subirade, M. Molecular and biopharmaceutical investigation of alginate-inulin synbiotic coencapsulation of probiotic to target the colon. J.Microencapsul. 4-19-2017; 1-13; PM: 28350268

ABSTRACT: Colon targeting, as a site-specific delivery for oral formulation, remains a major challenge, especially for sensitive bioactive components such as therapeutic forms of phages, live attenuated virus and prebiotics-probiotics association. Synbiotics could be used to protect encapsulated probiotics during the gastrointestinal tract and control their release in the colon. To achieve these goals, effective prebiotics, such as inulin, could be combined with alginate - the most exploited polymer used for probiotic encapsulation - in the form of beads. This work aimed to study the biopharmaceutical behaviour of alginate beads (A) and inulin-alginate beads of different inulin concentrations (5 or 20%) in 2% alginate (AI5, AI20). Beads were loaded with three probiotic strains (Pediococcus acidilactici UI5, Lactobacillus reuteri and Lactobacillus salivarius). Dissolution of beads was studied by USP4 under conditions simulating the gastrointestinal condition. The survival rates of the bacterial strains were measured by a specific qPCR bacterial count. Mucoadhesiveness of beads was studied by an ex vivo method using intestinal mucosa. To understand the behaviour of each formulation, the ultrastructure of the polymeric network was studied using scanning electron microscopy (SEM). Molecular interactions between alginate and inulin were studied by Fourier transform infra-red spectroscopy (FTIR). Dissolution results suggested that the presence of inulin in beads provided more protection for the tested bacterial strains against the acidic pH. AI5 was the most effective formulation to deliver probiotics to the colon

simulation conditions. FTIR and SEM investigations explained the differences in behaviour of each formula. The developed symbiotic form provided a promising matrix for the development of colonic controlled release systems.

Avershina, E., Cabrera, Rubio R., Lundgard, K., Perez, Martinez G., Collado, M. C., Storro, O., Oien, T., Dotterud, C. K., Johnsen, R., and Rudi, K. Effect of probiotics in prevention of atopic dermatitis is dependent on the intrinsic microbiota at early infancy. J.Allergy Clin.Immunol. 2017; 139(4):1399-1402; PM: 27931973

No Abstract Available.

Ayala, F. R., Bauman, C., Cogliati, S., Lenini, C., Bartolini, M., and Grau, R. Microbial flora, probiotics, Bacillus subtilis and the search for a long and healthy human longevity. Microb.Cell. 3-16-2017; 4(4):133-136; PM: 28435840

ABSTRACT: Probiotics are live microorganisms that have beneficial effects on host health, including extended lifespan, when they are administered or present in adequate quantities. However, the mechanisms by which probiotics stimulate host longevity remain unclear and very poorly understood. In a recent study (Nat. Commun. 8, 14332 (2017) doi: 10.1038/ncomms14332), we used the spore-forming probiotic bacterium Bacillus subtilis and the model organism Caenorhabditis elegans to study the mechanism by which a probiotic bacterium affects host longevity. We found that biofilm-proficient B. subtilis colonized the C. elegans gut and extended the worm lifespan significantly longer than did biofilm-deficient isogenic strains. In addition to biofilm proficiency, the quorum-sensing pentapeptide CSF and nitric oxide (NO) represent the entire B. subtilis repertoire responsible for the extended longevity of C. elegans. B. subtilis grown under biofilm-supporting conditions synthesized higher levels of NO and CSF than under planktonic growth conditions, emphasizing the key role of the biofilm in slowing host aging. Significantly, the prolongevity effect of B. subtilis was primarily due to a downregulation of the insulin-like signaling system that precisely is a key partaker in the healthy longevity of human centenarians. These findings open the possibility to test if the regular consumption of B. subtilis incorporated in foods and beverages could significantly extend human life expectancy and contribute to stop the development of age-related diseases.

az-Vergara, L., Pereyra, C. M., Montenegro, M., Pena, G. A., Aminahuel, C. A., and Cavaglieri, L. R. Encapsulated whey-native yeast Kluyveromyces marxianus as a feed additive for animal production. Food Addit.Contam Part A Chem.Anal.Control Expo.Risk Assess. 3-6-2017; 1-10; PM: 28277172

ABSTRACT: Whey is the main byproduct of the cheese industry. While the composition is variable, it retains up to 55% of milk nutrients. The beneficial features of whey indicates a promising source of new potentially probiotic strains for the development of food additives destined for animal production. The aim of this study was to identify Kluyveromyces spp. isolated from whey, to study some probiotic properties and to select the best strain to be encapsulated using derivatised chitosan. Kluyveromyces marxianus strains (VM003, VM004 and VM005) were isolated from whey and identified by phenotypic and molecular techniques. These three yeast strains were able to survive under gastrointestinal conditions. Moreover, they exhibited weak auto-aggregation and co-aggregation with pathogenic bacteria (Salmonella sp., Serratia sp., Escherichia coli

and Salmonella typhimurium). In general the K. marxianus strains had a strong antimicrobial activity against pathogenic bacteria. The potential probiotic K. marxianus VM004 strain was selected for derivatised-chitosan encapsulation. Material treated with native chitosan exhibited a strong antimicrobial activity of K. marxianus, showing a total growth inhibition at 10 min exposure. However, derivatised-chitosan encapsulation showed a reduced antimicrobial activity. This is the first study to show some probiotic properties of whey-native K. marxianus, in vitro. An encapsulation strategy was applied using derivatised chitosan.

Azimirad, M., Alebouyeh, M., and Naji, T. Inhibition of Lipopolysaccharide-Induced Interleukin 8 in Human Adenocarcinoma Cell Line HT-29 by Spore Probiotics: B. coagulans and B. subtilis (natto). Probiotics.Antimicrob.Proteins. 2017; 9(1):56-63; PM: 27785697

ABSTRACT: Probiotics are used as a treatment for different intestinal disorders. They confer health benefits by different ways. This study was aimed to investigate immunomodulatory effect of Bacillus probiotic spores on the production of lipopolysaccharide (LPS)-induced interleukin 8 (IL-8) in HT-29 intestinal epithelial cells. Differentiated intestinal epithelial cell line was used as a model for the study of colonization of purified spores (Bacillus subtilis (natto) and B. coagulans) and their anti-inflammatory effects. MTT assay and trypan blue staining were used for the detection of optimal concentration of the purified spores and LPS. Pre-treatment assay was done by treatment of the cells with the purified spores for 2 h, followed by challenges with LPS for 3 and 18 h. Post-treatment assay was done by initial treatment of the cells with LPS for 18 h, followed by the spores for 3 and 6 h. Levels of IL-8 secretion and its mRNA expression were measured by ELISA and relative Q real-time PCR. Our results showed similar rates of adherence to intestinal epithelial cells by the spore probiotics, while displaying no cytotoxic effect. In the pre-treatment assay, a significant decrease in IL-8, at both protein and mRNA levels, was measured for B. coagulans spores after the addition of LPS, which was higher than those observed for Bacillus subtilis (natto) spores. In the post-treatment assay, while Bacillus subtilis (but not B. coagulans) diminished the LPS-stimulated IL-8 levels after 3 h of incubation, the inhibitory effect was not constant. In conclusion, ability of Bacillus spore probiotics for adherence to intestinal epithelial cell and their anti-inflammatory effects, through interference with LPS/IL-8 signaling, was shown in this study. Further studies are needed to characterize responsible bacterial compounds associated with these effects.

Babot, J. D., Arganaraz, Martinez E., Lorenzo-Pisarello, M. J., Apella, M. C., and Perez, Chaia A. Lactic acid bacteria isolated from poultry protect the intestinal epithelial cells of chickens from in vitro wheat germ agglutinin-induced cytotoxicity. Br.Poult.Sci. 2017; 58(1):76-82; PM: 27845560

ABSTRACT: Poultry fed on wheat-based diets regularly ingest wheat germ agglutinin (WGA) that has toxic effects in vitro on intestinal epithelial cells (IEC) obtained from 14-d-old broilers. Cytotoxicity and the potential role of 14 intestinal bacterial strains in the removal of bound lectins in epithelial cell cultures were investigated. Cytotoxicity was dependent on time and lectin concentration; the lethal dose (LD50) was 8.36 microg/ml for IEC exposed for 2 h to WGA. Complementary sugars to WGA were detected on the surface of one Enterococcus and 9 Lactobacillus strains isolated from poultry. These strains were evaluated as a lectin removal tool for cytotoxicity prevention. Incubation of lactic acid bacteria with WGA before IEC-lectin interaction caused a substantial

reduction in the percentage of cell deaths. The protection was attributed to the amount of lectin bound to the bacterial surfaces and was strain-dependent. L. salivarius LET 201 and L. reuteri LET 210 were more efficient than the other lactic acid bacteria assayed. These results provide a basis for the development of probiotic supplements or cell-wall preparations of selected lactic acid bacteria intended to avoid harmful effects of a natural constituent of the grain in wheat-based diets.

Bahi, A., Guardiola, F. A., Messina, C., Mahdhi, A., Cerezuela, R., Santulli, A., Bakhrouf, A., and Esteban, M. A. Effects of dietary administration of fenugreek seeds, alone or in combination with probiotics, on growth performance parameters, humoral immune response and gene expression of gilthead seabream (Sparus aurata L.). Fish.Shellfish.Immunol. 2017; 60:50-58; PM: 27856325

ABSTRACT: The use of immunostimulants is considered a promising preventive practice that may help to maintain animal welfare and a healthy environment, while increasing production and providing higher profits. The purpose of this study was to evaluate the effects on gilthead seabream (Sparus aurata L.) of the dietary administration of fenugreek (Trigonella foenum graecum) seeds, alone or combined with one of the following probiotic strains: Bacillus licheniformis (TSB27), Lactobacillus plantarum or Bacillus subtilis (B46). Gilthead seabream were fed a control or one of the supplemented diets for 3 weeks. The effects of these supplemented diets on growth performance parameters and the humoral immune response (natural haemolytic complement, peroxidase, total IgM levels, proteases and antiproteases activities) were evaluated after 2 and 3 weeks of feeding. Simultaneously, the expression levels of some immune-relevant genes (igm, tcr-beta, csfr1 and bd) were measured in the head-kidney. Interestingly, all probiotic supplemented diets increased seabream growth rates, especially the B. licheniformis supplemented diet. Generally, humoral immune parameters were enhanced by the dietary supplementation at the different time points measured. The results showed a significant increases in the immune parameters, principally in fish fed only fenugreek or fenugreek combined with B. subtilis. Furthermore, real time qPCR revealed that dietary supplementation significantly enhances the expression of immune-associated genes in the head-kidney, particularly igm gene expression. These results suggest that fenugreek alone or combined with one of the probiotic strains mentioned enhances the immune response of gilthead seabream, a species with one of the highest rates of production in marine aquaculture.

Bakhshi, N., Soleimanian-Zad, S., and Sheikh-Zeinoddin, M. Dynamic surface tension measurement for the screening of biosurfactants produced by Lactobacillus plantarum subsp. plantarum PTCC 1896. Enzyme Microb.Technol. 2017; 101:1-8; PM: 28433185

ABSTRACT: Currently, screening of microbial biosurfactants (BSs) is based on their equilibrium surface tension values obtained using static surface tension measurement. However, a good surfactant should not only have a low equilibrium surface tension, but its dynamic surface tension (DST) should also decrease rapidly with time. In this study, screening of BSs produced by Lactobacillus plantarum subsp. plantarum PTCC 1896 (probiotic) was performed based on their DST values measured by Wilhelmy plate tensiometry. The relationship between DST and structural and functional properties (anti-adhesive activity) of the BSs was investigated. The results showed that the changes in the yield, productivity and structure of the BSs were growth medium and incubation time dependent ($p<0.05$). Structurally different BSs produced exhibited identical equilibrium

surface tension values. However, differences among the structure/yield of the BSs were observed through the measurement of their DST. The considerable dependence of DST on the concentration and composition of the BS proteins was observed ($p<0.05$). Moreover, the anti-adhesive activity of the BS was found to be positively correlated with its DST. The results suggest that the DST measurement could serve as an efficient method for the clever screening of BSs producer/production condition, and consequently, for the investigation of probiotic features of bacteria, since the anti-adhesive activity is an important criterion of probiotics.

Balamuralikrishnan, B., Lee, S. I., and Kim, I. H. Dietary inclusion of different multi-strain complex probiotics; effects on performance in broilers. Br.Poult.Sci. 2017; 58(1):83-86; PM: 27918205

ABSTRACT: This study was designed to evaluate the effects of two different complex probiotic supplementations on the growth performance, meat quality, excreta microflora, nutrient retention, blood metabolic profile and noxious gas emissions in broilers. A total of 612 conventional healthy 1-d-old Ross 308 broilers with body weight of 41 +/- 0.3 g were randomly divided into 3 treatments with 12 replicate cages, with 17 broilers in each cage and fed with the following diets: CON-Basal diet, T1-CON + Probiotic A, T2-CON + Probiotic B. Significant results were observed on body weight gain, but not on feed conversation ratio and feed intake, in the whole experimental period. Increased faecal lactobacillus counts were found with probiotics supplementation. However, no significant effects were found for meat quality, nutrient retention, blood metabolic profile or noxious gas emissions. In conclusion, both multi-strain probiotics had beneficial effects on growth performance, drip loss percentage and faecal Lactobacillus counts in broilers.

Balzaretti, S., Taverniti, V., Guglielmetti, S., Fiore, W., Minuzzo, M., Ngo, H. N., Ngere, J. B., Sadiq, S., Humphreys, P. N., and Laws, A. P. A Novel Rhamnose-Rich Hetero-exopolysaccharide Isolated from Lactobacillus paracasei DG Activates THP-1 Human Monocytic Cells. Appl.Environ.Microbiol. 2-1-2017; 83(3); PM: 27913418

ABSTRACT: Lactobacillus paracasei DG is a bacterial strain with recognized probiotic properties and is used in commercial probiotic products. However, the mechanisms underlying its probiotic properties are mainly unknown. In this study, we tested the hypothesis that the ability of strain DG to interact with the host is at least partly associated with its ability to synthesize a surface-associated exopolysaccharide (EPS). Comparative genomics revealed the presence of putative EPS gene clusters in the DG genome; accordingly, EPS was isolated from the surface of the bacterium. A sample of the pure EPS from strain DG (DG-EPS), upon nuclear magnetic resonance (NMR) and chemical analyses, was shown to be a novel branched hetero-EPS with a repeat unit composed of l-rhamnose, d-galactose, and N-acetyl-d-galactosamine in a ratio of 4:1:1. Subsequently, we demonstrated that DG-EPS displays immunostimulating properties by enhancing the gene expression of the proinflammatory cytokines tumor necrosis factor alpha (TNF-alpha) and interleukin 6 (IL-6), and particularly that of the chemokines IL-8 and CCL20, in the human monocytic cell line THP-1. In contrast, the expression of the cyclooxygenase enzyme COX-2 was not affected. In conclusion, DG-EPS is a bacterial macromolecule with the ability to boost the immune system either as a secreted molecule released from the bacterium or as a capsular envelope on the bacterial cell wall. This study provides additional information about the mechanisms supporting the cross talk between L. paracasei DG and the host. *IMPORTANCE*: The consumption of

food products and supplements called probiotics (i.e., containing live microbial cells) to potentially prevent or treat specific diseases is constantly gaining popularity. The lack of knowledge on the precise mechanisms supporting their potential health-promoting properties, however, greatly limits a more appropriate use of each single probiotic strain. In this context, we studied a well-known probiotic, Lactobacillus paracasei DG, in order to identify the constitutive molecules that can explain the documented health-promoting properties of this bacterium. We found a novel polysaccharide molecule, named DG-EPS, that is secreted by and covers the bacterium. We demonstrated that this molecule, which has a chemical structure never identified before, has immunostimulatory properties and therefore may contribute to the ability of the probiotic L. paracasei DG to interact with the immune system.

Bambling, M., Edwards, S. C., Hall, S., and Vitetta, L. A combination of probiotics and magnesium orotate attenuate depression in a small SSRI resistant cohort: an intestinal anti-inflammatory response is suggested. Inflammopharmacology. 2017; 25(2):271-274; PM: 28155119

ABSTRACT: Approximately, one-third of those who develop major depression will have a poor response to treatment and over time can become treatment resistant. Intestinal dysbiosis has been implicated in depression with systemic inflammation and vagal and enteric nerve impairment. We report on a sequel pilot study (n = 12) with a combination probiotics/magnesium orotate formulation adjuvant administered with SSRIs for treatment resistant depression. At the end of an 8-week intervention mean changes for depression scores and quality of life in the group was clinically significantly improved ($p < 0.001$) with all but 4 participants experiencing a benefit. An intestinal anti-inflammatory response was suggested. At 16-weeks follow-up while still on SSRI medications, the group had relapsed after cessation of the test intervention.

Bandara, H. M., Matsubara, V. H., and Samaranayake, L. P. Future therapies targeted towards eliminating Candida biofilms and associated infections. Expert.Rev.Anti.Infect.Ther. 2017; 15(3):299-318; PM: 27927053

ABSTRACT: INTRODUCTION: Candida species are common human commensals and cause either superficial or invasive opportunistic infections. The biofilm form of candida as opposed to its suspended, planktonic form, is predominantly associated with these infections. Alternative or adjunctive therapies are urgently needed to manage Candida infections as the currently available short arsenal of antifungal drugs has been compromised due to their systemic toxicity, cross-reactivity with other drugs, and above all, by the emergence of drug-resistant Candida species due to irrational drug use. *Areas covered*: Combination anti-Candida therapies, antifungal lock therapy, denture cleansers, and mouth rinses have all been proposed as alternatives for disrupting candidal biofilms on different substrates. Other suggested approaches for the management of candidiasis include the use of natural compounds, such as probiotics, plants extracts and oils, antifungal quorum sensing molecules, anti-Candida antibodies and vaccines, cytokine therapy, transfer of primed immune cells, photodynamic therapy, and nanoparticles. *Expert commentary*: The sparsity of currently available antifungals and the plethora of proposed anti-candidal therapies is a distinct indication of the urgent necessity to develop efficacious therapies for candidal infections. Alternative drug delivery approaches, such as probiotics, reviewed here is likely to be a reality in clinical settings in the not too distant future.

Banerjee, G. and Ray, A. K. The advancement of probiotics research and its application in fish farming industries. Res.Vet.Sci. 1-23-2017; 115:66-77; PM: 28157611

ABSTRACT: Fish are always susceptible to a variety of lethal diseases caused by different types of bacterial, fungal, viral and parasitic agents. The unscientific management practices such as, over feeding, high stock densities and destructive fishing techniques increase the probability of disease symptoms in aquaculture industries. According to Food and Agriculture Association (FAO), each and every year several countries such as China, India, Norway, Indonesia, etc. face a huge loss in aquaculture production due to mainly bacterial and viral diseases. The use of antibiotics is a common practice in fish farming sectors to control the disease outbreak. However, the antibiotics are not long term friend because it creates selective pressure for emergence of drug resistant bacteria. Probiotics are live microorganisms that confer several beneficial effects to host (enhances immunity, helps in digestion, protects from pathogens, improves water quality, promotes growth and reproduction) and can be used as an alternative of antibiotics. In recent year, a wide range of bacteria have reported as potential probiotics candidates in fish farming sectors, however, Lactobacillus sp. and Bacillus sp. gain special attention due to their high antagonistic activities, extracellular enzyme production and availability. In this present review, we have summarized the recent advancement in aquaculture probiotics research and its impact on fish health, nutrition, immunity, reproduction and water quality.

Barba-Vidal, E., Castillejos, L., Lopez-Colom, P., Rivero, Urgell M., Moreno Munoz, J. A., and Martin-Orue, S. M. Evaluation of the Probiotic Strain Bifidobacterium longum subsp. Infantis CECT 7210 Capacities to Improve Health Status and Fight Digestive Pathogens in a Piglet Model. Front Microbiol. 2017; 8:533; PM: 28443068

ABSTRACT: Probiotics have been demonstrated to be useful to enhance gut health and prevent gastrointestinal infections. The objective of this study is to demonstrate the potential of the probiotic strain Bifidobacterium longum subsp. infantis CECT 7210 (B. infantis IM1) to prevent and fight intestinal disease by using a Salmonella Typhimurium (Trial 1) or an enterotoxigenic Escherichia coli K88 (Trial 2) oral challenge in a weaning piglet model. Seventy-two piglets were used in each trial. After an adaptation period, animals were orally challenged. One animal per pen was euthanized at Days 4 and 8/9 (Trial 1/Trial 2) post-inoculation (PI). Animal performance, clinical signs, pathogen excretion, fermentation, immune response, and intestinal morphology were evaluated. In Trial 1, most parameters responded to the challenge, whereas, in Trial 2, effects were much milder. Consistent effects of the probiotic were detected in both experiments: Reduction of pathogen excretion ($P = 0.043$ on Day 3 PI, Trial 1) or ileal colonization (33% reduction of animals with countable coliforms; $P = 0.077$, Trial 2); increases in intraepithelial lymphocytes ($P = 0.002$ on Day 8 PI in Trial 1, $P = 0.091$ on Day 4 PI in Trial 2), and improvement of the fermentation profile by increasing butyric acid in non-challenged animals [P challenge x probiotic (interaction) = 0.092 in Trial 1 and $P = 0.056$ in Trial 2] concomitant with an enhancement of the villus:crypt ratio on Day 8/9 PI (P interaction = 0.091 for Trial 1 and $P = 0.006$ for Trial 2). Challenged animals treated with the probiotic showed reduced feed intakes (P interaction = 0.019 in Trial 1 and $P = 0.020$ in Trial 2) and had lower short-chain fatty acid concentrations in the colon (P interaction = 0.008 in Trial 1 and $P = 0.082$ in Trial 2). In conclusion, this probiotic demonstrated potential to reduce the intestinal colonization by pathogens and to stimulate local immune response. However, effects on feed intake, microbial fermentation, and

intestinal architecture showed a differential pattern between challenged and non-challenged animals. Effects of the probiotic intervention were dependent on the structure of the ecosystem in which it was applied.

bautret-Daly, A., Dempsey, E., Parra-Blanco, A., Medina, C., and Harkin, A. Gut-brain actions underlying comorbid anxiety and depression associated with inflammatory bowel disease. Acta Neuropsychiatr. 3-8-2017; 1-22; PM: 28270247

ABSTRACT: Introduction Inflammatory bowel disease (IBD) is a chronic relapsing and remitting disorder characterised by inflammation of the gastrointestinal tract. There is a growing consensus that IBD is associated with anxiety- and depression-related symptoms. Psychological symptoms appear to be more prevalent during active disease states with no difference in prevalence between Crohn's disease and ulcerative colitis. Behavioural disturbances including anxiety- and depression-like symptoms have also been observed in animal models of IBD. RESULTS: The likely mechanisms underlying the association are discussed with particular reference to communication between the gut and brain. The close bidirectional relationship known as the gut-brain axis includes neural, hormonal and immune communication links. Evidence is provided for a number of interacting factors including activation of the inflammatory response system in the brain, the hypothalamic-pituitary-adrenal axis, and brain areas implicated in altered behaviours, changes in blood brain barrier integrity, and an emerging role for gut microbiota and response to probiotics in IBD. Discussion The impact of psychological stress in models of IBD remains somewhat conflicted, however, it is weighted in favour of stress or early stressful life events as risk factors in the development of IBD, stress-induced exacerbation of inflammation and relapse. CONCLUSION: It is recommended that patients with IBD be screened for psychological disturbance and treated accordingly as intervention can improve quality of life and may reduce relapse rates.

Beilharz, J. E., Kaakoush, N. O., Maniam, J., and Morris, M. J. Cafeteria diet and probiotic therapy: cross talk among memory, neuroplasticity, serotonin receptors and gut microbiota in the rat. Mol.Psychiatry. 3-14-2017; PM: 28289278

ABSTRACT: The western diet is known to have detrimental effects on cognition and the gut microbiota, but few studies have investigated how these may be related. Here, we examined whether a probiotic could prevent diet-induced memory deficits. Rats were pre-exposed to vehicle, low or high doses of VSL#3 for 2 weeks before half were switched from chow to a cafeteria diet (Caf) for 25 days; VSL#3 treatment continued until death. High-dose VSL#3 prevented the diet-induced memory deficits on the hippocampal-dependent place task, but the probiotic caused deficits on the perirhinal-dependent object task, irrespective of diet or dose. No differences were observed in anxiety-like behaviour on the elevated plus maze. Gut microbial diversity was dramatically decreased by Caf diet and here, VSL#3 was able to increase the abundance of some taxa contained in the probiotic such as Streptococcus and Lactobacillus and also other taxa including Butyrivibrio, which were decreased by the Caf diet. This affected the predicted profile of microbial metabolic pathways related to antioxidant and bile biosynthesis, and fat and carbohydrate metabolism. In the hippocampus, the Caf diet increased the expression of many genes related to neuroplasticity and serotonin receptor (5HT) 1A, which was normalised in Caf-High rats. Distance-based linear modelling showed that these genes were the best predictors of place memory, and related to microbiota principal component (PC) 1. Neuroplasticity genes in the perirhinal

cortex were also affected and related to PC1 but object memory performance was correlated with perirhinal 5HT2C expression and microbiota PC3. These results show that probiotics can be beneficial in situations of gut dysbiosis where memory deficits are evident but may be detrimental in healthy subjects.Molecular Psychiatry advance online publication, 14 March 2017; doi:10.1038/mp.2017.38.

Bendali, F., Kerdouche, K., Hamma-Faradji, S., and Drider, D. In vitro and in vivo cholesterol lowering ability of Lactobacillus pentosus KF923750. Benef.Microbes. 4-26-2017; 8(2):271-280; PM: 28299945

ABSTRACT: Lactobacillus pentosus KF923750 was characterised for probiotic related properties and then characterised for cholesterol uptake in vitro as well as in vivo using rabbits fed a high-cholesterol diet. The survival percentage of L. pentosus KF923750 was 100% at pH 3, 52.18% at pH 2 and 36.21% at pH 2 plus pepsin. Similarly, this strain appeared resistant to bile (0.1% [98.42%], 0.3% [88.52%], 0.5% [75.60%] and 1% [71.15%]), after 4 h exposure. Moreover, L. pentosus KF923750 controlled growth of Escherichia coli ATCC 25922 and Staphylococcus aureus ATCC 25923 through the production of a bacteriocin-like inhibitory substance and anti-adhesive capabilities. L. pentosus KF923750 was non-cytotoxic to eukaryotic cells but sensitive to some antibiotics. Compared with rabbits fed a high-cholesterol diet but without L. pentosus KF923750 supplementation, the plasma total cholesterol, low-density lipoprotein cholesterol and triglycerides levels were significantly decreased in L. pentosus KF923750-fed rabbits by 11.54, 16.00 and 18.00%, respectively, with no significant change in high-density lipoprotein cholesterol levels. The histological sections of livers revealed lesions in all the rabbits that were fed a high-cholesterol diet, but these were less pronounced in rabbits ingesting L. pentosus KF923750. This study highlights the potential of lactobacilli, such as L. pentosus KF923750, in the treatment or prevention of hypercholesterolemia.

Berings, M., Jult, A., Vermeulen, H., De, Ruyck N., Derycke, L., Ucar, H., Ghekiere, P., Temmerman, R., Ellis, J., Bachert, C., Lambrecht, B. N., Dullaers, M., and Gevaert, P. Probiotics-impregnated bedding covers for house dust mite allergic rhinitis: A pilot randomized clinical trial. Clin.Exp.Allergy. 4-18-2017; PM: 28418228

No Abstract Available.

Berretta, M., Della, Pepa C., Tralongo, P., Fulvi, A., Martellotta, F., Lleshi, A., Nasti, G., Fisichella, R., Romano, C., De, Divitiis C., Taibi, R., Fiorica, F., Di, Francia R., Di, Mari A., Del, Pup L., Crispo, A., De, Paoli P., Santorelli, A., Quagliariello, V., Iaffaioli, R. V., Tirelli, U., and Facchini, G. Use of Complementary and Alternative Medicine (CAM) in cancer patients: An Italian multicenter survey. Oncotarget. 4-11-2017; 8(15):24401-24414; PM: 28212560

ABSTRACT: INTRODUCTION: Complementary and Alternative Medicine (CAM) include a wide range of products (herbs, vitamins, minerals, and probiotics) and medical practices, developed outside of the mainstream Western medicine. Patients with cancer are more likely to resort to CAM first or then in their disease history; the potential side effects as well as the costs of such practices are largely underestimated. *PATIENTS AND METHOD*: We conducted a descriptive survey in five Italian hospitals involving 468 patients with different malignancies. The survey consisted of a forty-two question questionnaire, patients were eligible if they were Italian-speaking and receiving an

anticancer treatment at the time of the survey or had received an anticancer treatment no more than three years before participating in the survey. *RESULTS*: Of our patients, 48.9% said they use or have recently used CAM. The univariate analysis showed that female gender, high education, receiving treatment in a highly specialized institute and receiving chemotherapy are associated with CAM use; at the multivariate analysis high education (Odds Ratio, (OR): 1.96 95% Confidence Interval, CI, 1.27-3.05) and receiving treatment in a specialized cancer center (OR: 2.75 95% CI, 1.53-4.94) were confirmed as risk factors for CAM use. *CONCLUSION*: Roughly half of our patients receiving treatment for cancer use CAM. It is necessary that health professional explore the use of CAM with their cancer patients, educate them about potentially beneficial therapies in light of the limited available evidence of effectiveness, and work towards an integrated model of health-care provision.

Berti, C., Agostoni, C., Davanzo, R., Hypponen, E., Isolauri, E., Meltzer, H. M., Steegers-Theunissen, R. P., and Cetin, I. Early-life nutritional exposures and lifelong health: immediate and long-lasting impacts of probiotics, vitamin D, and breastfeeding. Nutr.Rev. 2-1-2017; 75(2):83-97; PM: 28130504

ABSTRACT: Pregnancy and infancy comprise the most critical stages for conditioning an individual's health, with a number of implications for subsequent risks of morbidity, mortality, and reproductive health. Nutrition may influence both the overall pregnancy outcome and the growth trajectory and immune system of the fetus and infant, with short- and long-term effects on the health of the offspring. Within this context, leading experts at Expo Milano 2015 in Milan, Italy, discussed up-to-date knowledge while providing suggestions and challenges before, during, and after pregnancy. This narrative review summarizes the key issues raised by the experts concerning the interplay between the nutritional environment from conception to early infancy and the offspring's immediate and lifelong health, with a particular focus on epigenetic mechanisms, probiotics, vitamin D, and breastfeeding. Taken together, the findings strengthen the awareness that nutritional exposures occurring from preconception to the postnatal period may be strong determinants of the offspring's health and may provide supportive evidence for current nutritional recommendations and guidelines for pregnant women and infants. Critical topics to be addressed in future research and translated into recommendations of public health relevance are also highlighted.

Best, A. A., Porter, A. L., Fraley, S. M., and Fraley, G. S. Characterization of Gut Microbiome Dynamics in Developing Pekin Ducks and Impact of Management System. Front Microbiol. 2016; 7:2125; PM: 28101086

ABSTRACT: Little to no research has been conducted on the gut microbiome of the Pekin duck, yet over 24.5 million ducks are raised for human consumption each year in the United States alone. Knowledge of the microbiome could lead to an understanding of the effects of growing conditions such as the use of prebiotics, probiotics, and enzymes in feeding practices, the use of antibiotics, and the sources of pathogenic bacteria in diseased ducks. In order to characterize changes in the caecal microbiome that occur as ducks develop through a typical industry grow-out period, a 16S rRNA community analysis of caecal contents collected over a 6-week period was conducted using a next generation sequencing approach. Transitions in the composition of the caecal microbiome occurred throughout the lifespan, with a large shift during days 4 through 10 posthatch. Two major phyla of bacteria were found to be present within the caeca of

aviary raised ducks, with the relative abundance of each phylum varying by age of the duck. Proteobacteria is dominant for the first 3 days of age, and Firmicutes increases and dominates beginning at day 4. Barn raised ducks contained a significant population of Bacteroidetes in addition to Proteobacteria and Firmicutes at later developmental time points, though this phylum was absent in aviary raised ducks. Genera containing pathogens of anseriformes most often found in industry settings were either absent or found as normal parts of the caecal microbial populations. The high level differences in phylum abundance highlight the importance of well-designed sampling strategies for microbiome based studies. Results showed clear distinctions between Pekin Duck caecal contents and those of Broiler Chickens and Turkey in a qualitative comparison. These data provide a reference point for studies of the Pekin Duck through industry grow-out ages, provide a foundation for understanding the types of bacteria that promote health, and may lead to improved methods to increase yields and decrease instances of disease in agricultural production processes.

Beyitler, I. and Kavukcu, S. Clinical presentation, diagnosis and treatment of vulvovaginitis in girls: a current approach and review of the literature. World J.Pediatr. 2017; 13(2):101-105; PM: 28083751

ABSTRACT: BACKGROUND: Vulvovaginitis is the most common cause of gynecological complaints in children and young girls. Some of the factors which cause vulvovaginitis include hypoestrogenism, the anatomical proximity of rectum and delicate vulvar skin and vaginal mucosa. *DATA SOURCES*: We made a literature search with Pubmed, Medline and Cochrane database from January 2002 to May 2015 in English language using the key words vulvovaginitis, children, clinical, diagnosis and treatment. *RESULTS*: Vulvovaginitis in girls is usually caused by non-specific factors and hygiene measures, bioyoghurt and avoidance of chemical irritants are generally useful. Weight control if necessary and prevention of voiding dysfunction are effective. Vaginal flora is important in girls and results should be interpreted with clinical features to decide whether an isolated microorganism is part of the normal microflora or is the cause of symptomatic vulvovaginitis. Specific treatment is generally considered in case of a detected pathogen microorganism. Isolation of a sexually transmitted organism requires further investigation. Persistent disease may not always indicate a foreign body but it must be taken into account. Girls and parents are encouraged psychologically in all steps of evaluation, diagnosis and treatment. Probiotics, nanotechnology and petroleum jelly are other important treatment options used in vulvovaginitis. *CONCLUSIONS*: In this review, we present current approach to the presentation and management of vulvovaginitis in childhood. This disorder requires a comprehensive evaluation in all steps of diagnosis, differential diagnosis and treatment.

Bezagio, R. C., Colli, C. M., Romera, L. I., Ferreira, E. C., Falavigna-Guilherme, A. L., and Gomes, M. L. Synergistic effects of fenbendazole and metronidazole against Giardia muris in Swiss mice naturally infected. Parasitol.Res. 2017; 116(3):939-944; PM: 28039497

ABSTRACT: In this study were proposed different protocols for the treatment of mice naturally infected with Giardia muris. Male Swiss mice were divided into seven groups, with five animals each, in a blind, controlled, randomized by drawing lots and once-repeated experiment. Parasite detection and cure control were performed using the Faust method and search by trophozoites in the intestinal mucosa. Clinical parameters (weight, water and feed consumption, elimination of excreta, aspect of the fur and

feces) were also evaluated. All animals were treated with metronidazole (M), fenbendazole (F), and probiotics (P), administered intragastrically, during 7 days. M1, FM1, and F1 groups were treated 1x/day; M3, FM3, and PM3 groups 3x/day; and ST (control group) received only water. After the 5th and 7th days of treatment, the animals in FM1/FM3 and PM3/M3 groups presented, respectively, negative results and remained negative in the following 10 days. Animals in F1 group consumed less water ($p = 0.00010$) compared with FM1/FM3/PM3. The animals in M1 group compared with FM3/M3, F1 compared with M3, and ST compared with FM1/FM3/M3/PM3 consumed a larger amount of feed ($p = 0.00001$). The animals in F1 group compared with FM3/M1/M3/PM3, FM1 compared with FM3, and ST compared with FM3/M1/M3/PM3 eliminated lower volume of excreta ($p = 0.00001$). The results show that the association between F and M potentiates the effects, indicating a synergistic action of these two drugs, and FM1 is the best protocol due to early negativity in the animals, lower concentrations of the drugs, lower risk of toxicity and stress, and less alterations in clinical parameters.

Bhaskar, M. M., Sistla, S., and Kumaravel, S. A case of pyometrocolpos with Bifidobacterium species. Anaerobe. 2017; 44:48-50; PM: 28108392

ABSTRACT: Bifidobacterium species, a normal commensal of the human gastrointestinal tract, female genitourinary tract and vagina is usually considered non-pathogenic and is being used therapeutically as probiotic due to its beneficial effects. However, there are several case reports implicating Bifidobacteria as the causative agent in various infectious conditions. Infections with Bifidobacteria are often ignored or underreported as they are part of the normal gut microbiome. Here we discuss a case of pyometrocolpos with Bifidobacterium species. Clinical outcome of the patient was good after emergency drainage and antibiotic treatment with Cefoperazone sulbactam and Metronidazole.

Bhat, M. I. and Kapila, R. Dietary metabolites derived from gut microbiota: critical modulators of epigenetic changes in mammals. Nutr.Rev. 5-1-2017; 75(5):374-389; PM: 28444216

ABSTRACT: The mammalian gastrointestinal tract harbors trillions of commensal microorganisms, collectively known as the microbiota. The microbiota is a critical source of environmental stimuli and, thus, has a tremendous impact on the health of the host. The microbes within the microbiota regulate homeostasis within the gut, and any alteration in their composition can lead to disorders that include inflammatory bowel disease, allergy, autoimmune disease, diabetes, mental disorders, and cancer. Hence, restoration of the gut flora following changes or imbalance is imperative for the host. The low-molecular-weight compounds and nutrients such as short-chain fatty acids, polyamines, polyphenols, and vitamins produced by microbial metabolism of nondigestible food components in the gut actively participate in various epigenomic mechanisms that reprogram the genome by altering the transcriptional machinery of a cell in response to environmental stimuli. These epigenetic modifications are caused by a set of highly dynamic enzymes, notably histone acetylases, deacetylases, DNA methylases, and demethylases, that are influenced by microbial metabolites and other environmental cues. Recent studies have shown that host expression of histone acetylases and histone deacetylases is important for regulating communication between the intestinal microbiota and the host cells. Histone acetylases and deacetylases influence the molecular expression of genes that affect not only physiological functions but also behavioral shifts that occur via neuroepigenetic

modifications of genes. The underlying molecular mechanisms, however, have yet to be fully elucidated and thus provide a new area of research. The present review provides insights into the current understanding of the microbiota and its association with mammalian epigenomics as well as the interaction of pathogens and probiotics with host epigenetic machinery.

Bhatt, A. P., Redinbo, M. R., and Bultman, S. J. The role of the microbiome in cancer development and therapy. CA Cancer J.Clin. 5-8-2017; PM: 28481406

ABSTRACT: Answer questions and earn CME/CNE The human body harbors enormous numbers of microbiota that influence cancer susceptibility, in part through their prodigious metabolic capacity and their profound influence on immune cell function. Microbial pathogens drive tumorigenesis in 15% to 20% of cancer cases. Even larger numbers of malignancies are associated with an altered composition of commensal microbiota (dysbiosis) based on microbiome studies using metagenomic sequencing. Although association studies cannot distinguish whether changes in microbiota are causes or effects of cancer, a causative role is supported by rigorously controlled preclinical studies using gnotobiotic mouse models colonized with one or more specific bacteria. These studies demonstrate that microbiota can alter cancer susceptibility and progression by diverse mechanisms, such as modulating inflammation, inducing DNA damage, and producing metabolites involved in oncogenesis or tumor suppression. Evidence is emerging that microbiota can be manipulated for improving cancer treatment. By incorporating probiotics as adjuvants for checkpoint immunotherapy or by designing small molecules that target microbial enzymes, microbiota can be harnessed to improve cancer care. CA Cancer J Clin 2017. (c) 2017 American Cancer Society.

Biggs, M. B., Medlock, G. L., Moutinho, T. J., Lees, H. J., Swann, J. R., Kolling, G. L., and Papin, J. A. Systems-level metabolism of the altered Schaedler flora, a complete gut microbiota. ISME.J. 2017; 11(2):426-438; PM: 27824342

ABSTRACT: The altered Schaedler flora (ASF) is a model microbial community with both in vivo and in vitro relevance. Here we provide the first characterization of the ASF community in vitro, independent of a murine host. We compared the functional genetic content of the ASF to wild murine metagenomes and found that the ASF functionally represents wild microbiomes better than random consortia of similar taxonomic composition. We developed a chemically defined medium that supported growth of seven of the eight ASF members. To elucidate the metabolic capabilities of these ASF species-including potential for interactions such as cross-feeding-we performed a spent media screen and analyzed the results through dynamic growth measurements and non-targeted metabolic profiling. We found that cross-feeding is relatively rare (32 of 3570 possible cases), but is enriched between Clostridium ASF356 and Parabacteroides ASF519. We identified many cases of emergent metabolism (856 of 3570 possible cases). These data will inform efforts to understand ASF dynamics and spatial distribution in vivo, to design pre- and probiotics that modulate relative abundances of ASF members, and will be essential for validating computational models of ASF metabolism. Well-characterized, experimentally tractable microbial communities enable research that can translate into more effective microbiome-targeted therapies to improve human health.

Bimbo, F., Bonanno, A., Nocella, G., Viscecchia, R., Nardone, G., De, Devitiis B., and Carlucci, D. Consumers' acceptance and preferences for nutrition-modified and functional dairy products: A systematic review. Appetite. 6-1-2017; 113:141-154; PM: 28235616

ABSTRACT: This systematic literature review collects and summarizes research on consumer acceptance and preferences for nutrition-modified and functional dairy products, to reconcile, and expand upon, the findings of previous studies. We find that female consumers show high acceptance for some functional dairy products, such as yogurt enriched with calcium, fiber and probiotics. Acceptance for functional dairy products increases among consumers with higher diet/health related knowledge, as well as with aging. General interest in health, food-neophobia and perceived self-efficacy seem also to contribute shaping the acceptance for functional dairy products. Furthermore, products with "natural" matches between carriers and ingredients have the highest level of acceptance among consumers. Last, we find that brand familiarity drives consumers with low interest in health to increase their acceptance and preference for health-enhanced dairy products, such as probiotic yogurts, or those with a general function claim.

Bischoff, S. C. [The intestinal microbiome and metabolic diseases : From obesity to diabetes and nonalcoholic steatohepatitis]. Internist (Berl). 2017; 58(5):441-448; PM: 28432400

ABSTRACT: BACKGROUND: The intestinal microbiome consists of about 10 million genes, many of which encode digestive enzymes. This explains why animal and human experiments revealed that the intestinal microbiome adapts to food intake and optimizes energy harvest from food. This function is considered beneficial in states of lack of food, but following overnutrition, it might support the development of obesity. *OBJECTIVES*: The relevance of the intestinal microbiome for the pathogenesis of obesity and associated metabolic diseases such as fatty liver disease and type 2 diabetes mellitus and for the clinical management of such diseases shall be discussed. *MATERIALS AND METHODS*: Recent literature related to the topic has been selected, presented, and discussed with regard to the objectives. *RESULTS*: The intestinal microbiome plays a role in the pathogenesis of both obesity (by increasing the energy absorption from food) and fatty liver disease as well as type 2 diabetes mellitus (via induction of low-grade inflammation following translocation of lipopolysaccharides from the gut and dysregulation of metabolic pathways). *CONCLUSIONS*: The findings might have consequences for diagnosis (identification of risk groups) and therapy (usage of known and novel probiotics or bacterial metabolites) of metabolic diseases.

Blajman, J. E., Astesana, D. M., Zimmermann, J. A., Rossler, E., Scharpen, A. R., Berisvil, A. P., Zbrun, M. V., Soto, L. P., Rosmini, M. R., and Frizzo, L. S. Quantification of FITC-labelled probiotic Lactobacillus salivarius DSPV 001P during gastrointestinal transit in broilers. Benef.Microbes. 2-7-2017; 8(1):55-64; PM: 27903091

ABSTRACT: The knowledge related to the fate of probiotics in the complex environment of the intestinal microbiota in broilers is just beginning to be elucidated; however, it is not yet well understood. A good method to investigate the mechanisms by which probiotics mediate their effects is to mark probiotic bacteria and trace them. The aim of this research was to develop a new method to estimate in vivo fluorescein isothiocyanate (FITC)-labelled Lactobacillus salivarius DSPV 001P counts during passage through the gastrointestinal tract (GIT) of broilers. Forty-five, 1 d old Cobb broilers were used in this

trial. Programmed necropsies were performed 30 min, 6 h, and 12 h after the administration of the probiotic bacterium, and samples of liver, crop, duodenum, caecum, and bursa of fabricius were collected. To determine the spatial and temporal transit of L. salivarius DSPV 001P in broilers, the number of bacteria as well as its respective fluorescent signal produced by FITC were measured. In order to observe the relationship between the variables, a logistic regression analysis was applied. The amount of fluorescence could be used as an indicator of fluorescent probiotic bacteria in the crop and duodenum 30 min after probiotic bacterium supplementation. In addition, the fluorescent signal could be used to estimate bacterial counts in caecum 6 and 12 h after L. salivarius DSPV 001P administration. To the best of our knowledge, this research is the first in vivo trial to employ the bacterial FITC-labelling technique in order to enumerate probiotic bacteria during gastrointestinal transit in broilers.

Bogner, J. [Probiotics - is there evidence for use against antibiotic induced diarrhea, CDAD and travellers diarrhea?]. MMW.Fortschr.Med. 2017; 159(4):49-52; PM: 28265914

No Abstract Available.

Bohora, A. and Kokate, S. Evaluation of the Role of Probiotics in Endodontic Treatment: A Preliminary Study. J.Int.Soc.Prev.Community Dent. 2017; 7(1):46-51; PM: 28316949

ABSTRACT: AIMS AND OBJECTIVES: The principal goal of endodontics is the prevention of periapical infection. Acute and chronic apical periodontitis occur due to the persistence of pathogenic microorganisms such as Enterococcus faecalis and Candida albicans harboring the root canal systems of the teeth. The concept of the use of probiotics in addressing endodontic disease is new and has not been studied adequately. On the basis of the success of probiotics in periodontal treatment, this preliminary work was performed (a) to evaluate the antibacterial efficacy of probiotics against common endodontic pathogens, i.e. E. faecalis and C. albicans, and (b) to evaluate the potential use of probiotic therapy as an additive in endodontic treatment procedures. *MATERIALS AND METHODS*: Two commercial probiotics were selected and evaluated based upon the numbers and concentration of organisms. Pathogenic test organisms were C. albicans (ATCC 10231) and E. faecalis (ATCC 29212). Phase 1 of the study was conducted by agar cup method test to evaluate the antibacterial activity of the selected probiotics against E. faecalis and C. albicans by measuring zones of inhibition (ZOI) in mm. Microorganisms from probiotic samples were isolated following manufacturer's instructions. Pathogenic organisms were set to a 0.1 McFarland standard challenge. Circular wells of 8 mm diameter were punched in each of the poured plates. Appropriately diluted test samples were added to the above-punched wells. The volume of the solution added to each well was 100 mul. The plates were incubated in an upright position at 37 degrees C for 24 hours under aerobic conditions. Post incubation, ZOI was measured (mm). Phase 2 was conducted by mixing 9 ml of 30% poloxamer 407 and de Man, Rogosa and Sharpe (MRS) broth in a test tube with 500 mul of either E. faecalis or C. albicans set at an optical density (OD) of 0.252, together with 500 mul of test probiotic strain, set at a respective OD. Samples were then incubated at 37 degrees C for 48 hours, followed by serial dilutions by 1 ml till 108. This was done to calculate colony forming units (CFU)/ml counts. Controls used were endodontic pathogens in 30% poloxamer with MRS broth without any probiotic group. *RESULTS*: Probiotic groups showed inhibitory activity against E. faecalis by the agar cup method, whereas there was no effect on C. albicans. In the biofilm stage, both the test groups had an

antibacterial effect on pathogenic organisms. *CONCLUSION*: This study suggests that probiotic organisms of the species Lactobacillus and Bifidobacterium are effective for preventing the growth of E. faecalis and C. albicansin vitro. Because probiotics are available in varied compositions and concentrations, further evaluation for their role in treating endodontic infection is suggested and warranted. In addition, the study suggested that poloxamer 407 could be utilized as an ideal delivery vehicle for probiotics for use as a potential endodontic intracanal medicament.

Bohora, A. A. and Kokate, S. R. Good Bugs vs Bad Bugs: Evaluation of Inhibitory Effect of Selected Probiotics against Enterococcus faecalis. J.Contemp.Dent.Pract. 4-1-2017; 18(4):312-316; PM: 28349910

ABSTRACT: INTRODUCTION: The main goal of endodontics is the prevention of apical periodontitis. This is due to the presence of persistent pathogenic microorganisms, such as Enterococcus faecalis, and its ability to directly cause acute and chronic inflammation in the periapical tissues. Lactobacillus has been shown to promote health in the intestines as well as to inhibit the growth of certain problematic oral bacteria. This study explores shifting the established paradigm of endodontic treatment, which has focused on eliminating all bacteria from the canal system and on elimination of the problematic bacteria through introducing probiotics. A preliminary work was performed to evaluate the possible effectiveness of probiotics in preventing the growth of E. faecalis. *MATERIALS AND METHODS*: Two probiotic cultures Lactobacillus plantarum ATCC 8041 and Lactobacillus rhamnosus ATCC 7408 were selected to check their antimicrobial activity against E. faecalis ATCC 29212 by two methods: agar cup/well diffusion method and deferred antagonism test. Agar cup method: A total of 0.5 mL of requisite test pathogen culture was inoculated into 20 mL of molten sterile Mueller and Hinton agar and cooled to 45 +/- 2 degrees C. Circular wells of diameter 10 mm were punched in each of the poured plates. Appropriately diluted test samples were added to the above-punched wells. The plates were incubated upright position at 37 degrees C for 24 hours in aerobic conditions. Postincubation, zone of inhibition was measured. The cell-free supernatant of Lactobacillus species was also evaluated for antimicrobial activity. Deferred antagonism test: The test probiotic strain was standardized to 0.1 optical density (OD) at 600 nm and inoculated in a 1 cm wide diametric streak across the surface of trypticase soy agar + yeast extract + calcium carbonate (TSYCa) agar using a sterile cotton swab. Then, the plate agar containing the test strain was incubated at 37 degrees C for 24 hours under aero-philic condition and then standardized to 0.1 OD at 600 nm for overnight (18 hours, 37 degrees C). A purified culture of indicator strain (pathogen) was streaked at right angles to the line of original producer growth. Postincubation plates were observed for the inhibition zone width of the indicator strain. *RESULTS*: Under the conditions of this study, Lactobacilli had an inhibitory effect on the growth of E. faecalis by agar cup method but not by deferred antagonism test. *CONCLUSION*: This pilot study demonstrated that probiotics show a potential in root canal therapy. *CLINICAL SIGNIFICANCE*: If probioitcs are effective against end-odontic pathogens, they can be potentially used as intracanal medicaments. This will be a novel concept of introducing bac-teriotherapy in endodontics and replacing pathogenic bacteria by healthy bacteria, normal flora.

Bomko, T. V., Nosalskaya, T. N., Kabluchko, T. V., Lisnyak, Y. V., and Martynov, A. V. Immunotropic aspect of the Bacillus coagulans probiotic action. J.Pharm.Pharmacol. 4-11-2017; PM: 28397382

ABSTRACT: OBJECTIVES: Currently, probiotics are increasingly used as the alternative to antibiotics as well as the preventive measures in humans. In particular, probiotics occupy a key position in the treatment of antibiotics-associated intestinal dysbiosis. A spore-forming microorganism lactobacillus Bacillus coagulans is one of the most promising probiotics. However, some of its pharmacological effects remain poorly understood. This study was aimed at investigation of the effect of B. coagulans (Laktovit Forte) on the intestinal dysbiosis syndrome in mice caused by streptomycin against the background of cyclophosphamide-induced cellular immunodeficiency. *METHODS*: Pharmacological method: mouse model in vivo with immunodeficiency caused by cyclophosphamide. *KEY FINDINGS*: In mice with colitis caused by streptomycin treatment, the administration of B. coagulans (Laktovit Forte medicinal product) resulted in an antidiarrhoeal effect, normalisation of gastrointestinal motility and prevention of the animals' weight loss. Given the cyclophosphamide-induced immunosuppression and streptomycin-associated diarrhoea, the immunity was completely restored only under the action of B. coagulans. *CONCLUSIONS*: According to all parameters, B. coagulans has been proved to be more effective as compared to the Linex Forte reference product containing lacto- and bifidobacteria.

Bonacina, J., Suarez, N., Hormigo, R., Fadda, S., Lechner, M., and Saavedra, L. A genomic view of food-related and probiotic Enterococcus strains. DNA Res. 2-1-2017; 24(1):11-24; PM: 27773878

ABSTRACT: The study of enterococcal genomes has grown considerably in recent years. While special attention is paid to comparative genomic analysis among clinical relevant isolates, in this study we performed an exhaustive comparative analysis of enterococcal genomes of food origin and/or with potential to be used as probiotics. Beyond common genetic features, we especially aimed to identify those that are specific to enterococcal strains isolated from a certain food-related source as well as features present in a species-specific manner. Thus, the genome sequences of 25 Enterococcus strains, from 7 different species, were examined and compared. Their phylogenetic relationship was reconstructed based on orthologous proteins and whole genomes. Likewise, markers associated with a successful colonization (bacteriocin genes and genomic islands) and genome plasticity (phages and clustered regularly interspaced short palindromic repeats) were investigated for lifestyle specific genetic features. At the same time, a search for antibiotic resistance genes was carried out, since they are of big concern in the food industry. Finally, it was possible to locate 1617 FIGfam families as a core proteome universally present among the genera and to determine that most of the accessory genes code for hypothetical proteins, providing reasonable hints to support their functional characterization.

Bond, D. M., Morris, J. M., and Nassar, N. Study protocol: evaluation of the probiotic Lactobacillus Fermentum CECT5716 for the prevention of mastitis in breastfeeding women: a randomised controlled trial. BMC.Pregnancy.Childbirth. 5-19-2017; 17(1):148; PM: 28525984

ABSTRACT: BACKGROUND: Mastitis and accompanying pain have been associated with the cessation of breastfeeding. Mastitis is an inflammatory condition of the breast and may be a result of decreased immunity and a lowered resistance to infection. Mastitis affects up to one in five breastfeeding women with most episodes occurring in the first 6-

8 weeks postpartum. Antibiotics are often used in the treatment of mastitis, but have not been popular or proven effective as a preventative agent. The WHO has highlighted significant concerns relating to adverse harms of antibiotic use with the production of antibiotic-resistant strains of disease organisms. Increasing research suggests that specific probiotic bacteria possess significant anti-inflammatory properties and supports their potential use as immunomodulatory agents. While animal studies have shown promising results in the use of probiotics for preventing mastitis, their use in human trials has had limited investigation. The aim of this study is to evaluate the effectiveness of oral probiotics for the prevention of mastitis in breastfeeding women. *METHODS*: APProve (Can Probiotics Improve Breastfeeding Outcomes?) is a double-blind randomized controlled trial designed to assess outcomes between breastfeeding women ingesting a probiotic versus a placebo daily for 8 weeks following birth. A total of 600 women (300 to each arm) who intend to breastfeed will be randomized after the birth of a term, healthy infant. Daily and weekly surveys for 8 weeks and follow-up surveys at 2, 6 and 12 months after birth will assess the primary outcome of mastitis in the first 8 weeks following birth as well as secondary maternal outcomes of breastfeeding duration (total/partial), antibiotic use, maternal health and well-being, and treatment compliance; and infant outcomes including gastroenteritis, infant health and well-being and growth and development. The acceptability and compliance using a novel mobile phone application system will also be evaluated. *DISCUSSION*: There is an urgent need to explore safe and effective alternatives for preventing mastitis in breastfeeding women. This trial seeks to provide evidence for such an alternative in the form of probiotics, which may also increase breastfeeding duration, providing long-term health, cognitive and developmental benefits for children. Decreased antibiotic usage also benefits the community and health system. *TRIAL REGISTRATION*: Australian New Zealand Clinical Trials Registry: ACTRN12615000923561 . Date of registration: 4th September, 2015, retrospectively registered.

Bordalo, Tonucci L., Dos Santos, K. M., De Luces Fortes Ferreira CL, Ribeiro, S. M., De Oliveira, L. L., and Martino, H. S. Gut microbiota and probiotics: Focus on diabetes mellitus. Crit Rev.Food Sci.Nutr. 7-24-2017; 57(11):2296-2309; PM: 26499995

ABSTRACT: The characterization of gut microbiota has become an important area of research in several clinical conditions, including type 2 diabetes (T2DM). Changes in the composition and/or metabolic activity of the gut microbiota can contribute to human health. Thus, this review discusses the effects of probiotics and gut microbiota on metabolic control in these individuals. Relevant studies were obtained from electronic databases such as PubMed/Medline and ISI Web of Science. The main probiotics used in these studies belonged to the genera Lactobacillus and Bifidobacterium. The authors found seven randomized placebo-controlled clinical trials and 13 experimental studies directly related to the effect of probiotics on metabolic control in the context of T2DM. The hypothesis that gut microbiota plays a role in the development of diabetes indicates an important beginning, and the potential of probiotics to prevent and reduce the severity of T2DM is better observed in animal studies. In clinical trials, the use of probiotics in glycemic control presented conflicting results, and only few studies have attempted to evaluate factors that justify metabolic changes, such as markers of oxidative stress, inflammation, and incretins. Thus, further research is needed to assess the effects of probiotics in the metabolism of diabetic individuals, as well as the main mechanisms involved in this complex relationship.

Bosnea, L. A., Moschakis, T., and Biliaderis, C. G. Microencapsulated cells of Lactobacillus paracasei subsp. paracasei in biopolymer complex coacervates and their function in a yogurt matrix. Food Funct. 2-22-2017; 8(2):554-562; PM: 27935607

ABSTRACT: L. paracasei subsp. paracasei E6 cells were encapsulated by complex coacervation using whey protein isolate (WPI) and gum arabic and introduced in stirred yogurts after fermentation. For comparison purposes, yogurts without addition of L. paracasei and yogurts with free cells of L. paracasei were produced. The survival of free and microencapsulated L. paracasei cells was evaluated during storage of the yogurts for 45 days at 4 degrees C. In addition, yogurts were exposed to simulated gastric juice and the reduction in viable numbers of L. paracasei cells was assessed. The effect of complex coacervates' addition on the rheological properties of yogurts was also evaluated. Yogurts containing encapsulated L. paracasei cells showed a slightly improved cell survival (</=0.22 log CFU g-1 reduction) during storage when compared to yogurts containing free cells (</=0.64 log CFU g-1 reduction). Moreover, the microencapsulated L. paracasei cells exhibited greater survival compared to free cells upon exposure of the yogurt samples to simulated gastric juice (pH 2.0) for 3 h. Finally, the incorporation of complex coacervates did not significantly affect the rheological properties of yogurts especially when added at concentrations less than 10% w/w. Consequently, the inclusion of microencapsulated bacteria by complex coacervation in yogurts, could become an effective vehicle for successful delivery of probiotics to the gut, and hence contributing to the improvement of the gastrointestinal tract health, without altering the texture of the product.

Bozzetto, S., Pirillo, P., Carraro, S., Berardi, M., Cesca, L., Stocchero, M., Giordano, G., Zanconato, S., and Baraldi, E. Metabolomic profile of children with recurrent respiratory infections. Pharmacol.Res. 2017; 115:162-167; PM: 27888158

ABSTRACT: Recurrent respiratory infections (RRI) represent a widespread condition which has a severe social and economic impact. Immunostimulants are used for their prevention. It is crucial to better characterize children with RRI to refine their diagnosis and identify effective personalized prevention strategies. Metabolomics is a high-dimensional biological method that can be used for hypothesis-free biomarker profiling, examining a large number of metabolites in a given sample using spectroscopic techniques. Multivariate statistical data analysis then enables us to infer which metabolic information is relevant to the biological characterization of a given physiological or pathological condition. This can lead to the emergence of new, sometimes unexpected metabolites, and hitherto unknown metabolic pathways, enabling the formulation of new pathogenetic hypotheses, and the identification of new therapeutic targets. The aim of our pilot study was to apply mass-spectrometry-based metabolomics to the analysis of urine samples from children with RRI, comparing these children's biochemical metabolic profiles with those of healthy peers. We also compared the RRI children's and healthy controls' metabolomic urinary profiles after the former had received pidotimod treatment for 3 months to see whether this immunostimulant was associated with biochemical changes in the RRI children's metabolic profile. 13 children (age range 3-6 yeas) with RRI and 15 matched per age healthy peers with no history of respiratory diseases or allergies were enrolled. Their metabolomic urine samples were compared before and after the RRI children had been treated with pidotimod for a period of 3 months. Metabolomic analyses on the urine samples were done using mass spectrometry combined with ultra-performance liquid chromatography (UPLC-MS). The resulting spectroscopic data then underwent multivariate statistical analysis and the most

relevant variables characterizing the two groups were identified. Data modeling with post-transformation of PLS2-Discriminant Analysis (ptPLS2-DA) generated a robust model capable of discriminating the urine samples from children with RRI from those of healthy controls (R2=0.92,Q2CV7-fold=0.75, p-value<0.001). The dataset included 1502 time per mass variables, and 138 of them characterized the difference between the two groups. Thirty-five of these distinctive 138 variables persisted in the profiles of the children with RRI after pidotimod treatment. Metabolomics can discriminate children with RRI from healthy controls, suggesting that the former have a dysregulated metabolic profile. Among the variables characterizing children with RRI there are metabolites that may reflect the presence of a different microbiome. After pidotimod treatment, the metabolic profile of the children with RRI was no longer very different from that of the healthy controls, except for the persistence of some microbiome-related variables. We surmise that pidotimod partially "restores" the altered metabolic profile of children with RRI, without modifying the metabolites related to the composition of the gut microbiota. In the light of these results, we hypothesize a potential synergic effect of the combined use of immunostimulants and probiotics for the purpose of prevention in children with RRI.

Brandi, G., De, Lorenzo S., Candela, M., Pantaleo, M. A., Bellentani, S., Tovoli, F., Saccoccio, G., and Biasco, G. Microbiota, NASH, HCC and the potential role of probiotics. Carcinogenesis. 3-1-2017; 38(3):231-240; PM: 28426878

ABSTRACT: Hepatocellular carcinoma (HCC) accounts for the majority of primary liver cancers. Clearly identifiable risk factors are lacking in up to 30% of HCC patients and most of these cases are attributed to non-alcoholic fatty liver disease (NAFLD) and non-alcoholic steatohepatitis (NASH). Beyond the known risk factors for NAFLD, the intestinal microbiota, in particular dysbiosis (defined as any change in the composition of the microbiota commonly found in healthy conditions) is emerging as a new factor promoting the development of chronic liver diseases and HCC. Intestinal microbes produce a large array of bioactive molecules from mainly dietary compounds, establishing an intense microbiota-host transgenomic metabolism with a major impact on physiological and pathological conditions. A better knowledge of these 'new' pathways could help unravel the pathogenesis of HCC in NAFLD to devise new prevention strategies. Currently unsettled issues include the relative role of a 'negative microbiota' (in addition to the other known risk factors for NASH) and the putative prevention of NAFLD through modulation of the gut microbiota.

Brignardello-Petersen, R. Probiotics as adjuvant to scaling and root planing seem to improve periodontal parameters after 3 months of treatment. J.Am.Dent.Assoc. 2017; 148(4):e10; PM: 28193475

No Abstract Available.

Brignone, D., Radmann, P., Behr, J., and Vogel, R. F. Boosting the growth of the probiotic strain Lactobacillus paracasei ssp. paracasei F19. Arch.Microbiol. 3-18-2017; PM: 28315928

ABSTRACT: Single so-called booster substances were added to the fermentation medium of the probiotic strain Lactobacillus (L.) paracasei ssp. paracasei F19 to enhance its growth. A wide screening was carried out in microtiter plates and a statistical analysis of the growth parameters was performed. CFU counts were used to correlate the increase

in OD590nm with the increase in viable cell number. Sodium ascorbate, sodium pyruvate, manganese sulfate and cysteine had a remarkable boosting effect on the growth of L. paracasei F19. Three of the boosters increased the growth rate of the strain and led to a higher cell density and biomass yield in laboratory conditions. Cysteine significantly shortened the lag phase, therefore reducing the fermentation times. The boosters were tested on four additional Lactobacillus species and their growth boosting activity was retained. To investigate whether the growth boosters could improve the tolerance of L. paracasei F19 to the adverse condition in the GI tract, additional tests were performed. Sodium ascorbate and sodium pyruvate exerted a certain antioxidant effect, as they improved the tolerance of L. paracasei F19 to H2O2. Sodium ascorbate enhanced the growth of the strain in low pH.

Briskey, D., Tucker, P., Johnson, D. W., and Coombes, J. S. The role of the gastrointestinal tract and microbiota on uremic toxins and chronic kidney disease development. Clin.Exp.Nephrol. 2017; 21(1):7-15; PM: 26965149

ABSTRACT: It is well-established that uremic toxins are positively correlated with the risk of developing chronic kidney disease and cardiovascular disease. In addition, emerging data suggest that gut bacteria exert an influence over both the production of uremic toxins and the development of chronic kidney disease. As such, modifying the gut microbiota may have the potential as a treatment for chronic kidney disease. This is supported by data that suggest that rescuing microbiota dysbiosis may: reduce uremic toxin production; prevent toxins and pathogens from crossing the intestinal barrier; and, reduce gastrointestinal tract transit time allowing nutrients to reach the microbiota in the distal portion of the gastrointestinal tract. Despite emerging literature, the gut-kidney axis has yet to be fully explored. A special focus should be placed on examining clinically translatable strategies that might encourage improvements to the microbiome, thereby potentially reducing the risk of the development of chronic kidney disease. This review aims to present an overview of literature linking changes to the gastrointestinal tract with microbiota dysbiosis and the development and progression of chronic kidney disease.

Bron, P. A., Kleerebezem, M., Brummer, R. J., Cani, P. D., Mercenier, A., MacDonald, T. T., Garcia-Rodenas, C. L., and Wells, J. M. Can probiotics modulate human disease by impacting intestinal barrier function? Br.J.Nutr. 2017; 117(1):93-107; PM: 28102115

ABSTRACT: Intestinal barrier integrity is a prerequisite for homeostasis of mucosal function, which is balanced to maximise absorptive capacity, while maintaining efficient defensive reactions against chemical and microbial challenges. Evidence is mounting that disruption of epithelial barrier integrity is one of the major aetiological factors associated with several gastrointestinal diseases, including infection by pathogens, obesity and diabetes, necrotising enterocolitis, irritable bowel syndrome and inflammatory bowel disease. The notion that specific probiotic bacterial strains can affect barrier integrity fuelled research in which in vitro cell lines, animal models and clinical trials are used to assess whether probiotics can revert the diseased state back to homeostasis and health. This review catalogues and categorises the lines of evidence available in literature for the role of probiotics in epithelial integrity and, consequently, their beneficial effect for the reduction of gastrointestinal disease symptoms.

Brunkwall, L. and Orho-Melander, M. The gut microbiome as a target for prevention and treatment of hyperglycaemia in type 2 diabetes: from current human evidence to future possibilities. Diabetologia. 2017; 60(6):943-951; PM: 28434033

ABSTRACT: The totality of microbial genomes in the gut exceeds the size of the human genome, having around 500-fold more genes that importantly complement our coding potential. Microbial genes are essential for key metabolic processes, such as the breakdown of indigestible dietary fibres to short-chain fatty acids, biosynthesis of amino acids and vitamins, and production of neurotransmitters and hormones. During the last decade, evidence has accumulated to support a role for gut microbiota (analysed from faecal samples) in glycaemic control and type 2 diabetes. Mechanistic studies in mice support a causal role for gut microbiota in metabolic diseases, although human data favouring causality is insufficient. As it may be challenging to sort the human evidence from the large number of animal studies in the field, there is a need to provide a review of human studies. Thus, the aim of this review is to cover the current and future possibilities and challenges of using the gut microbiota, with its capacity to be modified, in the development of preventive and treatment strategies for hyperglycaemia and type 2 diabetes in humans. We discuss what is known about the composition and functionality of human gut microbiota in type 2 diabetes and summarise recent evidence of current treatment strategies that involve, or are based on, modification of gut microbiota (diet, probiotics, metformin and bariatric surgery). We go on to review some potential future gut-based glucose-lowering approaches involving microbiota, including the development of personalised nutrition and probiotic approaches, identification of therapeutic components of probiotics, targeted delivery of propionate in the proximal colon, targeted delivery of metformin in the lower gut, faecal microbiota transplantation, and the incorporation of genetically modified bacteria that express therapeutic factors into microbiota. Finally, future avenues and challenges for understanding the interplay between human nutrition, genetics and microbial genetics, and the need for integration of human multi-omic data (such as genetics, transcriptomics, epigenetics, proteomics and metabolomics) with microbiome data (such as strain-level variation, transcriptomics, proteomics and metabolomics) to make personalised treatments a successful future reality are discussed.

Bunesova, V., Killer, J., Javurkova, B., Vlkova, E., Tejnecky, V., Musilova, S., and Rada, V. Diversity of the subspecies Bifidobacterium animalis subsp. lactis. Anaerobe. 2017; 44:40-47; PM: 28108391

ABSTRACT: Strains of Bifidobacterium animalis subsp. lactis are well-known health-promoting probiotics used commercially. B. animalis subsp. lactis has been isolated from different sources, and little is known about animal isolates of this taxon. The aim of this study was to examine the genotypic and phenotypic diversity between B. animalis subsp. lactis strains different animal hosts including Cameroon sheep, Barbary sheep, okapi, mouflon, German shepard and to compare to BB12, food isolates and the collection strain DSM 10140. Ten strains of B. animalis subsp. lactis from different sources were characterised by phenotyping, fingerprinting, and multilocus sequence typing (MLST). Regardless of origin, MLST and phylogenetic analyses revealed a close relationship between strains of B. animalis subsp. lactis with commercial and animal origin with the exception of isolates from ovine cheese, mouflon and German Shepard dog. Moreover, isolates from dog and mouflon showed significant differences in fermentation profiles and peptide mass fingerprints (MALDI-TOF). Results indicated phenotypic and genotypic diversity among strains of B. animalis subsp. lactis.

Burke, D. G., Fouhy, F., Harrison, M. J., Rea, M. C., Cotter, P. D., O'Sullivan, O., Stanton, C., Hill, C., Shanahan, F., Plant, B. J., and Ross, R. P. The altered gut microbiota in adults with cystic fibrosis. BMC.Microbiol. 3-9-2017; 17(1):58; PM: 28279152

ABSTRACT: BACKGROUND: Cystic Fibrosis (CF) is an autosomal recessive disease that affects the function of a number of organs, principally the lungs, but also the gastrointestinal tract. The manifestations of cystic fibrosis transmembrane conductance regulator (CFTR) dysfunction in the gastrointestinal tract, as well as frequent antibiotic exposure, undoubtedly disrupts the gut microbiota. To analyse the effects of CF and its management on the microbiome, we compared the gut microbiota of 43 individuals with CF during a period of stability, to that of 69 non-CF controls using 454-pyrosequencing of the 16S rRNA gene. The impact of clinical parameters, including antibiotic therapy, on the results was also assessed. *RESULTS*: The CF-associated microbiome had reduced microbial diversity, an increase in Firmicutes and a reduction in Bacteroidetes compared to the non-CF controls. While the greatest number of differences in taxonomic abundances of the intestinal microbiota was observed between individuals with CF and the healthy controls, gut microbiota differences were also reported between people with CF when grouped by clinical parameters including % predicted FEV1 (measure of lung dysfunction) and the number of intravenous (IV) antibiotic courses in the previous 12 months. Notably, CF individuals presenting with severe lung dysfunction (% predicted FEV1 </= 40%) had significantly ($p < 0.05$) reduced gut microbiota diversity relative to those presenting with mild or moderate dysfunction. A significant negative correlation (-0.383, Simpson's Diversity Index) was also observed between the number of IV antibiotic courses and gut microbiota diversity. *CONCLUSIONS*: This is one of the largest single-centre studies on gut microbiota in stable adults with CF and demonstrates the significantly altered gut microbiota, including reduced microbial diversity seen in CF patients compared to healthy controls. The data show the impact that CF and it's management have on gut microbiota, presenting the opportunity to develop CF specific probiotics to minimise microbiota alterations.

Burns, P., Alard, J., Hrdy, J., Boutillier, D., Paez, R., Reinheimer, J., Pot, B., Vinderola, G., and Grangette, C. Spray-drying process preserves the protective capacity of a breast milk-derived Bifidobacterium lactis strain on acute and chronic colitis in mice. Sci.Rep. 2-24-2017; 7:43211; PM: 28233848

ABSTRACT: Gut microbiota dysbiosis plays a central role in the development and perpetuation of chronic inflammation in inflammatory bowel disease (IBD) and therefore is key target for interventions with high quality and functional probiotics. The local production of stable probiotic formulations at limited cost is considered an advantage as it reduces transportation cost and time, thereby increasing the effective period at the consumer side. In the present study, we compared the anti-inflammatory capacities of the Bifidobacterium animalis subsp. lactis (B. lactis) INL1, a probiotic strain isolated in Argentina from human breast milk, with the commercial strain B. animalis subsp. lactis BB12. The impact of spray-drying, a low-cost alternative of bacterial dehydration, on the functionality of both bifidobacteria was also investigated. We showed for both bacteria that the spray-drying process did not impact on bacterial survival nor on their protective capacities against acute and chronic colitis in mice, opening future perspectives for the use of strain INL1 in populations with IBD.

Bustamante, M., Oomah, B. D., Rubilar, M., and Shene, C. Effective Lactobacillus plantarum and Bifidobacterium infantis encapsulation with chia seed (Salvia hispanica L.) and flaxseed (Linum usitatissimum L.) mucilage and soluble protein by spray drying. Food Chem. 2-1-2017; 216:97-105; PM: 27596397

ABSTRACT: Mucilage (M) and soluble protein (SP) extracted from chia seed and flaxseed were used as encapsulating material for two probiotic bacteria: Bifidobacterium infantis and Lactobacillus plantarum by spray drying. Probiotic survival and viability after spray drying and during storage were evaluated. B. infantis and L. plantarum displayed high survival (98%) after encapsulation with mixtures of maltodextrin (MD) combined with M and SP from flaxseed (MD:FM.

Caillard, R. and Lapointe, N. In vitro gastric survival of commercially available probiotic strains and oral dosage forms. Int.J.Pharm. 3-15-2017; 519(1-2):125-127; PM: 28093323

ABSTRACT: Although the intestinal microbial community is still incompletely understood, there is strong evidence of the benefits of using probiotics to address some medical states or conditions. As a result, the probiotics oral supplements market has exploded during the last few years. However, while their sensitivity to gastric juices, acidic pH and bile is well known, most of these oral forms would not guarantee any survival of the strains in such conditions. In this work, we have studied the resistance to simulated gastric juices of several commercially available probiotics products. These included sixteen strains and ten oral forms such as enteric/non-enteric capsules/tablets and microencapsulated strains. Results demonstrated that all tested strains showed high sensitivity to acidic conditions and suggested that most of these microorganisms would not show any viability when immersed in the stomach at fasting. Most probiotics oral forms did not provide any protection to strains, unless these forms presented strong enteric protection. Consequently, the efficacy of non-enteric products to fully provide to the patient the benefits related to the consumption of probiotics supplement would be strongly questionable. This study underlines the chasm between the current opinion about probiotics protection needs and the products proposed by many companies in the dietary supplements area.

Calatayud, G. A. and Suarez, J. E. A new contribution to the history of probiotics. Benef.Microbes. 4-26-2017; 8(2):323-325; PM: 28403650

No Abstract Available.

Calderini, E., Celebioglu, H. U., Villarroel, J., Jacobsen, S., Svensson, B., and Pessione, E. Comparative proteomics of oxidative stress response of Lactobacillus acidophilus NCFM reveals effects on DNA repair and cysteine de novo synthesis. Proteomics. 2017; 17(5); PM: 28045221

ABSTRACT: Probiotic cultures encounter oxidative conditions during manufacturing, yet protein abundance changes induced by such stress have not been characterized for some of the most common probiotics and starters. This comparative proteomics investigation focuses on the response by Lactobacillus acidophilus NCFM to H2 O2, simulating an oxidative environment. Bacterial growth was monitored by BioScreen and batch cultures were harvested at exponential phase for protein profiling of stress

responses by 2D gel based comparative proteomics. Proteins identified in 19 of 21 spots changing in abundance due to H2 O2 were typically related to carbohydrate and energy metabolism, cysteine biosynthesis, and stress. In particular, increased cysteine synthase activity may accumulate a cysteine pool relevant for protein stability, enzyme catalysis, and the disulfide-reducing pathway. The stress response further included elevated abundance of biomolecules reducing damage such as enzymes from DNA repair pathways and metabolic enzymes with active site cysteine residues. By contrast, a protein-refolding chaperone showed reduced abundance, possibly reflecting severe oxidative protein destruction that was not overcome by refolding. The proteome analysis provides novel insight into resistance mechanisms in lactic acid bacteria against reactive oxygen species and constitutes a valuable starting point for improving industrial processes, food design, or strain engineering preserving microorganism viability.

Callewaert, C., Lambert, J., and Van de, Wiele T. Towards a bacterial treatment for armpit malodour. Exp.Dermatol. 2017; 26(5):388-391; PM: 27892611

ABSTRACT: Axillary malodour is a frustrating condition for many people. It can lead to significant discomforts and various psychological effects. The underarm microbiome plays a major role in axillary malodour formation. Not only the bacteria on the epidermis, but also and especially those living in the sweat glands, sweat pores and hair follicles play a pivotal role in malodour development. To treat underarm malodour, this viewpoint article envisions a bacterial treatment. Replacing the autochthonous malodour-causing microbiome with a non-odour-causing microbiome, through an armpit bacterial transplantation or direct application of probiotics/non-odour-causing bacteria, could resolve the condition. Selective steering of the microbiome with prebiotics, biochemicals or plant extracts can likewise greatly help in improving the underarm odour. Elimination/inhibition of the "bad bugs" and application/stimulation of the "good bugs" will be part of the future treatment for axillary body odour.

Camilleri, M., Park, S. Y., Scarpato, E., and Staiano, A. Exploring hypotheses and rationale for causes of infantile colic. Neurogastroenterol.Motil. 2017; 29(2); PM: 27647578

ABSTRACT: BACKGROUND: Infantile colic is a frequent problem in neonates and infants. This review addresses current management including the results for nutrient modifications; soy-based formulas; and prebiotics, probiotics, and synbiotics. *PURPOSE*: Given the evidence that there is still an unmet clinical need, as current treatments are incompletely efficacious, we have examined the evidence around three hypothetical mechanisms that could potentially be involved in etiopathogenesis of infantile colic: immaturity of bile acid mechanisms that alter intraluminal and absorptive mechanisms, immaturity in motility and alterations in the microbiome. Understanding these potential mechanisms may lead to the introduction of diagnostic procedures that should enhance the selection or individualization of therapy for infantile colic.

Campagnolo, N., Johnston, S., Collatz, A., Staines, D., and Marshall-Gradisnik, S. Dietary and nutrition interventions for the therapeutic treatment of chronic fatigue syndrome/myalgic encephalomyelitis: a systematic review. J.Hum.Nutr.Diet. 2017; 30(3):247-259; PM: 28111818

ABSTRACT: BACKGROUND: Chronic fatigue syndrome/myalgic encephalomyelitis

(CFS/ME) is characterised by unexplained fatigue for at least 6 months accompanied by a diverse but consistent set of symptoms. Diet modification and nutritional supplements could be used to improve patient outcomes, such fatigue and quality of life. We reviewed and discussed the evidence for nutritional interventions that may assist in alleviating symptoms of CFS/ME. *METHODS*: Medline, Cinahl and Scopus were systematically searched from 1994 to May 2016. All studies on nutrition intervention were included where CFS/ME patients modified their diet or supplemented their habitual diet on patient-centred outcomes (fatigue, quality of life, physical activity and/or psychological wellbeing). *RESULTS*: Seventeen studies were included that meet the inclusion criteria. Of these, 14 different interventions were investigated on study outcomes. Many studies did not show therapeutic benefit on CFS/ME. Improvements in fatigue were observed for nicotinamide adenine dinucleotide hydride (NADH), probiotics, high cocoa polyphenol rich chocolate, and a combination of NADH and coenzyme Q10. *CONCLUSIONS*: This review identified insufficient evidence for the use of nutritional supplements and elimination or modified diets to relieve CFS/ME symptoms. Studies were limited by the number of studies investigating the interventions, small sample sizes, study duration, variety of instruments used, and studies not reporting dietary intake method. Further research is warranted in homogeneous CFS/ME populations.

Carasi, P., Racedo, S. M., Jacquot, C., Elie, A. M., Serradell, M. L., and Urdaci, M. C. Enterococcus durans EP1 a Promising Anti-inflammatory Probiotic Able to Stimulate sIgA and to Increase Faecalibacterium prausnitzii Abundance. Front Immunol. 2017; 8:88; PM: 28239378

ABSTRACT: Enterococcus species, principally Enterococcus faecium are used as probiotics since a long time with preference in animal applications but safety considerations were updated and also new uses as probiotics can be envisaged. Fifteen Enterococcus strains isolated from different foods were identified and analyzed for virulence factors and antibiotic resistance. Three Enterococcus durans strains were selected to study their immunomodulatory properties on PBMC and Caco2 cells. Two strains presented a profile toward a mild inflammatory Th1 response considering TNF-alpha/IL-10 and IL-1beta/IL-10 cytokines ratios. The third strain EP1, presented an anti-inflammatory potential and was selected for in vivo studies. In mice, the strain was well tolerated and did not cause any adverse effects. EP1 administration increased the amount of IgA+ cells in mesenteric lymph node (MLN) after 7 days of administration. In fecal samples, the IgA content increased gradually and significantly from day 7 to day 21 in treated group. Additionally, IL-17, IL-6, IL-1beta, IFN-gamma, and CXCL1 gene expression significantly decreased on day 21 in Peyer's patches and IL-17 decreased in MLN. Mice treated with the probiotic showed significant lower mRNA levels of pro-inflammatory cytokines and mucins in the ileum at day 7 while their expression was normalized at day 21. Colonic expression of il-1beta, il6, and mucins remain diminished at day 21. Ileum and colon explants from treated mice stimulated in vitro with LPS showed a significant reduction in IL-6 and an increase in IL-10 secretion suggesting an in vivo protective effect of the probiotic treatment against a proinflammatory stimulus. Interestingly, analysis of feces microbiota demonstrated that EP1 administration increase the amount of Faecalibacterium prausnitzii, a butyrate-producing bacteria, which is known for its anti-inflammatory effects. In conclusion, we demonstrated that EP1 strain is a strong sIgA inducer and possess mucosal anti-inflammatory properties. This strain also modulates gut microbiota increasing Faecalibacterium prausnitzii, a functionally important bacterium. Thus, E. durans EP1 is not only a good candidate to increases F.

prausnitzii in some cases of dysbiosis but can also be interesting in gut inflammatory disorders therapy.

Caretto, M., Giannini, A., Russo, E., and Simoncini, T. Preventing urinary tract infections after menopause without antibiotics. Maturitas. 2017; 99:43-46; PM: 28364867¶

ABSTRACT: Urinary tract infections (UTIs) are the most common bacterial infections in women, and increase in incidence after the menopause. It is important to uncover underlying abnormalities or modifiable risk factors. Several risk factors for recurrent UTIs have been identified, including the frequency of sexual intercourse, spermicide use and abnormal pelvic anatomy. In postmenopausal women UTIs often accompany the symptoms and signs of the genitourinary syndrome of menopause (GSM). Antimicrobial prophylaxis has been demonstrated to be effective in reducing the risk of recurrent UTIs in women, but this may lead to drug resistance of both the causative microorganisms and the indigenous flora. The increasing prevalence of Escherichia coli (the most prevalent uropathogen) that is resistant to antimicrobial agents has stimulated interest in novel non-antibiotic methods for the prevention of UTIs. Evidence shows that topical estrogens normalize vaginal flora and greatly reduce the risk of UTIs. The use of intravaginal estrogens may be reasonable in postmenopausal women not taking oral estrogens. A number of other strategies have been used to prevent recurrent UTIs: probiotics, cranberry juice and d-mannose have been studied. Oral immunostimulants, vaginal vaccines and bladder instillations with hyaluronic acid and chondroitin sulfate are newer strategies proposed to improve urinary symptoms and quality of life. This review provides an overview of UTIs' prophylaxis without antibiotics, focusing on a practical clinical approach to women with UTIs.

Carmona-Sanchez, R., Gomez-Escudero, O., Zavala-Solares, M., Bielsa-Fernandez, M. V., Coss-Adame, E., Hernandez-Guerrero, A. I., Huerta-Iga, F., Icaza-Chavez, M. E., Lira-Pedrin, M. A., Lizarraga-Lopez, J. A., Lopez-Colombo, A., Noble-Lugo, A., Perez-Manauta, J., Rana-Garibay, R. H., Remes-Troche, J. M., Tamayo, J. L., Uscanga, L. F., Zamarripa-Dorsey, F., Valdovinos Diaz, M. A., and Velarde-Ruiz Velasco, J. A. Mexican consensus on dyspepsia. Rev.Gastroenterol.Mex. 4-13-2017; PM: 28413079

ABSTRACT: Since the publication of the 2007 dyspepsia guidelines of the Asociacion Mexicana de Gastroenterologia, there have been significant advances in the knowledge of this disease. A systematic search of the literature in PubMed (01/2007 to 06/2016) was carried out to review and update the 2007 guidelines and to provide new evidence-based recommendations. All high-quality articles in Spanish and English were included. Statements were formulated and voted upon using the Delphi method. The level of evidence and strength of recommendation of each statement were established according to the GRADE system. Thirty-one statements were formulated, voted upon, and graded. New definition, classification, epidemiology, and pathophysiology data were provided and include the following information: Endoscopy should be carried out in cases of uninvestigated dyspepsia when there are alarm symptoms or no response to treatment. Gastric and duodenal biopsies can confirm Helicobacter pylori infection and rule out celiac disease, respectively. Establishing a strong doctor-patient relationship, as well as dietary and lifestyle changes, are useful initial measures. H2-blockers, proton-pump inhibitors, prokinetics, and antidepressants are effective pharmacologic therapies. H.pylori eradication may be effective in a subgroup of patients. There is no evidence

that complementary and alternative therapies are beneficial, with the exception of Iberogast and rikkunshito, nor is there evidence on the usefulness of prebiotics, probiotics, or psychologic therapies. The new consensus statements on dyspepsia provide guidelines based on up-to-date evidence. A discussion, level of evidence, and strength of recommendation are presented for each statement.

Caroff, D. A., Yokoe, D. S., and Klompas, M. Evolving insights into the epidemiology and control of Clostridium difficile in hospitals. Clin.Infect.Dis. 5-17-2017; PM: 28520953

ABSTRACT: Typing studies suggest most cases of hospital-onset Clostridium difficile infection are unrelated to other cases of active disease in the hospital. New cases may instead be due to transmissions from asymptomatic carriers or progression of latent C.difficile present-on-admission to active infection. Direct exposure to antibiotics remains the primary risk factor for C.difficile infection but ward-level antibiotic use, antibiotic exposure of the prior room occupant, and C.difficile status of the prior room occupant increase risk for C.difficile acquisition while antibiotic exposure, gastric acid suppression, and immunosuppression increase risk for progression to infection. These insights suggest possible new approaches to prevent C.difficile infections, including screening to identify and isolate carriers, universal gloving, greater use of sporicidal cleaning methods, enhancing antibiotic and possibly proton pump inhibitor stewardship, and prescribing prophylactic vancomycin and/or probiotics to colonized patients to prevent progression from colonization to infection. We review current evidence and questions related to these interventions.

Carrieri, R., Manco, R., Sapio, D., Iannaccone, M., Fulgione, A., Papaianni, M., de, Falco B., Grauso, L., Tarantino, P., Ianniello, F., Lanzotti, V., Lahoz, E., and Capparelli, R. Structural data and immunomodulatory properties of a water-soluble heteroglycan extracted from the mycelium of an Italian isolate of Ganoderma lucidum. Nat.Prod.Res. 1-20-2017; 1-7; PM: 28105862

ABSTRACT: Mushrooms produce a wide range of bioactive polysaccharides, different from each other in chemical structure and biological effects. In the last years, the idea to develop functional foods or drugs containing fungal polysaccharides is attracting great attention. Fruiting bodies of Basidiomycetes Ganoderma lucidum are commonly used in Oriental medicine to treat several disorders. G. lucidum polysaccharides - mainly beta-glucans and heteroglycans - have numerous biological properties such as antitumour and immunomodulatory activities. This report shows, by gene expression analyses and bioenergetic assays, immunomodulatory properties and capacity to improve glucose metabolism of a water-soluble heteroglycan extracted from mycelium of an Italian isolate of G. lucidum. The findings suggest the use of the heteroglycan as probiotic or ingredient in functional foods, being easy to produce and disperse in a food matrix thanks to its water-solubility. Heteroglycan could exert protective effects in pro-inflammatory conditions and benefits for people characterised by suppressed immune response.

Carter, A., Adams, M., La Ragione, R. M., and Woodward, M. J. Colonisation of poultry by Salmonella Enteritidis S1400 is reduced by combined administration of Lactobacillus salivarius 59 and Enterococcus faecium PXN-33. Vet.Microbiol. 2017; 199:100-107; PM: 28110775

ABSTRACT: Salmonella Enteritidis remains a significant issue within the poultry industry and one potential solution is to use probiotic bacteria to prevent Salmonella colonisation through competitive exclusion (CE). We demonstrate that combined administration of Lactobacillus salivarius 59 and Enterococcus faecium PXN33 were effective competitive excluders of Salmonella Enteritidis S1400 in poultry. Two models were developed to evaluate the efficacy of probiotic where birds received Salmonella Enteritidis S1400 by a) oral gavage and b) sentinel bird to bird transmission. A statistically significant ($p<0.001$) 2 log reduction of Salmonella Enteritidis S1400 colonisation was observed in the ileum, caecum and colon at day 43 using combined administration of the two probiotic bacteria. However, no Salmonella Enteritidis S1400 colonisation reduction was observed when either probiotic was administered individually. In the sentinel bird model the combined probiotic administered at days 12 and 20 was more effective than one-off or double administrations at age 1 and 12days. In vitro cell free culture supernatant studies suggest the mechanism of Salmonella Enteritidis S1400 inhibition was due to a reduction in pH by the probiotic bacteria. Our current study provides further evidence that probiotics can significantly reduce pathogenic bacterial colonisation in poultry and that mixed preparation of probiotics provide superior performance when compared to individual bacterial preparations.

Castro-Osses, D., Carrera-Naipil, C., Gallardo-Escarate, C., and Goncalves, A. T. Functional diets modulate the acute phase protein response in Oncorhynchus mykiss subjected to chronic stress and challenged with Vibrio anguillarum. Fish.Shellfish.Immunol. 5-2-2017; 66:62-70; PM: 28476670

ABSTRACT: The acute phase response to pathogens alters the production of proinflammatory cytokines that, in turn, activate the synthesis of acute phase proteins. These proteins neutralize, prevent, and indicate tissue damage, thereby influencing the specific immune response and allowing the organism to regain homeostasis. Functional diets based in pre- and probiotics are used in aquaculture to improve fish health and resistance to diseases, but there is an information gap on the mechanisms involved in these effects and if these diets are efficient when fish are raised under high stocking densities. This study aimed an evaluation of the acute phase response in Oncorhynchus mykiss fed functional diets supplemented with pre- and probiotics (i.e. mannan-oligosaccharides and Saccharomyces cerevisiae, respectively) and challenged by either Vibrio anguillarum or chronic stress via maintenance under high stocking densities. For this, the relative expression of acute phase response related genes in liver, and of inflammatory response related genes in head kidney was evaluated by RT-qPCR. The supplemented diets differentially modulated the acute phase protein response to the assessed challenge conditions, specifically evidencing an overexpression of the genes HAPT, SAA, LECT2, and IL-1beta under chronic stress and of HAPT, IL-1beta, IL8, and LECT2 at 24 h post-challenge with V. anguillarum. The observed early-stage regulation of acute phase proteins and of the immune response by the probiotic S. cerevisiae and by prebiotic mannan-oligosaccharides suggests that both supplements have high immunostimulatory potentials for fish farmed under high stocking densities.

Cavallari, J. F., Fullerton, M. D., Duggan, B. M., Foley, K. P., Denou, E., Smith, B. K., Desjardins, E. M., Henriksbo, B. D., Kim, K. J., Tuinema, B. R., Stearns, J. C., Prescott, D., Rosenstiel, P., Coombes, B. K., Steinberg, G. R., and Schertzer, J. D. Muramyl Dipeptide-Based

Postbiotics Mitigate Obesity-Induced Insulin Resistance via IRF4. Cell Metab. 5-2-2017; 25(5):1063-1074; PM: 28434881

ABSTRACT: Intestinal dysbiosis contributes to obesity and insulin resistance, but intervening with antibiotics, prebiotics, or probiotics can be limited by specificity or sustained changes in microbial composition. Postbiotics include bacterial components such as lipopolysaccharides, which have been shown to promote insulin resistance during metabolic endotoxemia. We found that bacterial cell wall-derived muramyl dipeptide (MDP) is an insulin-sensitizing postbiotic that requires NOD2. Injecting MDP lowered adipose inflammation and reduced glucose intolerance in obese mice without causing weight loss or altering the composition of the microbiome. MDP reduced hepatic insulin resistance during obesity and low-level endotoxemia. NOD1-activating muropeptides worsened glucose tolerance. IRF4 distinguished opposing glycemic responses to different types of peptidoglycan and was required for MDP/NOD2-induced insulin sensitization and lower metabolic tissue inflammation during obesity and endotoxemia. IRF4 was dispensable for exacerbated glucose intolerance via NOD1. Mifamurtide, an MDP-based drug with orphan drug status, was an insulin sensitizer at clinically relevant doses in obese mice.

Cayzeele-Decherf, A., Pelerin, F., Leuillet, S., Douillard, B., Housez, B., Cazaubiel, M., Jacobson, G. K., Justen, P., and Desreumaux, P. Saccharomyces cerevisiae CNCM I-3856 in irritable bowel syndrome: An individual subject meta-analysis. World J.Gastroenterol. 1-14-2017; 23(2):336-344; PM: 28127207

ABSTRACT: AIM: To confirm previous conclusions on Saccharomyces cerevisiae (S. cerevisiae) CNCM I-3856 for irritable bowel syndrome (IBS) management. *METHODS*: An individual patient data meta-analysis was performed on two randomized clinical trials studying the effect of S. cerevisiae CNCM I-3856 supplementation on gastrointestinal (GI) symptoms in IBS subjects. A total of 579 IBS subjects were included. Outcomes were the daily Likert scale scores of abdominal pain/discomfort and bloating [area under the curve (AUC) and weekly means], responder status, and bowel movements (stool frequency and consistency). Statistical analyses were conducted in Intent to Treat (ITT) population, IBS-C subjects and IBS-C subjects with an abdominal pain/discomfort score higher than or equal to 2 at baseline ("IBS-C >/= 2 subpopulation"). *RESULTS*: S. cerevisiae CNCM I-3856 significantly improved abdominal pain/discomfort and bloating during the second month of supplementation [AUC (W5-W8)] with improvement up to the minimal clinically relevant threshold of 10%: a 12.3% reduction of abdominal pain/discomfort in the ITT population compared to the Placebo group (P = 0.0134) has been observed. In the IBS-C >/= 2 subpopulation, there were a 13.1% reduction of abdominal pain/discomfort and a 14.9% reduction of bloating compared to the Placebo group (P = 0.0194 and P = 0.0145, respectively). GI symptoms significantly decreased during supplementation but no statistical differences were reported between groups at the end of the supplementation period. Responder status was defined as a subject who experienced a decrease of 1 arbitrary unit (a.u.) or 50% of the abdominal discomfort score from baseline for at least 2 wk out of the last 4 wk of the study. A significant difference between groups was reported in the ITT population, when considering the first definition: subjects in the Active group had 1.510 higher odds to be a responder (reduction of 1 a.u. of abdominal pain/discomfort) compared with subjects in the Placebo group (P = 0.0240). At the end of supplementation period, stool consistency in the Active group of the ITT population was significantly improved and classified as "normal" compared to Placebo (respectively 3.13 +/- 1.197 a.u. vs 2.58 +/- 1.020 a.u., P = 0.0003). Similar results were seen in the IBS-C >/= 2 subpopulation (Active group: 3.14 +/-

1.219 a.u. vs Placebo group: 2.59 +/- 1.017 a.u., P = 0.0009). *CONCLUSION*: This meta-analysis supports previous data linking S. cerevisiae I-3856 and improvement of GI symptoms, in IBS overall population and in the IBS-C and IBS-C >/= 2 subpopulations.

Ceccarelli, D., van Essen-Zandbergen, A., Smid, B., Veldman, K. T., Boender, G. J., Fischer, E. A. J., Mevius, D. J., and van der Goot, J. A. Competitive Exclusion Reduces Transmission and Excretion of Extended-Spectrum-beta-Lactamase-Producing Escherichia coli in Broilers. Appl.Environ.Microbiol. 6-1-2017; 83(11);PM: 28314728

ABSTRACT: Extended-spectrum beta-lactamases (ESBLs) and plasmid-mediated AmpC beta-lactamases (pAmpC) are enzymes able to hydrolyze a large variety of beta-lactam antibiotics, including third-generation cephalosporins and monobactams. Broilers and broiler meat products can be highly contaminated with.

Cekin, A. H., Sahinturk, Y., Akbay, Harmandar F., Uyar, S., Yolcular, B. O., and Cekin, Y. Use of probiotics as an adjuvant to sequential H. pylori eradication therapy: impact on eradication rates, treatment resistance, treatment-related side effects, and patient compliance. Turk.J.Gastroenterol. 2017; 28(1):3-11; PM: 28007678

ABSTRACT: BACKGROUND/AIMS: To evaluate the effect of probiotics administered as an adjuvant to sequential Helicobacter pylori (H. pylori) eradication therapy on treatment outcome and patient compliance. *MATERIALS AND METHODS*: In total, 159 patients with H. pylori infection receiving sequential H. pylori eradication therapy were included in this randomized placebo-controlled study. Starting from day 0 of sequential eradication therapy (ERA), patients in the ERA+probiotic group [n=53, mean (SD) age: 47.7 (14.0) years, 54.7% were females] also received a probiotic supplement with Bifidobacterium animalis subsp. lactis B94 (1 capsule/day), patients in the ERA+placebo group [n=52, mean (SD) age: 46.4 (13.4) years, 51.9% were males] received placebo treatment (1 capsule/day), and patients in the ERA-only group [n=54, mean (SD) age: 46.3 (11.9) years, 55.6% were females] received no additional treatments. Eradication rates, patient compliance, and side effects of eradication therapy were recorded in each treatment group. *RESULTS*: Significantly higher eradication rates were noted in the ERA+probiotic group (86.8% vs. 70.8%, p=0.025) than in the combined ERA (ERA-only and ERA-placebo) group. Non-compliance with anti-H. pylori treatment was noted in 24 (15.1%) of 159 patients. Lower rates of first week treatment non-compliance due to diarrhea (1.88% vs. 12.26%, p=0.036) were noted in the ERA+probiotic group than in the combined ERA (ERA-only and ERA-placebo) group. Treatment resistance (p: 0.389) was similar between the groups, indicating pure antibiotic resistance without any compliance problems. The number needed to treat for an additional beneficial outcome (NNTB) was 6.2 (CI 95%, 3.5 to 28.9) for probiotic use. *CONCLUSION*: In conclusion, adjuvant administration of probiotic (B. animalis subsp. lactis) in 2-week sequential H. pylori eradication therapy is associated with a higher H. pylori eradication rate, lower first week diarrhea-related treatment discontinuation rates, less common self-reported side effects, and higher treatment compliance.

Celebioglu, H. U. and Svensson, B. Exo- and surface proteomes of the probiotic bacterium Lactobacillus acidophilus NCFM. Proteomics. 4-9-2017; PM: 28393464

ABSTRACT: Lactobacillus acidophilus NCFM is a well-known probiotic bacterium

extensively studied for its beneficial health effects. Exoproteome (proteins exported into culture medium) and surface proteome (proteins attached to S-layer) of this probiotic were identified by using 2DE followed by MALDI TOF MS to find proteins potentially involved in bacteria-host interactions. The exo- and surface proteomes included 43 and 39 different proteins from 72 and 49 successfully identified spots, respectively. Twenty-two proteins were shared between the two proteomes; both contained the major surface layer protein that participates in host interaction as well as several well-known and putative moonlighting proteins. The exoproteome contained 9 classically-secreted (containing a signal sequence) and 10 non-classically secreted proteins, while the surface proteome contained four classically-secreted and 8 non-classically secreted proteins. Identification of exo- and surface proteomes contributes describing potential protein-mediated probiotic-host interactions. This article is protected by copyright. All rights reserved.

Celiberto, L. S., Bedani, R., Rossi, E. A., and Cavallini, D. C. Probiotics: The scientific evidence in the context of inflammatory bowel disease. Crit Rev.Food Sci.Nutr. 6-13-2017; 57(9):1759-1768; PM: 25996176

ABSTRACT: Inflammatory bowel disease (IBD) generally comprises Crohn's disease (CD) and ulcerative colitis (UC), and their main characteristic is the intestinal mucosa inflammation. Although its origin is not yet fully known, there is growing evidence related to genetics, intestinal microbiota composition, and the immune system factors such as precursors for the initiation and progression of intestinal conditions. The use of certain probiotic microorganisms has been touted as a possible and promising therapeutic approach in reducing the risk of inflammatory bowel disease, specifically ulcerative colitis. Several mechanisms have been proposed to explain the benefits of probiotics, indicating that some bacterial strains are able to positively modulate the intestinal microbiota and the immune system, and to produce metabolites with anti-inflammatory properties. The aim of this paper is to bring together the various results and information, based on scientific evidence, that are related to probiotics and inflammatory bowel disease, emphasizing the possible mechanisms involved in this action.

Cepeda, M. S., Katz, E. G., and Blacketer, C. Microbiome-Gut-Brain Axis: Probiotics and Their Association With Depression. J.Neuropsychiatry Clin.Neurosci. 2017; 29(1):39-44; PM: 27539375

ABSTRACT: To assess the association of probiotics with depression, a large population-based cross-sectional study was conducted. National Health and Nutrition Examination Survey adult participants from 2005 through 2012 were included. Exposure was defined as having consumed any probiotic food or supplement on any of the interview days. Subjects were classified as depressed if Patient Health Questionnaire scores were >/=10. Of the 18,019 subjects included, 14.11% consumed probiotics. Unadjusted analysis suggested that subjects who consumed probiotics had lower odds of depression (OR=0.58, 95% CI=0.45-0.75). After adjustment for characteristics associated with depression and probiotic exposure, the effect was attenuated (OR=0.82, 95% CI=0.61-1.1) and no longer significant. Use of probiotics is not associated with lower rates of depression in this national sample.

Champer, M., Wong, A. M., Champer, J., Brito, I. L., Messer, P. W., Hou, J. Y., and Wright, J. D. The role of the vaginal microbiome in gynaecological cancer. BJOG. 3-9-2017; PM: 28278350

ABSTRACT: Human microbiome research has shown commensal bacteria to be a major factor in both wellness and disease pathogenesis. Interest in the microbiome has recently expanded beyond the gut to include a multitude of other organ systems for which the microbiome may have health implications. Here, we review the role of the vaginal microbiome in health and disease, with a particular focus on gynaecologic malignancies. Further, we suggest that it may be possible to expand the use of probiotics in the treatment of gynaecological cancers. TWEETABLE ABSTRACT: A review of the research to date on the relation between the vaginal microbiome and gynaecological cancers.

Chandel, D. S., Perez-Munoz, M. E., Yu, F., Boissy, R., Satpathy, R., Misra, P. R., Sharma, N., Chaudhry, R., Parida, S., Peterson, D. A., Gewolb, I. H., and Panigrahi, P. Changes in the Gut Microbiota After Early Administration of Oral Synbiotics to Young Infants in India. J.Pediatr.Gastroenterol.Nutr. 1-25-2017; PM: 28121648

ABSTRACT: OBJECTIVES: We examined the changes in the developing gut microbiota of Indian infants enrolled in a colonization study of an oral synbiotic (L. plantarum and fructo-oligosaccharides) preparation. *METHODS*: Frozen stool samples were available from a previously published clinical study of the synbiotic preparation administered daily for seven days to full term Indian infants delivered by C-section. 16S rRNA gene sequencing of fecal bacterial community-DNA was done in 11 infants sampled at Day-7 and Day-60 of life. *RESULTS*: All infants showed changes in bacterial diversity with age. While Firmicutes and Proteobacteria were predominant in all, Actinobacteria and Bacteroidetes were initially low at day-7. In control infants, we observed a significant increase ($p = 0.012$) in the proportions of Actinobacteria at day-60. In the treated group, over the 60-day period, there was a 10-fold increase in Bacteroidetes, a somewhat smaller increase in Firmicutes, and a reduction in Proteobacteria. Compared to controls, treated infants were increasingly colonized by different Gram positive genera including Enterococcus, Lactobacillus and Bifidobacteria. Relatively less known taxa and some unassigned sequence reads added to enriched diversity observed in the treated group. *CONCLUSIONS*: There was a high level of bacterial diversity among infants examined in this study. Synbiotic treatment induced an increase in overall taxa and Gram positive diversity, especially in the first week of life. Changes in the microbiota during early infancy should be used as a rationale for selecting probiotics in diverse clinical settings.

Chang, H. Y., Chen, J. H., Chang, J. H., Lin, H. C., Lin, C. Y., and Peng, C. C. Multiple strains probiotics appear to be the most effective probiotics in the prevention of necrotizing enterocolitis and mortality: An updated meta-analysis. PLoS.One. 2017; 12(2):e0171579; PM: 28182644

ABSTRACT: BACKGROUND: Some oral probiotics have been shown to prevent necrotizing enterocolitis (NEC) and decrease mortality effectively in preterm very low birth weight (PVLBW) infants. However, it is unclear whether a single probiotic or a mixture of probiotics is most effective for the prevention of NEC. *OBJECTIVE*: A meta-analysis was conducted by reviewing the most up to date literature to investigate whether multiple strains probiotics are more effective than a single strain in reducing NEC and death in PVLBW infants. *DATA SOURCES*: Relevant studies were identified by searches of the

MEDLINE, EMBASE, and Cochrane CENTRAL databases, from 2001 to 2016. *DATA EXTRACTION AND SYNTHESIS*: The inclusion criteria were randomized controlled trials of any enteral probiotic supplementation that was initiated within the first 7 days and continued for at least 14 days in preterm infants (</= 34 weeks' gestation) and/or those of a birth weight </=1500 g. *RESULTS*: A total of 25 trials (n = 7345 infants) were eligible for inclusion in the meta-analysis using a fixed-effects model. Multiple strains probiotics were associated with a marked reduction in the incidence of NEC, with a pooled OR of 0.36 (95% CI, 0.24-0.53; P < .00001). Single strain probiotic using Lactobacillus species had a borderline effect in reducing NEC (OR of 0.60; 95% CI 0.36-1.0; P = .05), but not mortality. Multiple strains probiotics had a greater effectiveness in reducing mortality and were associated with a pooled OR of 0.58 (95% CI, 0.43-0.79; P = .0006). Trials using single strain of Bifidobacterium species and Saccharomyces boulardii did not reveal any beneficial effects in terms of reducing NEC or mortality. *CONCLUSION*: This updated report found that multiple strains probiotics appear to be the most feasible and effective strategy for the prevention of NEC and reduction of mortality in PVLBW neonates. Further clinical trials should focus on which probiotic combinations are most effective.

Chapple, I. L., Bouchard, P., Cagetti, M. G., Campus, G., Carra, M. C., Cocco, F., Nibali, L., Hujoel, P., Laine, M. L., Lingstrom, P., Manton, D. J., Montero, E., Pitts, N., Range, H., Schlueter, N., Teughels, W., Twetman, S., Van, Loveren C., Van der, Weijden F., Vieira, A. R., and Schulte, A. G. Interaction of lifestyle, behaviour or systemic diseases with dental caries and periodontal diseases: consensus report of group 2 of the joint EFP/ORCA workshop on the boundaries between caries and periodontal diseases. J.Clin.Periodontol. 2017; 44 Suppl 18:S39-S51; PM: 28266114

ABSTRACT: Periodontal diseases and dental caries are the most common diseases of humans and the main cause of tooth loss. Both diseases can lead to nutritional compromise and negative impacts upon self-esteem and quality of life. As complex chronic diseases, they share common risk factors, such as a requirement for a pathogenic plaque biofilm, yet they exhibit distinct pathophysiologies. Multiple exposures contribute to their causal pathways, and susceptibility involves risk factors that are inherited (e.g. genetic variants), and those that are acquired (e.g. socio-economic factors, biofilm load or composition, smoking, carbohydrate intake). Identification of these factors is crucial in the prevention of both diseases as well as in their management. AIM: To systematically appraise the scientific literature to identify potential risk factors for caries and periodontal diseases. *METHODS*: One systematic review (genetic risk factors), one narrative review (role of diet and nutrition) and reference documentation for modifiable acquired risk factors common to both disease groups, formed the basis of the report. *RESULTS & CONCLUSIONS*: There is moderately strong evidence for a genetic contribution to periodontal diseases and caries susceptibility, with an attributable risk estimated to be up to 50%. The genetics literature for periodontal disease is more substantial than for caries and genes associated with chronic periodontitis are the vitamin D receptor (VDR), Fc gamma receptor IIA (Fc-gammaRIIA) and Interleukin 10 (IL10) genes. For caries, genes involved in enamel formation (AMELX, AMBN, ENAM, TUFT, MMP20, and KLK4), salivary characteristics (AQP5), immune regulation and dietary preferences had the largest impact. No common genetic variants were found. Fermentable carbohydrates (sugars and starches) were the most relevant common dietary risk factor for both diseases, but associated mechanisms differed. In caries, the fermentation process leads to acid production and the generation of biofilm components such as Glucans. In periodontitis, glycaemia drives oxidative stress and advanced glycation end-products may also trigger a hyper inflammatory state. Micronutrient deficiencies, such as for vitamin C, vitamin D or vitamin B12, may be

related to the onset and progression of both diseases. Functional foods or probiotics could be helpful in caries prevention and periodontal disease management, although evidence is limited and biological mechanisms not fully elucidated. Hyposalivation, rheumatoid arthritis, smoking/tobacco use, undiagnosed or sub-optimally controlled diabetes and obesity are common acquired risk factors for both caries and periodontal diseases.

Chaves, B. D., Brashears, M. M., and Nightingale, K. K. Applications and safety considerations of Lactobacillus salivarius as a probiotic in animal and human health. J.Appl.Microbiol. 3-3-2017; PM: 28256040

ABSTRACT: The goals of this review are to summarize the current knowledge on the application of Lactobacillus salivarius as a probiotic in animals and humans, and to address safety concerns with its use on live hosts. Overall, several strains of L. salivarius are well established probiotics with multiple applications in animal health, particularly to reduce colonization by gastrointestinal pathogens, and to a lesser extent, as a production and quality aid. In humans, L. salivarius has been used to prevent and treat a variety of chronic diseases, including asthma, cancer, atopic dermatitis and halitosis, and to a much limited extent, to prevent or treat infections. Based on the results from primary research evidence, it seems that L. salivarius does not pose a health risk to animals or humans in the doses currently used for a variety of applications; however, there is a systematic lack of studies assuring the safety of many of the strains intended for clinical use. This review provides researchers in the field with up-to-date information regarding applications and safety of L. salivarius. Furthermore, it helps researchers identify knowledge gaps and potential opportunities for microbiological and clinical research.

Cheifetz, A. S., Gianotti, R., Luber, R., and Gibson, P. R. Complementary and Alternative Medicines Used by Patients With Inflammatory Bowel Diseases. Gastroenterology. 2017; 152(2):415-429; PM: 27743873

ABSTRACT: Patients and physicians often have many questions regarding the role of complementary and alternative medicines (CAMs), or nonallopathic therapies, for inflammatory bowel diseases (IBDs). CAMs of various forms are used by more than half of patients with IBD during some point in their disease course. We summarize the available evidence for the most commonly used and discussed CAMs. We discuss evidence for the effects of herbs (such as cannabis and curcumin), probiotics, acupuncture, exercise, and mind-body therapy. There have been few controlled studies of these therapies, which have been limited by their small sample sizes; most studies have been uncontrolled. In addition, there has been a lack of quality control for herbal preparations. It has been a challenge to design rigorous, randomized, placebo-controlled trials, in part owing to problems of adequate blinding for psychological interventions, acupuncture, and exercise. These barriers have limited the acceptance of CAMs by physicians. However, such therapies might be used to supplement conventional therapies and help ease patient symptoms. We conclude that physicians should understand the nature of and evidence for CAMs for IBD so that rational advice can be offered to patients who inquire about their use. CAMs have the potential to aid in the treatment of IBD, but further research is needed to validate these approaches.

Chen, J., Wang, Q., Liu, C. M., and Gong, J. Issues deserve attention in encapsulating probiotics: Critical review of existing literature. Crit Rev.Food Sci.Nutr. 4-13-2017; 57(6):1228-1238; PM: 26054762

ABSTRACT: Probiotic bacteria are being increasingly added to food for developing products with health-promoting properties. However, the efficacy of probiotics in commercial products is often questioned due to the loss of their viability during shelf storage and in human gastrointestinal tracts. Encapsulation of probiotics has been expected to provide protection to probiotics, but not many commercial products contain encapsulated and viable probiotic cells owing to various reasons. To promote the development and application of encapsulation technologies, this paper has critically reviewed previous publications with a focus on the areas where studies have fallen short, including insufficient consideration of structural effects of encapsulating material, general defects in encapsulating methods and issues in evaluation methodologies and risk assessments for application. Corresponding key issues that require further studies are highlighted. Some emerging trends in the field, such as current treads in encapsulating material and recently advanced encapsulation techniques, have also been discussed.

Chen, M., Wang, M. C., Ni, R., Wang, J., Wang, L., Wang, G. N., and Zhang, L. Y. [Role of probiotics in treatment of nonalcoholic fatty liver disease]. Zhonghua Gan Zang.Bing.Za Zhi. 1-20-2017; 25(1):77-80; PM: 28297790

ABSTRACT: Nonalcoholic fatty liver disease (NAFLD) is one of the most common chronic liver diseases in China and manifests as simple fatty liver, non-alcoholic steatohepatitis, liver cirrhosis, and hepatocellular carcinoma. Studies have shown that intestinal flora can affect the development and progression of NAFLD via the "gut-liver axis". Probiotics are active microorganisms with beneficial effects on the host, and more and more studies have found that probiotics play a positive role in improving NAFLD. They are cheaper, less harmful, and safer compared with antibiotics and surgery, and therefore, it may become a new method for the prevention and treatment of NAFLD. This article reviews the research advances in probiotics in the treatment of NAFLD, in order to provide a basis for the treatment of NAFLD using probiotics.

Chen, M. F., Weng, K. F., Huang, S. Y., Liu, Y. C., Tseng, S. N., Ojcius, D. M., and Shih, S. R. Pretreatment with a heat-killed probiotic modulates monocyte chemoattractant protein-1 and reduces the pathogenicity of influenza and enterovirus 71 infections. Mucosal.Immunol. 2017; 10(1):215-227; PM: 27072606

ABSTRACT: It has been proposed that inactivated probiotics may modulate the host immune system and contribute to mitigation of viral infections. This study demonstrated that administration of heat-killed Enterococcus faecalis, a widely used probiotic, can protect host animals against viral infections. The influenza-mediated morbidity and lung inflammation in E. faecalis-treated mice decreased significantly compared with those of the control mice. Furthermore, we found that the protection is associated with production of monocyte chemoattractant protein-1 (MCP-1). The intratracheal injection of a recombinant mouse MCP-1 protein abrogated the antiviral effects elicited by pretreatment with E. faecalis. CC chemokine receptor 2 (CCR2) is a receptor for MCP-1, and the intraperitoneal administration of a CCR2 antagonist effectively inhibited viral pathogenicity. The reduced pathogenicity was also observed in CCR2-deficient mice. Finally, E. faecalis significantly attenuated neuropathogenicity induced by another RNA

virus, enterovirus 71. This study demonstrates that killed probiotics can reduce viral disease severity and identify that the MCP-1 pathway might act as a key mediator in the improved antiviral immune response. Our findings suggest that MCP-1 and its related signaling pathway can serve as critical therapeutic targets for development of new antiviral strategies.

Chen, P. W., Liu, Z. S., Kuo, T. C., Hsieh, M. C., and Li, Z. W. Prebiotic effects of bovine lactoferrin on specific probiotic bacteria. Biometals. 2017; 30(2):237-248; PM: 28185076

ABSTRACT: Bovine lactoferrin (bLf) is a natural iron-binding protein and it has been suggested to be a prebiotic agent, but this finding remains inconclusive. This study explores the prebiotic potential of bLf in 14 probiotics. Initially, bLf (1-32 mg/mL) treatment showed occasional and slight prebiotic activity in several probiotics only during the late experimental period (48, 78 h) at 37 degrees C. We subsequently supposed that bLf exerts stronger prebiotic effects when probiotic growth has been temperately retarded. Therefore, we incubated the probiotics at different temperatures, namely 37 degrees C, 28 degrees C, room temperature (approximately 22-24 degrees C), and 22 degrees C, to retard or inhibit their growth. As expected, bLf showed more favorable prebiotic activity in several probiotics when their growth was partially retarded at room temperature. Furthermore, at 22 degrees C, the growth of Bifidobacterium breve, Lactobacillus coryniformis, L. delbrueckii, L. acidophilus, B. angulatum, B. catenulatum, and L. paraplantarum were completely blocked. Notably, these probiotics started regrowing in the presence of bLf (1-32 mg/mL) in a significant and dose-dependent manner. Accordingly, bLf significantly increased the growth of Pediococcus pentosaceus, L. rhamnosus, and L. paracasei (BCRC 17483; a locally isolated strain) when their growth was retarded by incubation at 22 degrees C. In conclusion, bLf showed inconsistent prebiotic activity in the 14 probiotics at 37 degrees C, but revealed strong prebiotic activity in 10 probiotic strains at 22 degrees C. Therefore, this study enables determining additional roles of Lf in probiotic strains, which can facilitate developing novel combinational approaches by simultaneously using Lf and specific probiotics.

Cheng, Y., Chen, Y., Li, X., Yang, W., Wen, C., Kang, Y., Wang, A., and Zhou, Y. Effects of synbiotic supplementation on growth performance, carcass characteristics, meat quality and muscular antioxidant capacity and mineral contents in broilers. J.Sci.Food Agric. 1-23-2017; PM: 28111775

ABSTRACT: BACKGROUND: The present study aimed to investigate the effects of dietary synbiotic supplementation on growth performance, carcass composition, meat quality and muscular antioxidant capacity, and mineral contents in broilers. Accordingly, 96 day-old male broiler chicks (Arbor Acres Plus; Aviagen, Huntsville, AL, USA) were randomly allocated to two groups, and each group consisted of six replicates with eight chicks each. Birds were fed a corn-soybean meal basal diet supplemented with either 0 or 1.5 g kg-1 synbiotic, consisting of probiotics (Bacillus subtilis, Bacillus licheniformis and Clostridium butyricum) and prebiotics (yeast cell wall and xylooligosaccharide) from 1 to 42 days of age. *RESULTS*: Compared with the control group, supplementation with a synbiotic increased average daily gain ($P < 0.05$) but reduced feed/gain ratio ($P < 0.01$) in broilers from 1 to 42 days of age. Similalrly, dietary synbiotic inclusion increased breast yield ($P < 0.05$) but decreased abdominal fat ($P < 0.01$) in broilers. The breast muscle pH value at 24 h postmortem in broilers was elevated with the incorporation of synbiotic ($P < 0.05$). By contrast, synbiotic supplementation lowered the cooking loss during heat

treatment in a water bath, malondialdehyde content, and total Cr content in the thigh muscle in broilers (P < 0.05). *CONCLUSION*: Dietary synbiotic supplementation into the diet of broilers may be an effective method for improving growth performance and carcass compositions, resulting in the production of meat with a favorable quality and oxidative stability. (c) 2017 Society of Chemical Industry.

Chiodelli, G., Pellizzoni, M., Ruzickova, G., and Lucini, L. Effect of Different Aloe Fractions on the Growth of Lactic Acid Bacteria. J.Food Sci. 2017; 82(1):219-224; PM: 27886374

ABSTRACT: Several foods on the market, such as yogurt and fermented milk, include mixtures of prebiotics and probiotic microorganisms effective in promoting the proliferation and equilibrium of intestinal bacteria, thus improving gut health. Particularly, researchers and the public have shown increasing interest in the combination of probiotics with natural substances that promote health or that can act as substrates to promote bacterial growth. The aim of this study is to evaluate the effects of different extracts of Aloe barbadensis and Aloe arborescens in fermented milk, taking into account both the prebiotic effect of aloe polysaccharides and the antimicrobial activity of several secondary metabolites. The results demonstrate a beneficial effect of 5% aloe inner gel on Lactobacillus growth and confirm the antimicrobial activity of the phenolic compounds peculiar of green rind extracts.

Chong, J. H. and Koh, M. J. Non-topical management of recalcitrant paediatric atopic dermatitis. Arch.Dis.Child. 2-16-2017; PM: 28209661

ABSTRACT: Atopic dermatitis (AD) is a common chronic, pruritic skin disease in children. As the incidence of AD increases, especially in high-income countries, paediatricians may see an increasing number of recalcitrant AD cases in their practice. Although these cases are principally managed by paediatric dermatologists, it is important for paediatricians to be aware of the use and side effects of non-topical treatment like phototherapy and systemic agents as well as the evidence for alternative treatment, which caregivers may ask about. This review presents paediatric evidence for the practical use of phototherapy and certain oral immunosuppressants for paediatric AD including doses, duration of use and monitoring of adverse effects. The use of alternative therapy including traditional medicine, probiotics and the role of nutrition are also discussed. Narrow band ultraviolet B phototherapy is effective in recalcitrant paediatric AD. When phototherapy is ineffective or contraindicated, systemic drugs may be administered cautiously with close surveillance of side effects. The use of azathioprine, ciclosporin, methotrexate and mycophenolate mofetil is generally safe in the short term under close monitoring and can be effective alongside compliance to topical treatment. Alternative complementary treatment is not known to be effective. Holistic management including therapeutic patient education is important. Good quality paediatric studies for non-topical AD treatment are needed for definitive guidelines.

Chua, K. J., Kwok, W. C., Aggarwal, N., Sun, T., and Chang, M. W. Designer probiotics for the prevention and treatment of human diseases. Curr.Opin.Chem.Biol. 5-4-2017; 40:8-16; PM: 28478369

ABSTRACT: Various studies have shown the beneficial effects of probiotics in humans. The use of synthetic biology to engineer programmable probiotics that specifically targets cancer, infectious agents, or other metabolic diseases has gained much interest since

the last decade. Developments made in synthetic probiotics as therapeutics within the last three years will be discussed in this review.

Chung, K. F. Airway microbial dysbiosis in asthmatic patients: A target for prevention and treatment? J.Allergy Clin.Immunol. 2017; 139(4):1071-1081; PM: 28390574

ABSTRACT: There has been long-standing interest in the role of bacterial communities in the complex and heterogeneous disease of asthma. With the advent of 16s rRNA sequencing replacing traditional culture methods, a strong association between the presence of bacterial communities with asthma has emerged. These microbiota can be modulated by various environmental factors, including diet, antibiotics, and early-life microbial exposures. Microbiota in the gut and lungs can influence both the inception and progress of asthma. In babies and infants the presence of pathogenic bacteria in the lungs and gut has been associated with subsequent development of allergic sensitization and asthma. Lung microbiota are present in the airways of healthy subjects but are dysregulated in adults with asthma, with a reduced diversity and community composition that has been linked to severity and inflammatory phenotypes. Causality between certain gut microbiota and the development of allergic asthma has been shown in experiments conducted in neonatal mice. Manipulation of the airway microbiome, particularly in early life, might be a strategy to prevent or treat asthma, although the results of studies of probiotics used together with prebiotics have been overall negative. A better understanding of the regulation of both the lung and gut microbiota to derive appropriate targets for prevention or treatment of asthma is needed.

Cicero, A. F. and Colletti, A. Nutraceuticals and dietary supplements to improve quality of life and outcomes in heart failure patients. Curr.Pharm.Des. 1-24-2017; PM: 28120718

ABSTRACT: BACKGROUND: Heart failure (HF) is a complex clinical syndrome that can result from any structural or functional cardiac disorder that impairs the ability of the ventricle to fill or eject blood. It represents a major public health issue, with a prevalence of over 23 million worldwide. The lifetime risk of developing HF is one in five and the most important risk factors identified are ischemic heart disease, hypertension, smoking, obesity and diabetes. Preventive approaches are based on improvements of lifestyle, associated with pharmacological therapy. Several nutraceuticals have shown interesting clinical results in prevention of HF as well as in the treatment of the early stages of the disease, alone or in association with pharmacological therapy. *AIM*: The aim of this review is to resume the available clinical evidence on phytochemicals effect on HF prevention and/or treatment. *METHODS*: A systematic search strategy was developed to identify trials in PubMed (January 1980 to April 2016). The terms 'nutraceuticals', 'dietary supplements', 'herbal drug' and 'heart failure' were incorporated into an electronic search strategy. *RESULTS*: Clinical trials reported that the intake of some nutraceuticals (hawthorn, coenzyme Q10, L-carnitine, D-ribose, Carnosine, Vitamin D, Some probiotics, Omega-3 PUFAs, Beet nitrates) is associated with improvements in functional parameters such as ejection fraction, stroke volume and cardiac output in HF patients, with minimal side effects. These findings were sometimes reinforced by subsequent meta-analyses, which further concluded that benefits tended to be greater in earlier stage HF. The main mechanisms involved are antioxidant, antinflammatory, anti-ischemic and antiaggregant effects. *CONCLUSIONS*: Evidence suggests that the supplementation with

nutraceuticals may be a useful option for effective management of HF, with the advantage of excellent clinical tolerance.

Ciernikova, S., Mego, M., Semanova, M., Wachsmannova, L., Adamcikova, Z., Stevurkova, V., Drgona, L., and Zajac, V. Probiotic Survey in Cancer Patients Treated in the Outpatient Department in a Comprehensive Cancer Center. Integr.Cancer Ther. 2017; 16(2):188-195; PM: 27151581

ABSTRACT: PURPOSE: Availability without prescription restriction, low cost, and simple oral administration allow cancer patients to use probiotics without knowledge of potential risks. We present a survey of probiotic use and the association with patient tumor characteristics in cancer patients treated at the outpatient department of the National Cancer Institute in Slovakia. *PATIENTS AND METHODS*: Between March and December 2014, 499 patients were asked to evaluate their overall experience with probiotics by questionnaire form, including the length and method of use relative to anticancer therapy, expectations, side-effect experiences, understanding of the possible risks, dietary supplement use, and others. The relevant data were statistically evaluated. *RESULTS*: The cohort consisted of 323 women (64.7%) and 176 men (35.3%); 91.6% were undergoing chemotherapy (2.6% together with radiotherapy) and 8.4% had no anticancer therapy. The prevalence of probiotic use was 28.5% and only 12 patients using probiotics (8.5%) described negative side effects. Most patients declared consideration of probiotic use based on recommendation from a physician (37.3%) or a pharmacist (14.8%). Nevertheless, up to 86.6% of patients declared no knowledge of possible risks. Statistically significant correlation was found between probiotic use and age of patients ($P < .008$), gender ($P < .023$), and taking other dietary supplements ($P < .000002$). *CONCLUSIONS*: In this prospective study, we present for the first time the prevalence, side-effect experience, and aspects that most likely influence probiotic use in cancer patients. Minimal knowledge of risks underlines the importance of an active approach by oncologists to inform patients about probiotic safety.

Cigarran, Guldris S., Gonzalez, Parra E., and Cases, Amenos A. Gut microbiota in chronic kidney disease. Nefrologia. 2017; 37(1):9-19; PM: 27553986

ABSTRACT: The intestinal microflora maintains a symbiotic relationship with the host under normal conditions, but its imbalance has recently been associated with several diseases. In chronic kidney disease (CKD), dysbiotic intestinal microflora has been reported with an increase in pathogenic flora compared to symbiotic flora. An enhanced permeability of the intestinal barrier, allowing the passage of endotoxins and other bacterial products to the blood, has also been shown in CKD. By fermenting undigested products that reach the colon, the intestinal microflora produce indoles, phenols and amines, among others, that are absorbed by the host, accumulate in CKD and have harmful effects on the body. These gut-derived uraemic toxins and the increased permeability of the intestinal barrier in CKD have been associated with increased inflammation and oxidative stress and have been involved in various CKD-related complications, including cardiovascular disease, anaemia, mineral metabolism disorders or the progression of CKD. The use of prebiotics, probiotics or synbiotics, among other approaches, could improve the dysbiosis and/or the increased permeability of the intestinal barrier in CKD. This article describes the situation of the intestinal microflora in CKD, the alteration of the intestinal barrier and its clinical consequences, the harmful effects of intestinal flora-derived

uraemic toxins, and possible therapeutic options to improve this dysbiosis and reduce CKD-related complications.

Cinque, B., La, Torre C., Lombardi, F., Palumbo, P., Evtoski, Z., Jr, Santini S., Falone, S., Cimini, A., Amicarelli, F., and Cifone, M. G. VSL#3 probiotic differently influences IEC-6 intestinal epithelial cell status and function. J.Cell Physiol. 1-21-2017; PM: 28109129

ABSTRACT: The data here reported introduce the wound-healing assay as a tool for testing probiotics aimed at protecting gastrointestinal mucosal surfaces and to verify the consistency of their manufacturing. At the scope, we compared the in vitro effects of two multi-strain high concentration formulations both commercialized under the same brand VSL#3 but sourced from different production sites (USA and Italy) on a non-transformed small-intestinal epithelial cell line, IEC-6. The effects on cellular morphology, viability, migration, and H2 O2 -induced damage, were assessed before and after the treatment with both VSL#3 formulations. While the USA-sourced product ("USA-made") VSL#3 did not affect monolayer morphology and cellular density, the addition of bacteria from the Italy-derived product ("Italy-made") VSL#3 caused clear morphological cell damage and strongly reduced cellularity. The treatment with "USA-made" lysate led to a higher rate of wounded monolayer healing, while the addition of "Italy-made" bacterial lysate did not influence the closure rate as compared to untreated cells. While lysates from "USA-made" VSL#3 clearly enhanced the formation of elongated and aligned stress fibers, "Italy-made" lysates had not similar effect. "USA-made" lysate was able to cause a total inhibition of H2 O2 -induced cytotoxic effect whereas "Italy-made" VSL#3 lysate was unable to protect IEC-6 cells from H2 O2 -induced damage. ROS generation was also differently influenced, thus supporting the hypotesis of a protective action of "USA-made" VSL#3 lysates, as well as the idea that "Italy-made" formulation was unable to prevent significantly the H2 O2 -induced oxidative stress.

Clark, A. K., Haas, K. N., and Sivamani, R. K. Edible Plants and Their Influence on the Gut Microbiome and Acne. Int.J.Mol.Sci. 5-17-2017; 18(5); PM: 28513546

ABSTRACT: Acne vulgaris affects most people at some point in their lives. Due to unclear etiology, likely with multiple factors, targeted and low-risk treatments have yet to be developed. In this review, we explore the multiple causes of acne and how plant-based foods and supplements can control these. The proposed causative factors include insulin resistance, sex hormone imbalances, inflammation and microbial dysbiosis. There is an emerging body of work on the human gut microbiome and how it mediates feedback between the foods we eat and our bodies. The gut microbiome is also an important mediator of inflammation in the gut and systemically. A low-glycemic load diet, one rich in plant fibers and low in processed foods, has been linked to an improvement in acne, possibly through gut changes or attenuation of insulin levels. Though there is much interest in the human microbiome, there is much more unknown, especially along the gut-skin axis. Collectively, the evidence suggests that approaches such as plant-based foods and supplements may be a viable alternative to the current first line standard of care for moderate acne, which typically includes antibiotics. Though patient compliance with major dietary changes is likely much lower than with medications, it is a treatment avenue that warrants further study and development.

Compare, D., Rocco, A., Coccoli, P., Angrisani, D., Sgamato, C., Iovine, B., Salvatore, U., and Nardone, G. Lactobacillus casei DG and its postbiotic reduce the inflammatory mucosal response: an ex-vivo organ culture model of post-infectious irritable bowel syndrome. BMC.Gastroenterol. 4-14-2017; 17(1):53; PM: 28410580

ABSTRACT: BACKGROUND: The evidence on the role of gut microbiota in post-infectious irritable bowel syndrome (PI-IBS) is convincing. Lactobacillus spp. positively affect IBS symptoms, although the mechanisms through which probiotics exert their beneficial effects are largely unknown. The aim of the study is to evaluate the role of Lactobacillus casei DG (LC-DG) and its postbiotic (PB) in modulating the inflammatory/immune-response in PI-IBS in an ex-vivo organ culture model. *METHODS*: Ex vivo cultures of ileal and colonic mucosa from 10 PI-IBS, diarrhea predominant subtype (D) patients, and 10 healthy controls (HC) were treated with LPS, LC-DG and PB. Interleukin (IL)-1alpha, IL-6, IL-8 and IL-10 mRNA levels were assessed by real-time PCR and Toll like receptor 4 (TLR-4) protein expression by Western blotting. *RESULTS*: At baseline, IL-1alpha, IL-6 and IL-8 mRNA levels as well as TLR-4 protein expression were significantly higher while IL-10 mRNA levels were lower in PI-IBS D than in HC in both ileum and colon. LC-DG and PB significantly reduced the mRNA levels of pro-inflammatory cytokines and TLR-4 while increased that of IL-10 after LPS stimulation. The protective effect was more pronounced for PB than LC-DG treatment. *CONCLUSION*: LC-DG and its PB attenuate the inflammatory mucosal response in an ex-vivo organ culture model of PI-IBS D.

Constante, M., Fragoso, G., Lupien-Meilleur, J., Calve, A., and Santos, M. M. Iron Supplements Modulate Colon Microbiota Composition and Potentiate the Protective Effects of Probiotics in Dextran Sodium Sulfate-induced Colitis. Inflamm.Bowel.Dis. 2017; 23(5):753-766; PM: 28368910

ABSTRACT: BACKGROUND: Iron is an important nutrient for both the host and colonizing bacteria. Oral iron supplementation may impact the composition of the microbiota and can be particularly damaging to patients suffering from inflammatory bowel disease (IBD). However, patients with IBD may require iron supplementation to treat their anemia. *METHODS*: We fed mice with diets supplemented with ferrous sulfate at different doses (5, 50, and 500 mg of iron/kg chow) and with different iron formulations (ferrous sulfate, ferrous bisglycinate and ferric ethylenediaminetetraacetic acid [FEDTA]), and analyzed the effects on the composition of the gut microbiota by 16S ribosomal RNA gene sequencing. Using the dextran sodium sulfate (DSS)-induced colitis mouse model, we investigated the effects of iron supplementation in colitis severity, as well as the use of the probiotic Escherichia coli Nissle 1917 (EcN) in combination with iron supplementation. *RESULTS*: Iron supplementation at different doses induced shifts in the gut microbial communities and inferred metabolic pathways. However, depending on the iron formulation used in the diets, iron supplementation during dextran sodium sulfate-induced colitis was either beneficial (ferrous bisglycinate) or highly detrimental (FEDTA). Finally, the beneficial effect of the probiotic EcN in the dextran sodium sulfate-induced colitis model was potentiated by oral iron supplementation with ferrous sulfate. *CONCLUSIONS*: These results show that the iron formulations used to treat iron deficiency influence the gut microbiota and colitis in mice and suggest that distinct iron compounds may be of particular relevance to patients with IBD. In addition, the beneficial action of probiotics in IBD may be enhanced by oral iron supplementation.

Cooper, P., Bolton, K. D., Velaphi, S., de, Groot N., Emady-Azar, S., Pecquet, S., and Steenhout, P. Early Benefits of a Starter Formula Enriched in Prebiotics and Probiotics on the Gut

Microbiota of Healthy Infants Born to HIV+ Mothers: A Randomized Double-Blind Controlled Trial. Clin.Med.Insights.Pediatr. 2016; 10:119-130; PM: 28096702

ABSTRACT: The gut microbiota of infants is shaped by both the mode of delivery and the type of feeding. The gut of vaginally and cesarean-delivered infants is colonized at different rates and with different bacterial species, leading to differences in the gut microbial composition, which may persist up to 6 months. In a multicenter, randomized, controlled, double-blind trial conducted in South Africa, we tested the effect of a formula supplemented with a prebiotic (a mixture of bovine milk-derived oligosaccharides [BMOS] generated from whey permeate and containing galactooligosaccharides and milk oligosaccharides such as 3'- and 6'-sialyllactose) and the probiotic Bifidobacterium animalis subsp. lactis (B. lactis) strain CNCM I-3446 on the bifidobacteria levels in the gut of infants born vaginally or via cesarean section in early life. Additionally, the safety of the new formulation was evaluated. A total of 430 healthy, full-term infants born to HIV-positive mothers who had elected to feed their child beginning from birth (</=3 days old) exclusively with formula were randomized into this multicenter trial of four parallel groups. A total of 421 infants who had any study formula intake were included in the full analysis set (FAS). The first two groups consisted of cesarean-delivered infants assigned to the Test formula (n = 92) (a starter infant formula [IF] containing BMOS at a total oligosaccharide concentration of 5.8 +/- 1.0 g/100 g of powder formula [8 g/L in the reconstituted formula] + B. lactis [1 x 107 colony-forming units {cfu}/g]) or a Control IF (n = 101); the second two groups consisted of vaginally delivered infants randomized to the same Test (n = 115) or Control (n = 113) formulas from the time of enrollment to 6 months. The primary efficacy outcome was fecal bifidobacteria count at 10 days, and the primary safety outcome was daily weight gain (g/d) between 10 days and 4 months. At 10 days, fecal bifidobacteria counts were significantly higher in the Test formula than in the Control formula group among infants with cesarean birth (median [range] log: 9.41 [6.30-10.94] cfu/g versus 6.30 [6.30-10.51] cfu/g; P = 0.002) but not among those with vaginal birth (median [range] log: 10.06 [5.93-10.77] cfu/g versus 9.85 [6.15-10.79] cfu/g; P = 0.126). The lower bound of the two-sided 95% confidence interval of the difference in the mean daily weight gain between the Test and Control formula groups was more than -3 g/d in both the vaginally and cesarean-delivered infants, indicating that growth in the Test formula-fed infants was not inferior to that of Control formula-fed infants. At 10 days and 4 weeks, the fecal pH of infants fed the Test formula was significantly lower than in those fed the Control formula, irrespective of mode of delivery: for vaginal delivery: 4.93 versus 5.59; P < 0.001 (10 days) and 5.01 versus 5.71; P < 0.001 (4 weeks); for cesarean delivery: 5.14 versus 5.65, P = 0.009 (10 days) and 5.06 versus 5.75, P < 0.001 (4 weeks). At 3 months, this acidification effect only persisted among cesarean-born infants. IF supplemented with the prebiotic BMOS and probiotic B. lactis induced a strong bifidogenic effect in both delivering modes, but more explicitly correcting the low bifidobacteria level found in cesarean-born infants from birth. The supplemented IF lowered the fecal pH and improved the fecal microbiota in both normal and cesarean-delivered infants. The use of bifidobacteria as a probiotic even in infants who are immunologically at risk is safe and well tolerated.

Cordonnier, C., Thevenot, J., Etienne-Mesmin, L., Alric, M., Livrelli, V., and Blanquet-Diot, S. Probiotic and enterohemorrhagic Escherichia coli: An effective strategy against a deadly enemy? Crit Rev.Microbiol. 2017; 43(1):116-132; PM: 27798976

ABSTRACT: Enterohemorrhagic Escherichia coli (EHEC) are major food-borne pathogens that constitute a serious public health threat. Currently, there is no specific treatment

available for EHEC infections in human creating an urgent need for the development of alternative therapeutic strategies. Among them, one of the most promising approaches is the use of probiotic microorganisms. Even if many studies have shown the antagonistic effects of probiotic bacteria or yeast on EHEC survival, virulence, adhesion on intestinal epithelium or pathogen-induced inflammatory responses, mechanisms mediating their beneficial effects remain unclear. This review describes EHEC pathogenesis and novel therapeutic strategies, with a particular emphasis on probiotics. The interests and limits of a probiotic-based approach and the way it might be incorporated into global health strategies against EHEC infections will be discussed.

Costantini, E., Giannitsas, K., and Illiano, E. The role of nonantibiotic treatment of community-acquired urinary tract infections. Curr.Opin.Urol. 2017; 27(2):120-126; PM: 27898456

ABSTRACT: PURPOSE OF REVIEW: To summarize evidence on the efficacy of nonantibiotic treatments in the prevention of recurrent urinary tract infections (UTIs). The need for antibiotic-free regimens seems to be imperative given the worldwide rates of resistance of uropathogens to available antibiotics. *RECENT FINDINGS*: In the recently published literature, cranberry products and probiotics are the focus of research. They both seem to be effective in preventing recurrent UTIs compared with placebo, but their benefit becomes less clear when they are compared with antibiotics. *SUMMARY*: A number of nonantibiotic-containing alternatives are available for the prevention of recurrent UTIs. For the majority of these alternatives, contradictory results have been published. These can be, at least partially, explained by variation in doses administered and duration of treatment. Selection of patients more likely to benefit from these interventions seems to be a realistic approach from a clinical-practice perspective, as well a worthwhile focus for future research.

Cresci, G. A. M., Mayor, P. C., and Thompson, S. A. Effect of butyrate and Lactobacillus GG on a butyrate receptor and transporter during Campylobacter jejuni exposure. FEMS Microbiol.Lett. 3-1-2017; 364(6);PM: 28333199

ABSTRACT: Campylobacter jejuni frequently infects humans causing many gastrointestinal symptoms, fever, fatigue and several long-term debilitating diseases. Current treatment for campylobacteriosis includes rehydration and in some cases, antibiotic therapy. Probiotics are used to treat several gastrointestinal diseases. Butyrate is a short-chain fatty acid known to promote intestinal health. Interaction of butyrate with its respective receptor (HCAR2) and transporter (SLC5A8), both expressed in the intestine, is associated with water and electrolyte absorption as well as providing defense against colon cancer and inflammation. Alterations in gut microbiota influence the presence of HCAR2 and SLC5A8 in the intestine. We hypothesized that adherence and/or invasion of C. jejuni and alterations in HCAR2 and SLC5A8 expression would be minimized with butyrate or Lactobacillus GG (LGG) pretreatment of Caco-2 cells. We found that both C. jejuni adhesion but not invasion was reduced with butyrate pretreatment. While LGG pretreatment did not prevent C. jejuni adhesion, it did result in reduced invasion which was associated with altered cell supernate pH. Both butyrate and LGG protected HCAR2 and SLC5A8 protein expression following C. jejuni infection. These results suggest that the first stages of C. jejuni infection of Caco-2 cells may be minimized by LGG and butyrate pretreatment.

Crisol-Martinez, E., Stanley, D., Geier, M. S., Hughes, R. J., and Moore, R. J. Understanding the mechanisms of zinc bacitracin and avilamycin on animal production: linking gut microbiota and growth performance in chickens. Appl.Microbiol.Biotechnol. 2-28-2017; PM: 28243710

ABSTRACT: Unravelling the mechanisms of how antibiotics influence growth performance through changes in gut microbiota can lead to the identification of highly productive microbiota in animal production. Here we investigated the effect of zinc bacitracin and avilamycin on growth performance and caecal microbiota in chickens and analysed associations between individual bacteria and growth performance. Two trials were undertaken; each used 96 individually caged 15-day-old Cobb broilers. Trial 1 had a control group (n = 48) and a zinc bacitracin (50 ppm) treatment group (n = 48). Trial 2 had a control group (n = 48) and an avilamycin (15 ppm) treatment group (n = 48). Chicken growth performance was evaluated over a 10-day period, and caecal microbiota was characterised by sequencing of bacterial 16S rRNA gene amplicons. Avilamycin produced no effect on growth performance and exhibited little significant disturbance of the microbiota structure. However, zinc bacitracin reduced the feed conversion ratio (FCR) in treated birds, changed the composition and increased the diversity of their caecal microbiota by reducing dominant species. Avilamycin only produced minor reductions in the abundance of two microbial taxa, whereas zinc bacitracin produced relatively large shifts in a number of taxa, primarily Lactobacillus species. Also, a number of phylotypes closely related to lactobacilli species were positively or negatively correlated with FCR values, suggesting contrasting effects of Lactobacillus spp. on chicken growth performance. By harnessing such bacteria, it may be possible to develop high-productivity strategies in poultry that rely on the use of probiotics and less on in-feed antibiotics.

Cuomo, R., Cargiolli, M., Andreozzi, P., Zito, F. P., and Sarnelli, G. Rationale and evidences for treatment of symptomatic uncomplicated diverticular disease. Minerva Gastroenterol.Dietol. 2017; 63(2):130-142; PM: 27973463

ABSTRACT: INTRODUCTION: Symptomatic uncomplicated diverticular disease (SUDD) is one of the possible clinical manifestations of diverticular disease. It is a common disorder characterized by chronic abdominal symptoms ranging from lower left abdominal pain to alteration of bowel habit, that significantly reduce quality of life of subject affected. The present article aims to review the current data for medical management of SUDD. *EVIDENCE ACQUISITION*: We analyzed the existing literature on the factors involved in the pathogenesis of SUDD and we highlighted the possible target for treatment. Treatment for SUDD should be direct to relieve chronic symptoms and prevent diverticulitis and its complications. In particular we focused on the role of probiotics, fiber-diet, mesalazine and rifaximin on these two aspects. In this setting, we conducted a PubMed search for guidelines, systematic reviews and meta-analyses and updated information to October 2016. *EVIDENCE SYNTHESIS*: Each topic was evaluated according to the best evidences available. Best results seemed to be obtained with combined therapies and in particular with rifaximin associated to high fiber-diet. This regimen seems to guarantee better symptoms control compared to fiber alone and it is more effective in preventing acute diverticulitis. On the contrary, no clear evidences about the efficacy of mesalazine and probiotics are available. *CONCLUSIONS*: The results of the studies available in literature are controversial and debatable, for this reason a clear and defined algorithm for treatment of SUDD has not yet been defined. Further randomized, double-blind, placebo controlled study are necessary.

Curro, D., Ianiro, G., Pecere, S., Bibbo, S., and Cammarota, G. Probiotics, fibre and herbal medicinal products for functional and inflammatory bowel disorders. Br.J.Pharmacol. 2017; 174(11):1426-1449; PM: 27696378

ABSTRACT: Functional bowel disorders (FBD), mainly irritable bowel syndrome (IBS) and functional constipation (FC, also called chronic idiopathic constipation), are very common worldwide. Inflammatory bowel disease (IBD), including ulcerative colitis and Crohn's disease, although less common, has a strong impact on patients' quality of life, as well as being highly expensive for our healthcare. A definite cure for those disorders is still yet to come. Over the years, several therapeutic approaches complementary or alternative to traditional pharmacological treatments, including probiotics, prebiotics, synbiotics, fibre and herbal medicinal products, have been investigated for the management of both groups of diseases. However, most available studies are biased by several drawbacks, including small samples and poor methodological quality. Probiotics, in particular Saccharomyces boulardii and Lactobacilli (among which Lactobacillus rhamnosus), synbiotics, psyllium, and some herbal medicinal products, primarily peppermint oil, seem to be effective in ameliorating IBS symptoms. Synbiotics and fibre seem to be beneficial in FC patients. The probiotic combination VSL#3 may be effective in inducing remission in patients with mild-to-moderate ulcerative colitis, in whom Escherichia coli Nissle 1917 seems to be as effective as mesalamine in maintaining remission. No definite conclusions can be drawn as to the efficacy of fibre and herbal medicinal products in IBD patients due to the low number of studies and the lack of randomized controlled trials that replicate the results obtained in the individual studies conducted so far. Thus, further, well-designed studies are needed to address the real role of these therapeutic options in the management of both FBD and IBD. LINKED ARTICLES: This article is part of a themed section on Principles of Pharmacological Research of Nutraceuticals. To view the other articles in this section visit http://onlinelibrary.wiley.com/doi/10.1111/bph.v174.11/issuetoc.

d'Ettorre, G., Rossi, G., Scagnolari, C., Andreotti, M., Giustini, N., Serafino, S., Schietroma, I., Scheri, G. C., Fard, S. N., Trinchieri, V., Mastromarino, P., Selvaggi, C., Scarpona, S., Fanello, G., Fiocca, F., Ceccarelli, G., Antonelli, G., Brenchley, J. M., and Vullo, V. Probiotic supplementation promotes a reduction in T-cell activation, an increase in Th17 frequencies, and a recovery of intestinal epithelium integrity and mitochondrial morphology in ART-treated HIV-1-positive patients. Immun.Inflamm.Dis. 4-20-2017; PM: 28474815

ABSTRACT: INTRODUCTION: HIV infection is characterized by a persistent immune activation associated to a compromised gut barrier immunity and alterations in the profile of the fecal flora linked with the progression of inflammatory symptoms. The effects of high concentration multistrain probiotic (Vivomixx(R), Viale del Policlinico 155, Rome, Italy in EU; Visbiome(R), Dupont, Madison, Wisconsin in USA) on several aspects of intestinal immunity in ART-experienced HIV-1 patients was evaluated. *METHODS*: A sub-study of a longitudinal pilot study was performed in HIV-1 patients who received the probiotic supplement twice a day for 6 months (T6). T-cell activation and CD4+ and CD8+ T-cell subsets expressing IFNgamma (Th1, Tc1) or IL-17A (Th17, Tc17) were stained

by cytoflorimetric analysis. Histological and immunohistochemical analyses were performed on intestinal biopsies while enterocytes apoptosis index was determined by TUNEL assay. *RESULTS*: A reduction in the frequencies of CD4+ and CD8+ T-cell subsets, expressing CD38+ , HLA-DR+ , or both, and an increase in the percentage of Th17 cell subsets, especially those with central or effector memory phenotype, was recorded in the peripheral blood and in gut-associated lymphoid tissue (GALT) after probiotic intervention. Conversely, Tc1 and Tc17 levels remained substantially unchanged at T6, while Th1 cell subsets increase in the GALT. Probiotic supplementation was also associated to a recovery of the integrity of the gut epithelial barrier, a reduction of both intraepithelial lymphocytes density and enterocyte apoptosis and, an improvement of mitochondrial morphology sustained in part by a modulation of heat shock protein 60. *CONCLUSIONS*: These findings highlight the potential beneficial effects of probiotic supplementation for the reconstitution of physical and immunological integrity of the mucosal intestinal barrier in ART-treated HIV-1-positive patients.

Dafe, A., Etemadi, H., Zarredar, H., and Mahdavinia, G. R. Development of novel carboxymethyl cellulose/k-carrageenan blends as an enteric delivery vehicle for probiotic bacteria. Int.J.Biol.Macromol. 2017; 97:299-307; PM: 28064052

ABSTRACT: This study reports a novel carrier based on blends of carboxymethyl cellulose (CMC) and k-carrageenan (k-Carr) for probiotic colon delivery. Lactobacillus plantarum ATCC:13643 (L. plantarum) cells were encapsulated in CMC/k-Carr blends by extrusion method. k-Carrageenan was used as a coating agent to improve encapsulation of L. plantarum cells in carboxymethyl cellulose biopolymer. K-Carrageenan and carboxymethyl cellulose were ionically cross-linked with K+ and Ca2+ ions, respectively. Optical and scanning electron microscopy obviously showed the random distribution of L. plantarum cells throughout the blend network. The viability of encapsulated cells in simulated gastric fluid (SGF) and bile salt solution were conducted. Results indicated that CMC/k-Carr blends could successfully protect L. plantarum cells against adverse conditions of the gastro-intestinal tract and bile salt solution. After sequential exposure to SGF for 2h almost complete death of free cells was observed. However, the number of surviving cells was 5.20 and 7.30 Log CFU/g for uncoated free CMC and CMC/k-Carr blends, respectively. Cumulatively the results of this research offer a suitable media to potentially deliver probiotics to colon site.

Dahiya, D. K., Renuka, Puniya, M., Shandilya, U. K., Dhewa, T., Kumar, N., Kumar, S., Puniya, A. K., and Shukla, P. Gut Microbiota Modulation and Its Relationship with Obesity Using Prebiotic Fibers and Probiotics: A Review. Front Microbiol. 2017; 8:563; PM: 28421057

ABSTRACT: In the present world scenario, obesity has almost attained the level of a pandemic and is progressing at a rapid rate. This disease is the mother of all other metabolic disorders, which apart from placing an added financial burden on the concerned patient also has a negative impact on his/her well-being and health in the society. Among the various plausible factors for the development of obesity, the role of gut microbiota is very crucial. In general, the gut of an individual is inhabited by trillions of microbes that play a significant role in host energy homeostasis by their symbiotic interactions. Dysbiosis in gut microbiota causes disequilibrium in energy homeostasis that ultimately leads to obesity. Numerous mechanisms have been reported by which gut microbiota induces obesity in experimental models. However, which microbial community is directly linked to obesity is still unknown due to the complex nature of gut

microbiota. Prebiotics and probiotics are the safer and effective dietary substances available, which can therapeutically alter the gut microbiota of the host. In this review, an effort was made to discuss the current mechanisms through which gut microbiota interacts with host energy metabolism in the context of obesity. Further, the therapeutic approaches (prebiotics/probiotics) that helped in positively altering the gut microbiota were discussed by taking experimental evidence from animal and human studies. In the closing statement, the challenges and future tasks within the field were discussed.

Dai, S. X., Gu, H. X., Lin, Q. Y., Huang, S. Z., Xing, T. S., Zhang, Q. F., Wu, G., Chen, M. H., Tan, W. E., Jian, H. J., Zheng, Z. W., Zhong, T., Zhang, M. H., Cheng, X. F., Huang, P., Liao, G. J., and Sha, W. H. CD8+CD28+/CD8+. Clin.Res.Hepatol.Gastroenterol. 5-10-2017; PM: 28502591

ABSTRACT: BACKGROUND/AIM: The balance of blood CD8+CD28+/CD8+.

Dai, Y. J., Wang, H. Y., Wang, X. J., Kaye, A. D., and Sun, Y. H. Potential Beneficial Effects of Probiotics on Human Migraine Headache: A Literature Review. Pain Physician. 2017; 20(2):E251-E255; PM: 28158162

ABSTRACT: BACKGROUND: Recent studies have shown that migraine headache is often associated with concomitant gastrointestinal diseases. There is a higher prevalence of headaches in patients with gastrointestinal disorders. These associations between migraine and gastrointestinal disorders suggest a potential link to a bidirectional modulation of gut microbiota and brain function. The underlying working mechanistic links between migraine and gastrointestinal diseases may include increased intestinal epithelial permeability and inflammation. *OBJECTIVE*: This review presents an overview of the relationship between gut microbiota and brain function, especially with regard to migraine headache. *STUDY DESIGN*: Literature review. *SETTING*: Anesthesia and Operation Center, Department of Anesthesiology, Chinese PLA General Hospital. *METHODS*: The present investigation included a PubMed search using the following terms: migraine headache, gut microbiota, brain function, and probiotics. RESULTS: In this literature review, we mainly discussed the relationship between gut microbiota and brain function, especially with regard to migraine headache. The potential effects of probiotics supplement on migraine headache were also included. *LIMITATIONS*: There is limited evidence from clinical studies of the positive effects of probiotics in patients with migraine headache. Large-scale randomized, placebo-controlled clinical trials are warranted to evaluate the clinical efficacy and safety of probiotics in patients with migraine headache. *CONCLUSIONS*: Similar to migraine headache, disorders of the brain involving depression and anxiety have been demonstrated to be associated with increased gut permeability. An improvement in gut microbiota and reduction of inflammation can have positive effects on strengthening gut and brain function. Moreover, it can be inferred that probiotics may have a beneficial effect on the frequency and severity of migraine headache attacks. Large-scale randomized, placebo-controlled studies are warranted in the future to evaluate the clinical efficacy and safety of probiotics in patients with migraine headache.Key words: Migraine headache, gut microbiota, brain function, probiotics.

Dalal, R., McGee, R. G., Riordan, S. M., and Webster, A. C. Probiotics for people with hepatic encephalopathy. Cochrane.Database.Syst.Rev. 2-23-2017; 2:CD008716; PM: 28230908

ABSTRACT: BACKGROUND: Hepatic encephalopathy is a disorder of brain function as a result of liver failure or portosystemic shunt or both. Both hepatic encephalopathy (clinically overt) and minimal hepatic encephalopathy (not clinically overt) significantly impair patient's quality of life and daily functioning, and represent a significant burden on healthcare resources. Probiotics are live micro-organisms, which when administered in adequate amounts, may confer a health benefit on the host. *OBJECTIVES*: To determine the beneficial and harmful effects of probiotics in any dosage, compared with placebo or no intervention, or with any other treatment for people with any grade of acute or chronic hepatic encephalopathy. This review did not consider the primary prophylaxis of hepatic encephalopathy. *SEARCH METHODS*: We searched The Cochrane Hepato-Biliary Group Controlled Trials Register, CENTRAL, MEDLINE, Embase, Science Citation Index Expanded, conference proceedings, reference lists of included trials, and the World Health Organization International Clinical Trials Registry Platform until June 2016. *SELECTION CRITERIA*: We included randomised clinical trials that compared probiotics in any dosage with placebo or no intervention, or with any other treatment in people with hepatic encephalopathy. *DATA COLLECTION AND ANALYSIS*: We used standard methodological procedures expected by The Cochrane Collaboration. We conducted random-effects model meta-analysis due to obvious heterogeneity of participants and interventions. We defined a P value of 0.05 or less as significant. We expressed dichotomous outcomes as risk ratio (RR) and continuous outcomes as mean difference (MD) with 95% confidence intervals (CI). *MAIN RESULTS*: We included 21 trials with 1420 participants, of these, 14 were new trials. Fourteen trials compared a probiotic with placebo or no treatment, and seven trials compared a probiotic with lactulose. The trials used a variety of probiotics; the most commonly used group of probiotic was VSL#3, a proprietary name for a group of eight probiotics. Duration of administration ranged from 10 days to 180 days. Eight trials declared their funding source, of which six were independently funded and two were industry funded. The remaining 13 trials did not disclose their funding source. We classified 19 of the 21 trials at high risk of bias.We found no effect on all-cause mortality when probiotics were compared with placebo or no treatment (7 trials; 404 participants; RR 0.58, 95% CI 0.23 to 1.44; low-quality evidence). No-recovery (as measured by incomplete resolution of symptoms) was lower for participants treated with probiotic (10 trials; 574 participants; RR 0.67, 95% CI 0.56 to 0.79; moderate-quality evidence). Adverse events were lower for participants treated with probiotic than with no intervention when considering the development of overt hepatic encephalopathy (10 trials; 585 participants; RR 0.29, 95% CI 0.16 to 0.51; low-quality evidence), but effects on hospitalisation and change of/or withdrawal from treatment were uncertain (hospitalisation: 3 trials, 163 participants; RR 0.67, 95% CI 0.11 to 4.00; very low-quality evidence; change of/or withdrawal from treatment: 9 trials, 551 participants; RR 0.70, 95% CI 0.46 to 1.07; very low-quality evidence). Probiotics may slightly improve quality of life compared with no intervention (3 trials; 115 participants; results not meta-analysed; low-quality evidence). Plasma ammonia concentration was lower for participants treated with probiotic (10 trials; 705 participants; MD -8.29 mumol/L, 95% CI -13.17 to -3.41; low-quality evidence). There were no reports of septicaemia attributable to probiotic in any trial.When probiotics were compared with lactulose, the effects on all-cause mortality were uncertain (2 trials; 200 participants; RR 5.00, 95% CI 0.25 to 102.00; very low-quality evidence); lack of recovery (7 trials; 430 participants; RR 1.01, 95% CI 0.85 to 1.21; very low-quality evidence); adverse events considering the development of overt hepatic encephalopathy (6 trials; 420 participants; RR 1.17, 95% CI 0.63 to 2.17; very low-quality evidence); hospitalisation (1 trial; 80 participants; RR 0.33, 95% CI 0.04 to 3.07;

very low-quality evidence); intolerance leading to discontinuation (3 trials; 220 participants; RR 0.35, 95% CI 0.08 to 1.43; very low-quality evidence); change of/or withdrawal from treatment (7 trials; 490 participants; RR 1.27, 95% CI 0.88 to 1.82; very low-quality evidence); quality of life (results not meta-analysed; 1 trial; 69 participants); and plasma ammonia concentration overall (6 trials; 325 participants; MD -2.93 mumol/L, 95% CI -9.36 to 3.50; very low-quality evidence). There were no reports of septicaemia attributable to probiotic in any trial. *AUTHORS' CONCLUSIONS*: The majority of included trials suffered from a high risk of systematic error ('bias') and a high risk of random error ('play of chance'). Accordingly, we consider the evidence to be of low quality. Compared with placebo or no intervention, probiotics probably improve recovery and may lead to improvements in the development of overt hepatic encephalopathy, quality of life, and plasma ammonia concentrations, but probiotics may lead to little or no difference in mortality. Whether probiotics are better than lactulose for hepatic encephalopathy is uncertain because the quality of the available evidence is very low. High-quality randomised clinical trials with standardised outcome collection and data reporting are needed to further clarify the true efficacy of probiotics.

Daliri, E. B., Lee, B. H., and Oh, D. H. Current Perspectives on Antihypertensive Probiotics. Probiotics.Antimicrob.Proteins. 2017; 9(2):91-101; PM: 27900619

ABSTRACT: Hypertension is a major risk factor for cardiovascular diseases. Optimizing blood pressure results in an overall health outcome. Over the years, the gut microbiota has been found to play a significant role in host metabolic processes, immunity, and physiology. Dietary strategies have therefore become a target for restoring disturbed gut microbiota to treat metabolic diseases. Probiotics and their fermented products have been shown in many studies to lower blood pressure by suppressing nitrogen oxide production in microphages, reducing reactive oxygen species, and enhancing dietary calcium absorption. Other studies have shown that hypertension could be caused by many factors including hypercholesterolemia, chronic inflammation, and inconsistent modulation of the renin-angiotensin system. This review discusses the antihypertensive roles of probiotics and their fermented products via the reduction of serum cholesterol levels, anti-inflammation, and inhibition of angiotensin-converting enzyme. The ability of recombinant probiotics to reduce high blood pressure has also been discussed.

Dalziel, J. E., Anderson, R. C., Peters, J. S., Lynch, A. T., Spencer, N. J., Dekker, J., and Roy, N. C. Promotility Action of the Probiotic Bifidobacterium lactis HN019 Extract Compared with Prucalopride in Isolated Rat Large Intestine. Front Neurosci. 2017; 11:20; PM: 28184185

ABSTRACT: Attention is increasingly being focussed on probiotics as potential agents to restore or improve gastrointestinal (GI) transit. Determining mechanism of action would support robust health claims. The probiotic bacterium Bifidobacterium lactis HN019 reduces transit time, but its mechanisms of action and effects on motility patterns are poorly understood. The aim of this study was to investigate changes in GI motility induced by an extract of HN019 on distinct patterns of colonic motility in isolated rat large intestine, compared with a known promotility modulator, prucalopride. The large intestines from male Sprague Dawley rats (3-6 months) were perfused with Kreb's buffer at 37 degrees C in an oxygenated tissue bath. Isometric force transducers recorded changes in circular muscle activity at four independent locations assessing contractile propagation between the proximal colon and the rectum. HN019 extract was perfused through the tissue bath and differences in tension and frequency quantified relative to pre-treatment controls. Prucalopride (1 muM) increased the frequency of propagating

contractions (by 75 +/- 26%) in the majority of preparations studied (10/12), concurrently decreasing the frequency of non-propagating contractions (by 50 +/- 11%). HN019 extract had no effect on contractile activity during exposure (n = 8). However, following wash out, contraction amplitude of propagating contractions increased (by 55 +/- 18%) in the distal colon, while the frequency of non-propagating proximal contractions decreased by 57 +/- 7%. The prokinetic action of prucalopride increased the frequency of synchronous contractions along the length of colon, likely explaining increased colonic rate of transit in vivo. HN019 extract modified motility patterns in a different manner by promoting propagating contractile amplitude and inhibiting non-propagations, also demonstrating prokinetic activity consistent with the reduction of constipation by B. lactis HN019 in humans.

Damaceno, Q. S., Souza, J. P., Nicoli, J. R., Paula, R. L., Assis, G. B., Figueiredo, H. C., Azevedo, V., and Martins, F. S. Evaluation of Potential Probiotics Isolated from Human Milk and Colostrum. Probiotics.Antimicrob.Proteins. 4-3-2017; PM: 28374172

ABSTRACT: Several studies have demonstrated a diversity of bacterial species in human milk, even in aseptically collected samples. The present study evaluated potential probiotic bacteria isolated from human milk and associated maternal variables. Milk samples were collected from 47 healthy women and cultured on selective and universal agar media under aerobic and anaerobic conditions. Bacterial isolates were counted and identified by Biotyper Matrix-Assisted Laser Desorption Ionization-Time of Flight mass spectrometry and then tested for probiotic properties. Total bacteria in human milk ranged from 1.5 to 4.0 log10 CFU/mL. The higher bacterial counts were found in colostrum (mean = 3.9 log10 CFU/mL, 95% CI 3.14-4.22, p = 0.00001). The most abundant species was Staphylococcus epidermidis (n = 76). The potential probiotic candidates were Lactobacillus gasseri (n = 4), Bifidobacterium breve (n = 1), and Streptococcus salivarius (n = 4). Despite the small sample size, L. gasseri was isolated only in breast milk from mothers classified into a normal weight range and after a vaginally delivered partum. No potential probiotics showed antagonism against pathogens, but all of them agglutinated different pathogens. Nine bacterial isolates belonging to the species L. gasseri, B. breve, and S. salivarius were selected as potential probiotics. The present study confirms the presence in breast milk of a bacterial microbiota that could be the source of potential probiotic candidates to be used in the formula of simulated maternal milk.

Damm, J. A., Smith, B., Greisen, G., Krogfelt, K. A., Clausen, M. L., and Agner, T. The influence of probiotics for preterm neonates on the incidence of atopic dermatitis-results from a historically controlled cohort study. Arch.Dermatol.Res. 2017; 309(4):259-264; PM: 28271213

ABSTRACT: Probiotic supplementation is a promising preventive strategy for atopic dermatitis (AD). To help clarifying the significance of timing with respect to prevention of AD, we here evaluate the benefit of prophylactic use of probiotic supplementation in neonates younger than 30 weeks of gestation. Preterm children from the Department of Neonatology, Rigshospitalet, Denmark from two different admission periods were included in a historically controlled cohort study. Neonates from January 2007 to February 2010, not treated with and neonates from March 2010 to February 2013 treated with probiotic were enrolled. Main outcome was prevalence of AD, and secondary outcomes were use of topical corticosteroids, and number of skin-related visits to GPs and dermatologists. 527 preterm neonates were included in the study, 249 treated and

278 not treated with probiotics. Response rate for the two cohorts was 76.7 and 77.7% respectively. The prevalence of AD was similar in the two groups (20.9% in the probiotic treated group versus 17.1% in the not treated group, p = 0.33). No significant differences were found between the groups with respect to treatment with topical corticosteroids, or visits at GPs or dermatologist. We found no indication that probiotics may prevent AD when administered to neonates <30 gestation weeks from birth until discharge home. Factors influencing the early maturation of the immune system have been assumed to be of particular importance in atopic dermatitis, and hence, our unique cohorts contribute information on how probiotic supplementation may affect the extremely immature immune systems of preterm infants.

Danilo, C. A., Constantopoulos, E., McKee, L. A., Chen, H., Regan, J. A., Lipovka, Y., Lahtinen, S., Stenman, L. K., Nguyen, T. V., Doyle, K. P., Slepian, M. J., Khalpey, Z. I., and Konhilas, J. P. Bifidobacterium animalis subsp. lactis 420 mitigates the pathological impact of myocardial infarction in the mouse. Benef.Microbes. 4-26-2017; 8(2):257-269; PM: 28409534

ABSTRACT: There is a growing appreciation that our microbial environment in the gut plays a critical role in the maintenance of health and the pathogenesis of disease. Probiotic, beneficial gut microbes, administration can directly attenuate cardiac injury and post-myocardial infarction (MI) remodelling, yet the mechanisms of cardioprotection are unknown. We hypothesised that administration of Bifidobacterium animalis subsp. lactis 420 (B420), a probiotic with known anti-inflammatory properties, to mice will mitigate the pathological impact of MI, and that anti-inflammatory T regulatory (Treg) immune cells are necessary to impart protection against MI as a result of B420 administration. Wild-type male mice were administered B420, saline or Lactobacillus salivarius 33 (Ls-33) by gavage daily for 14 or 35 days, and underwent ischemia/reperfusion (I/R). Pretreatment with B420 for 10 or 28 days attenuated cardiac injury from I/R and reduced levels of inflammatory markers. Depletion of Treg cells by administration of anti-CD25 monoclonal antibodies eliminated B420-mediated cardio-protection. Further cytokine analysis revealed a shift from a pro-inflammatory to an anti-inflammatory environment in the probiotic treated post-MI hearts compared to controls. To summarise, B420 administration mitigates the pathological impact of MI. Next, we show that Treg immune cells are necessary to mediate B420-mediated protection against MI. Finally, we identify putative cellular, epigenetic and/or post-translational mechanisms of B420-mediated protection against MI.

Darbaky, Y., Evrard, B., Patrier, S., Falenta, J., Garcin, S., Tridon, A., Dapoigny, M., Silberberg, C., Nivoliez, A., and Diop, L. Oral probiotic treatment of Lactobacillus rhamnosus Lcr35(R) prevents visceral hypersensitivity to a colonic inflammation and an acute psychological stress. J.Appl.Microbiol. 2017; 122(1):188-200; PM: 27718511

ABSTRACT: *AIMS*: This study evaluated the efficacy of a repeated oral treatment with two active pharmaceutical ingredients (Lcr Lenio(R) and Lcr Restituo(R)) derivated from the probiotic bacterial strain Lactobacillus rhamnosus Lcr35(R) in two animal models mimicking different features of irritable bowel syndrome (IBS). IBS is characterized by visceral pain associated with alteration of bowel transit. IBS patients present visceral hypersensitivity with peripheral and central origins. *METHODS AND RESULTS*: The injection of 2,4,6-trinitrobenzenesulfonic acid (TNBS) into the proximal colon as well as an acute

partial restraint stress (PRS) produces colonic hypersensitivity measured in conscious rats by a decrease in pain threshold in response to distal colonic distension. Visceral hypersensitivity was produced by injection of TNBS 7 days before colonic distension or by acute PRS on testing day. Treatments were performed once a day during eight consecutive days. *CONCLUSIONS*: This study indicates that an 8-day probiotic treatment (Lcr Lenio and Lcr Restituo) produces an antihypersensitivity activity in both TNBS and PRS visceral pain models. As this probiotic strain attenuates peripherally and centrally induced visceral hypersensitivity in rats, it may be active in treatment of IBS symptoms. An immunomodulatory effect of the probiotics was highlighted in the TNBS model on the IL-23 secretion, suggesting a mechanism of action involving a regulation of the local IL-23/Th17 immune activation. *SIGNIFICANCE AND IMPACT OF THE STUDY*: Two formulas of Lcr35(R) probiotic strain show very encouraging results for the treatment of IBS patients. Further studies are needed to better understand the role and mechanisms of probiotics on the pathogenesis of IBS.

Dawood, M. A., Koshio, S., Ishikawa, M., El-Sabagh, M., Yokoyama, S., Wang, W. L., Yukun, Z., and Olivier, A. Physiological response, blood chemistry profile and mucus secretion of red sea bream (Pagrus major) fed diets supplemented with Lactobacillus rhamnosus under low salinity stress. Fish.Physiol Biochem. 2017; 43(1):179-192; PM: 27542150

ABSTRACT: Environmental stressors caused by inadequate aquaculture management strategies suppress the immune response of fish and make them more susceptible to diseases. Therefore, efforts have been made to relieve stress in fish by using various functional feed additives in the diet, including probiotics. The present work evaluates the effects of Lactobacillus rhamnosus (LR) on physiological stress response, blood chemistry and mucus secretion of red sea bream (Pagrus major) under low salinity stress. Fish were fed four diets supplemented with LR at [0 (LR0), 1 x 102 (LR1), 1 x 104 (LR2) and 1 x 106 (LR3) cells g-1] for 56 days. Before stress, blood cortisol, urea nitrogen (BUN) and total bilirubin (T-BIL) showed no significant difference ($P > 0.05$), whereas plasma glucose and triglyceride (TG) of fish-fed LR2 and LR3 diets were significantly lower ($P < 0.05$) than those of the other groups. Plasma total cholesterol (T-CHO) of fish-fed LR3 diet was significantly ($P < 0.05$) lower than that of the other groups. Furthermore, total plasma protein, mucus myeloperoxidase activity and the amount of mucus secretion were significantly enhanced in LR-supplemented groups when compared with the control group ($P < 0.05$). After the application of the low salinity stress test, plasma cortisol, glucose, T-CHO and TG contents in all groups showed an increased trend significantly ($P < 0.01$) compared to the fish before the stress challenge. However, plasma total protein and the amount of secreted mucus showed a decreased trend in all groups. On the other hand, BUN, T-BIL and mucus myeloperoxidase activity showed no significant difference after exposure to the low salinity stress ($P > 0.05$). In addition, the fish that received LR-supplemented diets showed significantly higher tolerance against low salinity stress than the fish-fed LR-free diet ($P < 0.05$). The physiological status and the detected immune responses, including total plasma protein and mucus myeloperoxidase activity in red sea bream, will provide a more comprehensive outlook of the effects of probiotics to relieve stress in fish.

de Llano, D. G., Arroyo, A., Cardenas, N., Rodriguez, J. M., Moreno-Arribas, M. V., and Bartolome, B. Strain-specific inhibition of the adherence of uropathogenic bacteria to bladder cells by probiotic Lactobacillus spp. Pathog.Dis. 6-1-2017; 75(4); PM: 28402532

ABSTRACT: Urinary tract infections (UTIs), one of most common infections worldwide, face high recurrence rates and increasing antimicrobial resistance. Probiotic bacteria, especially of the genus Lactobacillus, are considered a promising preventive and/or treatment therapy against UTIs. In order to elucidate the mechanisms involved in these beneficial effects, we studied the impact of different Lactobacillus strains (Lactobacillus salivarius UCM572, L. plantarum CLC17 and L. acidophilus 01) in the adherence of reference and clinical uropathogenic strains (Escherichia coli ATCC(R) 53503, E. coli 10791, Enterococcus faecalis 04-1, En. faecalis 08-1 and Staphylococcus epidermidis 08-3) to T24 epithelial bladder cells. In general, the Lactobacillus strains with previous in vivo evidence of beneficial effects against UTIs (L. salivarius UCM572 and L. acidophilus 01) significantly inhibited the adherence of the five uropathogens to T24 cells, displaying percentages of inhibition ranging between 22.2% and 43.9%, and between 16.5% and 53.7%, respectively. On the other hand, L. plantarum CLC17, a strain with no expected effects on UTIs, showed almost negligible anti-adherence effects.Therefore, these in vitro results suggest that inhibition of the adherence of uropathogens to epithelial bladder cells may be one of the mechanisms involved in the potential beneficial effects of probiotics against UTIs in vivo.

De, Angelis M., Garruti, G., Minervini, F., Bonfrate, L., Portincasa, P., and Gobbetti, M. The food-gut human axis: the effects of diet on gut microbiota and metabolome. Curr.Med.Chem. 4-27-2017; PM: 28462705

ABSTRACT: Gut microbiota, the largest symbiont community hosted in human organism, is emerging as a pivotal player in the relationship between dietary habits and health. Oral and, especially, intestinal microbes metabolize dietary components, affecting human health by producing harmful or beneficial metabolites, which are involved in the incidence and progression of several intestinal related and non-related diseases. Habitual diet (Western, Agrarian and Mediterranean omnivore diets, vegetarian, vegan and gluten-free diets) drives the composition of the gut microbiota and metabolome. Within the dietary components, polymers (mainly fibers, proteins, fat and polyphenols) that are not hydrolyzed by human enzymes seem to be the main leads of the metabolic pathways of gut microbiota, which in turn directly influences the human metabolome. Specific relationships between diet and microbes, microbes and metabolites, microbes and immune functions and microbes and/or their metabolites and some human diseases are being established. Dietary treatments with fibers are the most effective to benefit the metabolome profile, by improving the synthesis of short chain fatty acids and decreasing the level of molecules, such as p-cresyl sulfate, indoxyl sulfate and trimethylamine N-oxide, involved in disease state. Based on the axis diet-microbiota-health, this review aims at describing the most recent knowledge oriented towards a profitable use of diet to provide benefits to human health, both directly and indirectly, through the activity of gut microbiota.

de, Timary P., Starkel, P., Delzenne, N. M., and Leclercq, S. A role for the peripheral immune system in the development of alcohol use disorders? Neuropharmacology. 4-8-2017; PM: 28400259

ABSTRACT: Preclinical studies have largely supported that alcohol-consumption induces the development of an important neuro-inflammation and this neuro-inflammation contributes to alcohol-drinking behaviors, notably through TLR4 and LPS related mechanisms. The neuro-inflammation originates from a direct interaction of ethanol with

the neuronal and immune brain cells, but also from the generation of an inflammation at the periphery. Ethanol in particular interacts with the intestine to develop a gut dysbiosis and an increase in gut permeability, that allows the liberation of bacterial fragments to the systemic circulation and induces a pro-inflammatory response in the systemic circulation and peripheral organs, and in particular the liver. Peripheral cytokines or activated peripheral cells may cross the blood-brain barrier and activate neuro-inflammation. In humans, peripheral inflammation and intestinal dysbiosis are related to symptoms of alcohol use disorders (AUD), such as depression, anxiety and alcohol-craving, However, the dysbiosis, could also participate in a different manner to the symptomatology of the addiction, possibly by interacting with the stress system, by interfering with the sleep processes and altering the abilities for social interactions. The role of the gut suggests that interventions with probiotics or prebiotics might in the future be of interest for the treatment of the addiction.

Del'arco, A. P., Magalhaes, P., and Quilici, F. A. SIM BRASIL ST. Arq Gastroenterol. 2-23-2017; 0; PM: 28273276

ABSTRACT: BACKGROUND: Gastrointestinal symptoms seem to affect more women, due to hormonal and emotional issues, impacting the quality of life. The emotional state can affect the bowel functioning through a bidirectional communication system between the gut and the brain involving the neuroendocrine system. Altered bowel functioning and gastrointestinal symptoms can alter quality of life. *OBJECTIVE*: The SIM study aimed to describe, characterize and quantify gastrointestinal symptoms reported by Brazilian women, their causes, feelings and impact. *METHODS*: A structured electronic questionnaire was developed following qualitative phase for semantic formatting, and was administered to volunteer women in ten Brazilian cities. Descriptive and Bayesian statistics analyses were used. *RESULTS*: From the 3029 respondent, 66% reported gastrointestinal symptoms. The most prevalent symptoms were gases (46%), abdominal distention and constipation (43%). The main causes were lifestyle and eating habits. Gastrointestinal symptoms affected quality of life in most women (62%), especially constipation (mood (89%), concentration (88%) and sexual life (79%)). Most common solutions were drinking water, teas, eating foods rich in fiber and probiotics. *CONCLUSION*: Gastrointestinal symptoms are highly prevalent in Brazilian women and negatively impact different aspects of quality of life (mood, concentration and sexuality). The bowel is an important emotional catalyst that can modulate the psychologic behavior. Better understanding of the interaction between the gut and the brain should help in the management of gastrointestinal symptoms to improve women's quality of life.

Dermyshi, E., Wang, Y., Yan, C., Hong, W., Qiu, G., Gong, X., and Zhang, T. The "Golden Age" of Probiotics: A Systematic Review and Meta-Analysis of Randomized and Observational Studies in Preterm Infants. Neonatology. 2-15-2017; 112(1):9-23; PM: 28196365

ABSTRACT: BACKGROUND: Over the last few years, probiotics have been one of the most studied interventions in neonatal medicine. *OBJECTIVES*: The aim of this work was to analyse all studies (randomized controlled trials, RCTs, and observational studies) assessing the use of probiotics in very low birth weight (VLBW) preterm infants. *SEARCH METHODS*: A systematic literature search was conducted using PubMed, Embase, Cochrane Library, and Web of Science. The data from RCTs and observational studies were pooled and analysed separately. *SELECTION CRITERIA*: RCTs and observational

studies that enrolled VLBW infants with enteral administration of probiotics were considered. Extracted study data included probiotic characteristics and at least 1 clinical outcome (necrotizing enterocolitis [NEC], late-onset sepsis or all-cause mortality). *DATA COLLECTION AND ANALYSIS*: Forty-four studies were eligible for our review: 30 RCTs and 14 observational studies. Severe NEC rates (stage II or more) and all-cause mortality were reduced among the probiotic groups in both the RCTs (RR 0.57, 95% CI 0.47-0.70, and RR 0.77, 95% CI 0.65-0.92, respectively) and the observational studies (RR 0.51, 95% CI 0.37-0.70, and RR 0.71, 95% CI 0.62-0.81, respectively). Furthermore, there was a 12% reduction in the risk of sepsis in RCTs and a 19% reduction in observational studies. The meta-analysis of observational studies showed a reduction in the risk of NEC in extremely low birth weight infants. However, this was not statistically significant. *CONCLUSIONS*: This meta-analysis of RCT and observational studies found that the use of probiotics was beneficial for the prevention of severe NEC, late-onset sepsis, and all-cause mortality in VLBW infants.

Derrien, M. and Veiga, P. Rethinking Diet to Aid Human-Microbe Symbiosis. Trends Microbiol. 2017; 25(2):100-112; PM: 27916707

ABSTRACT: The spread of the Western lifestyle has been accompanied by microbial changes thought to underlie the emergence of chronic, nontransmissible, immune-related diseases. The past decade has seen the unprecedented development of therapies for 'replenishing' the microbiota of sick individuals. However, functional and ecological solutions helping the host and the gut microbiota to cope with the ecological stressors of modern life are still lacking. In this review, we discuss how recent advances in gut microbiome science are leading to the identification of microbe-derived and health-relevant metabolites. These molecules will guide the selection of the next-generation of probiotics and dietary recommendations, which should also take the resident gut microbiota into account, to optimise efficacy. These solutions for maintaining a well-functioning gut ecosystem and promoting good health should be customised, palatable, and as widely accessible as possible.

Diab, R., Canilho, N., Pavel, I. A., Haffner, F. B., Girardon, M., and Pasc, A. Silica-based systems for oral delivery of drugs, macromolecules and cells. Adv.Colloid Interface Sci. 4-20-2017; PM: 28473052

ABSTRACT: According to the US Food and Drug Administration and the European Food Safety Authority, amorphous forms of silica and silicates are generally recognized to be safe as oral delivery ingredients in amounts up to 1500mg per day. Silica is used in the formulation of solid dosage forms, e.g. tablets, as glidant or lubricant. The synthesis of silica-based materials depends on the payload nature, drug, macromolecule or cell, and on the target release (active or passive). In the literature, most of the examples deal with the encapsulation of drugs in mesoporous silica nanoparticles. Still to date limited reports concerning the delivery of encapsulated macromolecules and cells have been reported in the field of oral delivery, despite the multiple promising examples demonstrating the compatibility of the sol-gel route with biological entities, likewise the interest of silica as an oral carrier. Silica diatoms appear as an elegant, cost-effective and promising alternative to synthetic sol-gel-based materials. This review reports the latest advances silica-based systems and discusses the potential benefits and drawbacks of using silica for oral delivery of drugs, macromolecules or cells.

Dickerson, F., Severance, E., and Yolken, R. The microbiome, immunity, and schizophrenia and bipolar disorder. Brain Behav.Immun. 2017; 62:46-52; PM: 28003152

ABSTRACT: Schizophrenia and bipolar disorder are serious neuropsychiatric disorders of uncertain etiology. Recent studies indicate that immune activation may contribute to the etiopathogenesis of these disorders. Numerous studies in animal models indicate that the mucosal microbiome may influence cognition and behavior by altering the functioning of the immune system. It is thus likely that the microbiome plays a role in human psychiatric disorders. The study of immune alterations and the microbiome in schizophrenia and bipolar disorder is in its infancy. Two recent investigations of the oro-pharyngeal microbiota in schizophrenia found differences between cases and controls. Other studies have found increased gastrointestinal inflammation in schizophrenia and bipolar disorder based on measures of microbial translocation. Several studies have also found an association between the receipt of antibiotics and an increased incidence of psychiatric disorders, perhaps due to alterations in the microbiome. Studies to characterize the intestinal microbiome of individuals with these disorders are in progress. The ultimate test of the role of the microbiome and immune-mediated pathology in schizophrenia and bipolar disorder will come from clinical trials of therapeutic agents which alter gut microbiota or gastrointestinal inflammation. The successful development of such modalities would represent a novel strategy to prevent and treat serious psychiatric disorders.

Dimidi, E., Christodoulides, S., Scott, S. M., and Whelan, K. Mechanisms of Action of Probiotics and the Gastrointestinal Microbiota on Gut Motility and Constipation. Adv.Nutr. 2017; 8(3):484-494; PM: 28507013

ABSTRACT: Constipation is a common and burdensome gastrointestinal disorder that may result from altered gastrointestinal motility. The effect of probiotics on constipation has been increasingly investigated in both animal and human studies, showing promising results. However, there is still uncertainty regarding the mechanisms of action of probiotics on gut motility and constipation. Several factors are vital to normal gut motility, including immune and nervous system function, bile acid metabolism and mucus secretion, and the gastrointestinal microbiota and fermentation; an imbalance or dysfunction in any of these components may contribute to aberrant gut motility and, consequently, symptoms of constipation. For example, adults with functional constipation have significantly decreased numbers of bifidobacteria (with one study showing a mean difference of 1 log10/g) and lactobacilli (mean difference, 1.4 log10/g) in stool samples, as well as higher breath methane, compared with control subjects. Modifying the gut luminal environment with certain probiotic strains may affect motility and secretion in the gut and, hence, provide a benefit for patients with constipation. Therefore, this review explores the mechanisms through which probiotics may exert an effect on gut motility and constipation. Nevertheless, the majority of current evidence is derived from animal studies, and therefore, further human studies are needed to determine the mechanisms through specific probiotic strains that might be effective in constipation.

Dinan, T. G. and Cryan, J. F. The Microbiome-Gut-Brain Axis in Health and Disease. Gastroenterol.Clin.North Am. 2017; 46(1):77-89; PM: 28164854

ABSTRACT: Gut microbes are capable of producing most neurotransmitters found in the human brain. Evidence is accumulating to support the view that gut microbes influence central neurochemistry and behavior. Irritable bowel syndrome is regarded as the prototypic disorder of the brain-gut-microbiota axis that can be responsive to probiotic therapy. Translational studies indicate that certain bacteria may have an impact on stress responses and cognitive functioning. Manipulating the gut microbiota with psychobiotics, prebiotics, or even antibiotics offers a novel approach to altering brain function and treating gut-brain axis disorders, such as depression and autism.

Dinan, T. G. and Cryan, J. F. Microbes, Immunity, and Behavior: Psychoneuroimmunology Meets the Microbiome. Neuropsychopharmacology. 2017; 42(1):178-192; PM: 27319972

ABSTRACT: There is now a large volume of evidence to support the view that the immune system is a key communication pathway between the gut and brain, which plays an important role in stress-related psychopathologies and thus provides a potentially fruitful target for psychotropic intervention. The gut microbiota is a complex ecosystem with a diverse range of organisms and a sophisticated genomic structure. Bacteria within the gut are estimated to weigh in excess of 1 kg in the adult human and the microbes within not only produce antimicrobial peptides, short chain fatty acids, and vitamins, but also most of the common neurotransmitters found in the human brain. That the microbial content of the gut plays a key role in immune development is now beyond doubt. Early disruption of the host-microbe interplay can have lifelong consequences, not just in terms of intestinal function but in distal organs including the brain. It is clear that the immune system and nervous system are in continuous communication in order to maintain a state of homeostasis. Significant gaps in knowledge remain about the effect of the gut microbiota in coordinating the immune-nervous systems dialogue. However, studies using germ-free animals, infective models, prebiotics, probiotics, and antibiotics have increased our understanding of the interplay. Early life stress can have a lifelong impact on the microbial content of the intestine and permanently alter immune functioning. That early life stress can also impact adult psychopathology has long been appreciated in psychiatry. The challenge now is to fully decipher the molecular mechanisms that link the gut microbiota, immune, and central nervous systems in a network of communication that impacts behavior patterns and psychopathology, to eventually translate these findings to the human situation both in health and disease. Even at this juncture, there is evidence to pinpoint key sites of communication where gut microbial interventions either with drugs or diet or perhaps fecal microbiota transplantation may positively impact mental health.

Djaldetti, M. and Bessler, H. Probiotic strains modulate cytokine production and the immune interplay between human peripheral blood mononucear cells and colon cancer cells. FEMS Microbiol.Lett. 2-1-2017; 364(3); PM: 28104778

ABSTRACT: Human health is tightly connected with a great number of gut microbial cells designated as microbiome or microbiota. We have examined the effect of six microbial strains (MS) included in a commercial probiotic on cytokine production by human peripheral blood mononuclear cells (PBMC) and on their immune dialog with colon carcinoma cells. Non-stimulated and lipopolysaccharide (LPS)-stimulated PBMC were incubated for 24 h with MS. The secretion of tumor necrosis factor alpha (TNFalpha), IL-1beta, IL-6, interferon gamma, IL-10 and IL-1ra and the effect of MS on the immune

interplay between PBMC and cells from HT-29 and RKO colon carcinoma lines were evaluated. MS incubated with non-stimulated PBMC induced high expression of all cytokines examined, whereas in those stimulated by LPS, variability in the results was observed. MS added to PBMC co-cultivated with HT-29 or RKO colon cancer cells resulted in downregulation of most cytokines except IL-6 and TNFalpha, and enhanced production of TNFalpha and IL-1beta. The MS incorporated in the probiotic affected PBMC' cytokine production and altered the cross-talk between immune and colon cancer cells. The results may clarify the way by which probiotics modify the intestinal environment resulting in a decline of colon cancer development.

Djurasevic, S., Jama, A., Jasnic, N., Vujovic, P., Jovanovic, M., Mitic-Culafic, D., Knezevic-Vukcevic, J., Cakic-Milosevic, M., Ilijevic, K., and Djordjevic, J. The Protective Effects of Probiotic Bacteria on Cadmium Toxicity in Rats. J.Med.Food. 2017; 20(2):189-196; PM: 27976972

ABSTRACT: One of the useful properties of probiotic bacteria is their capacity to bind different targets, thus eliminating them through feces. It is supposed that one of these targets could be cadmium, a widespread environmental toxicant that causes various disturbances in biological systems. This study examined the protective effects of probiotic supplementation against cadmium-induced toxicity in the rat. The experiment was conducted in the course of 5 weeks. Animals were divided into four groups: (1) controls, (2) probiotics treated, (3) cadmium treated, and (4) probiotics + cadmium treated. The cadmium concentration was measured in the blood, liver, kidney, and feces, as well as the blood alanine aminotransferase (ALT) and aspartate aminotransferase (AST) as biomarkers of the liver function. Histomorphological changes in the liver and kidney were also determined. Our results revealed that probiotics combined with cadmium increase this metal concentration in feces. As a result, blood, liver, and kidney Cd levels, as well as blood ALT and AST activities were lessened compared to the rat group treated with cadmium only. Besides, probiotics consumed simultaneously with cadmium attenuated histomorphological changes in the liver and kidney caused by cadmium. The rise in lactobacilli number in feces of rats treated simultaneously with cadmium and probiotics results in strong correlation with the increase of Cd concentration in their feces and the decrease of Cd concentration in their blood. We speculate that probiotics actively contribute to cadmium excretion through feces, probably, by its binding to their bacterial cell wall.

Do, J., Zafar, H., and Saier, M. H., Jr. Comparative genomics of transport proteins in probiotic and pathogenic Escherichia coli and Salmonella enterica strains. Microb.Pathog. 3-24-2017; 107:106-115; PM: 28344124

ABSTRACT: Escherichia coli is a genetically diverse species that can be pathogenic, probiotic, commensal, or a harmless laboratory strain. Pathogenic strains of E. coli cause urinary tract infections, diarrhea, hemorrhagic colitis, and pyelonephritis, while the two known probiotic E. coli strains combat inflammatory bowel disease and play a role in immunomodulation. Salmonella enterica, a close relative of E. coli, includes two important pathogenic serovars, Typhi and Typhimurium, causing typhoid fever and enterocolitis in humans, respectively, with the latter strain also causing a lethal typhoid fever-like disease in mice. In this study, we identify the transport systems and their substrates within seven E. coli strains: two probiotic strains, two extracellular pathogens, two intracellular pathogens, and K-12, as well as the two intracellular pathogenic S.

enterica strains noted above. Transport systems characteristic of each probiotic or pathogenic species were thus identified, and the tabulated results obtained with all of these strains were compared. We found that the probiotic and pathogenic strains generally contain more iron-siderophore and sugar transporters than E. coli K-12. Pathogens have increased numbers of pore-forming toxins, protein secretion systems, decarboxylation-driven Na+ exporters, electron flow-driven monovalent cation exporters, and putative transporters of unknown function compared to the probiotic strains. Both pathogens and probiotic strains encode metabolite transporters that reflect their intracellular versus extracellular environments. The results indicate that the probiotic strains live extracellularly. It seems that relatively few virulence factors can convert a beneficial or commensal microorganism into a pathogen. Taken together, the results reveal the distinguishing features of these strains and provide a starting point for future engineering of beneficial enteric bacteria.

Donders, G. G. G., Bellen, G., Grinceviciene, S., Ruban, K., and Vieira-Baptista, P. Aerobic vaginitis: no longer a stranger. Res.Microbiol. 5-11-2017; PM: 28502874

ABSTRACT: Aerobic vaginitis (AV) is the name given in 2002 to a vaginal infectious entity which was not recognized as such before. It is characterized by abnormal (dysbiotic) vaginal microflora containing aerobic, enteric bacteria, variable levels of vaginal inflammation and deficient epithelial maturation. Although AV and bacterial vaginosis (BV) share some characteristics, such as a diminished number or absence of lactobacilli, increased discharge (fishy smelling in BV, while in severe forms of AV, a foul, rather rotten smell may be present) and increased pH (often more pronounced in AV), there are also striking differences between the two. There is no inflammation in women with BV, whereas the vagina of women with AV often appears red and edematous, and may even display small erosions or ulcerations. The color of the discharge in BV is usually whitish or gray and of a watery consistency, whereas in AV it is yellow to green and rather thick and mucoid. Women with BV do not have dyspareunia, while some women with AV do. Finally, the microscopic appearance differs in various aspects, such as the presence of leucocytes and parabasal or immature epithelial cells in AV and the absence of the granular aspect of the microflora, typical of BV. Despite all these differences, the distinction between AV and BV was not recognized in many former studies, leading to incomplete and imprecise diagnostic workouts and erroneous management of patients in both clinical and research settings. The prevalence of AV ranges between 7 and 12%, and is therefore less prevalent than BV. Although still largely undiagnosed, many researchers and clinicians increasingly take it into account as a cause of symptomatic vaginitis. AV can co-occur with other entities, such as BV and candidiasis. It can be associated with dyspareunia, sexually transmitted infections (such as human papilloma virus, human immunodeficiency virus, Trichomonas vaginalis and Chlamydia trachomatis), chorioamnionitis, fetal infection, preterm birth and cervical dysplasia. Many other possible pathological associations are currently under investigation. The diagnosis of AV is made using wet mount microscopy, ideally using phase contrast. An AV score is calculated, according to: lactobacillary grade, presence of inflammation, proportion of toxic leucocytes, characteristics of the microflora and presence of immature epithelial cells. To circumvent the hurdle of microscopic investigation, some groups have begun to develop nucleic-acid-based and enzymatic diagnostic tests, but the detailed information obtained with phase contrast microscopy is irreplaceable. The best treatment is not yet fully determined, but it must be tailored according to the microscopic findings and the patient's needs. There is a role for local

estrogen therapy, corticosteroids, antimicrobials and probiotics. Further research will reveal more precise data on diagnosis, pathogenesis, management and prevention.

Dong, J. L., Yu, X., Dong, L. E., and Shen, R. L. In vitro fermentation of oat beta-glucan and hydrolysates by fecal microbiota and selected probiotic strains. J.Sci.Food Agric. 2-28-2017; PM: 28244112

ABSTRACT: BACKGROUND: Emerging evidence suggested that the prebiotic ability of beta-glucan was intimately related to its molecular weight (Mw). However, the effect of oat beta-glucan with differing Mw on gut homeostasis was inconsistent. Importantly, knowledge of the fermentation properties of oat beta-glucan fractions was still limited. The present study aimed to evaluate the prebiotic potential of raw and hydrolyzed oat beta-glucan during in vitro fermentation by fecal microbiota and selected probiotic strains. *RESULTS*: The results obtained showed that both oat beta-glucan (OG) and hydrolysates (OGH) comparably promoted the growth of fecal Lactobacillus counts ($P < 0.05$). Importantly, OGH revealed greater fermentability compared to OG as denoted by lower pH value and higher short-chain fatty acid concentration ($P < 0.05$). Moreover, OGH was found to be more favorable to provide growth substrates for Lactobacillus helveticus R389 (LR389), Lactobacillus rhamnosus GG ATCC 53103 (LGG) and Bifidobacterium longum BB536 (BB536) than OG, and was preferentially utilized by LR389, LGG and BB536 as the sole carbon source. *CONCLUSION*: The results of the present study indicate that oat beta-glucan hydrolysates could serve as a more promising material for developing novel symbiotic foods. (c) 2017 Society of Chemical Industry.

Dos Reis, S. A., da Conceicao, L. L., Siqueira, N. P., Rosa, D. D., da Silva, L. L., and Peluzio, M. D. Review of the mechanisms of probiotic actions in the prevention of colorectal cancer. Nutr.Res. 2017; 37:1-19; PM: 28215310

ABSTRACT: The purpose of this review is to discuss the potential mechanisms of probiotics action in colorectal cancer prevention. In this regard, the composition of the intestinal microbiota is considered as an important risk factor in the development of colorectal cancer, and probiotics are able to positively modulate the composition of this microbiota. Studies have shown that the regular consumption of probiotics could prevent the development of colorectal cancer. In this respect, in vitro and experimental studies suggest some potential mechanisms responsible for this anticarcinogenic action. The mechanisms include modification of the intestinal microbiota composition, changes in metabolic activity of the microbiota, binding and degradation of carcinogenic compounds present in the intestinal lumen, production of compounds with anticarcinogenic activity, immunomodulation, improvement of the intestinal barrier, changes in host physiology, inhibition of cell proliferation, and induction of apoptosis in cancer cells. In contrast, very few reports demonstrate adverse effects of probiotic oral supplementation. In light of the present evidence, more specific studies are needed on probiotic bacteria, especially regarding the identification of the bacterial strains with greater anticarcinogenic potential; the verification of the viability of these strains after passing through the gastrointestinal tract; the investigation of potential adverse effects in immunocompromised individuals; and finally establishing the dosage and frequency of use.

Dos Santos Pereira Andrade AC, Lima, M. T., Oliveira, G. P., Calixto, R. S., de Sales E Souza EL, da Gloria de, Souza D., de Almeida Leite, C. M., Ferreira, J. M., Kroon, E. G., de Oliveira, D. B.,

Dos Santos, Martins F., and Abrahao, J. S. Daily ingestion of the probiotic Lactobacillus paracasei ST11 decreases Vaccinia virus dissemination and lethality in a mouse model. Benef.Microbes. 2-7-2017; 8(1):73-80; PM: 27873547

ABSTRACT: Vaccinia virus (VACV) is an important pathogen. Although studies have shown relationships between probiotics and viruses, the effect of probiotics on VACV infection is unknown. Therefore, this work aims to investigate the probiotics effects on VACV infection. Mice were divided into four groups, two non-infected groups, one receiving the probiotic, the other one not receiving it, and two groups infected intranasally with VACV Western Reserve (VACV-WR) receiving or not receiving the probiotic. Viral titres in organs and cytokine production in the lungs were analysed. Lung samples were also subjected to histological analysis. The intake of probiotic results in reduction in viral spread with a significant decrease of VACV titer on lung, liver and brain of treated group. In addition,treatment with the probiotic results in attenuated mice lung inflammation showing fewer lesions on histological findings and decreased lethality in mice infected with VACV. The ingestion of Lactobacillus paracasei ST11 (LPST11) after VACV infection resulted in 2/9 animal lethality compared with 4/9 in the VACV group. This is the first study on probiotics and VACV interactions, providing not only information about this interaction, but also proposing a model for future studies involving probiotics and other poxvirus.

Dos Santos, K. M., de, Oliveira, I, Lopes, M. A., Cruz, A. P., Buriti, F. C., and Cabral, L. M. Addition of grape pomace extract to probiotic fermented goat milk: the effect on phenolic content, probiotic viability and sensory acceptability. J.Sci.Food Agric. 2017; 97(4):1108-1115; PM: 27282819

ABSTRACT: BACKGROUND: Grape pomace is a source of phenolic compounds, which are associated with health benefits in humans. Additionally, fermented dairy foods with probiotics can be good vehicles to deliver these bioactive compounds. The effects of the addition of grape pomace extract (GPE) on the total phenolic (TP) content, physico-chemical characteristics and viability of Lactobacillus acidophilus LA-5 or Lactobacillus rhamnosus HN001 in fermented goat milks prepared with grape juice were investigated. *RESULTS*: The TP concentration increased significantly in fermented milks with the addition of GPE. A protective effect of GPE on the viability of L. acidophilus was observed. However, after 14 days of storage, the populations of L. acidophilus were significantly lower when compared with those of L. rhamnosus, and only the last probiotic maintained its viability above 7 log CFU mL-1 throughout the period investigated. The sensory scores of flavor, color and overall acceptability of the fermented milk containing L. rhamnosus HN001 were significantly increased when GPE was added. *CONCLUSION*: The use of GPE might increase the functionality of probiotic fermented goat milk processed with L. rhamnosus HN001 and grape juice because grape polyphenols are known for their antioxidant properties and positive effect on the modulation of gut microbiota. (c) 2016 Society of Chemical Industry.

Dossett, M. L., Cohen, E. M., and Cohen, J. Integrative Medicine for Gastrointestinal Disease. Prim.Care. 2017; 44(2):265-280; PM: 28501229

ABSTRACT: Gastrointestinal conditions are prevalent in the population and account for significant morbidity and health care costs. Patients with gastrointestinal conditions use integrative medicine. There is growing evidence that integrative medicine approaches

can improve symptoms and affect physiology and disease course. This article reviews data on some common and well-studied approaches, including mind-body therapies, acupuncture, diet, probiotics, and dietary supplements and herbs. Although clear recommendations can be made for some conditions, in others there are challenges in translating these findings owing to small study size, lack of standardization, and trial heterogeneity.

Doulberis, M., Kotronis, G., Gialamprinou, D., Kountouras, J., and Katsinelos, P. Non-alcoholic fatty liver disease: An update with special focus on the role of gut microbiota. Metabolism. 2017; 71:182-197; PM: 28521872

ABSTRACT: Non-alcoholic fatty liver disease (NAFLD) is a significant global health burden in children, adolescents and adults with substantial rise in prevalence over the last decades. Accumulating data from manifold studies support the idea of NAFLD as a hepatic manifestation of metabolic syndrome, being rather a systemic metabolic disease than a liver confined pathology. Emerging data support that the gut microbiome represents a significant environmental factor contributing to NAFLD development and progression. Apart from other regimens, probiotics may have a positive role in the management of NAFLD through a plethora of possible mechanisms. The current review focuses on the NAFLD multifactorial pathogenesis, including mainly the role of intestinal microbiome and all relevant issues are raised. Furthermore, the clinical manifestations and appropriate diagnostic approach of the disease are discussed, with all possible therapeutic measures that can be taken, also including the potential beneficial effect of probiotics.

Draper, K., Ley, C., and Parsonnet, J. A survey of probiotic use practices among patients at a tertiary medical centre. Benef.Microbes. 4-13-2017; 1-8; PM: 28403649

ABSTRACT: Probiotic use has skyrocketed in recent years. Little is known, however, about patient knowledge and practices regarding probiotic use, especially in the context of antibiotic use. An invitation to complete a short, anonymous, electronic survey was sent by email to 965 patients at a tertiary medical centre in California who had agreed to be contacted for participation in research studies. Questions were asked about both probiotic and antibiotic use in the prior three months. Of 333 survey respondents, 55% had recently used probiotics, including food products and/or supplements (90 and 60% of probiotic users, respectively). Women were more likely than men to have used probiotics (odds ratio (OR): 1.99; 95% confidence interval (CI): 1.2-3.4). Health care providers (HCP) had prescribed antibiotics to 79 (24%) respondents in the preceding three months. Among antibiotic users, 33% had initiated or changed probiotics at the time of antibiotic use, usually without a recommendation from their prescribing HCP (72%). Only 12% of those who took probiotics with antibiotics had received a specific recommendation from their HCP. Most patients chose to take probiotic mixtures (56%), with few selecting evidence-based strains, such as Lactobacillus rhamnosus GG (11%). Regular probiotic use among patients is common. Typically, these probiotics are not recommended by a HCP, even in conjunction with antibiotic prescriptions. While a growing body of evidence supports specific probiotic strains for the prevention of antibiotic-associated diarrhoea, patients are often not receiving a specific recommendation from their HCP and appear to be taking strains without guidance from supporting evidence.

Drissi, F., Raoult, D., and Merhej, V. Metabolic role of lactobacilli in weight modification in humans and animals. Microb.Pathog. 2017; 106:182-194; PM: 27033001

ABSTRACT: Obesity represents a worldwide public health crisis. Trials suggested that intestinal microbiota may contribute to the development of obesity and highlighted the involvement of bacteria, including Lactobacillus spp., in changes to the host metabolism. Several experiments have shown significant effects of Lactobacillus probiotics on weight modification. Lactobacillus spp. are involved in the digestion of complex carbohydrates not digested by the host in the colon and also participate in the degradation of lipids and simple sugars in the duodenum and jejunum. Moreover, Lactobacillus species survive throughout the gastrointestinal tract, as they are able to survive in the presence of bile and low pH, and produce an antimicrobial agent, allowing them to reduce the number of bacteria in the gut. Hence, Lactobacillus spp. can have a significant impact on microbiota and, consequently, on weight change. Here, we review current studies of Lactobacillus spp. involved in weight change and discuss the different mechanisms of action by which Lactobacillus spp. acts on host digestion and appears to influence weight.

Dror, T., Dickstein, Y., Dubourg, G., and Paul, M. Microbiota manipulation for weight change. Microb.Pathog. 2017; 106:146-161; PM: 26792677

ABSTRACT: Manipulation of the intestinal microbiota has been linked to weight changes and obesity. To explore the influence of specific agents that alter the intestinal flora on weight in different patient groups we conducted a meta-analysis of randomized controlled trials (RCTs) reporting on the effects of probiotics, prebiotics, synbiotics, and antibiotics on weight. We searched the Pubmed and Cochrane Library databases for trials on adults, children, and infants evaluating the effects of these substances on weight. Our primary outcome was weight change from baseline. Standardized mean differences (SMDs) with 95% confidence intervals were calculated. We identified and included 13 adult, 17 children, and 23 infant RCTs. Effects were opposite among adults and children, showing weight loss among adults (SMD -0.54 [-0.83, -0.25]) and minor weight gains among children (SMD 0.20 [0.04, 0.36]) and infants (SMD 0.30 [-0.01, 0.62]) taking mainly Lactobacillus probiotic supplements. Heterogeneity was substantial in the adult and infant analyses and could not be explained by intervention or patient characteristics. Azithromycin administration in children with pulmonary disease was associated with weight gain (SMD 0.39 [0.24, 0.54]), without heterogeneity. A high risk of selective reporting and attrition bias was detected across the studies, making it difficult to draw firm conclusions. Overall, our meta-analysis suggests that there may be a role for probiotics in promoting weight loss in adults and weight gain in children, however additional studies are needed. Though we cannot recommend antibiotic administration for weight manipulation, its use provides advantageous weight gain in children with cystic fibrosis and bronchiectasis.

Dunfield, K. and Yost, C. Editorial foreword to Dr. Gregor Reid's review paper: The development of probiotics for women's health. Can.J.Microbiol. 2017; 63(4):iii; PM: 28256909

No Abstract Available.

Dunislawska, A., Slawinska, A., Stadnicka, K., Bednarczyk, M., Gulewicz, P., Jozefiak, D., and Siwek, M. Synbiotics for Broiler Chickens-In Vitro Design and Evaluation of the Influence on Host and Selected Microbiota Populations following In Ovo Delivery. PLoS.One. 2017; 12(1):e0168587; PM: 28045927

ABSTRACT: Synbiotics are synergistic combinations of prebiotics and probiotics. In chickens, synbiotics can be delivered in ovo to expedite colonization of the gut by beneficial bacteria. We therefore aimed to design synbiotics in vitro and validate them in broiler chickens upon in ovo delivery. The probiotic components of the synbiotics were Lactobacillus salivarius and Lactobacillus plantarum. Their growth was assessed in MRS medium supplemented with different prebiotics. Based on in vitro results (hatchability and growth curve), two synbiotics were designed: S1 -Lactobacillus salivarius with galactooligosaccarides (GOS) and S2 -Lactobacillus plantarum with raffinose family oligosaccharides (RFO). These synbiotics were delivered to Cobb broiler chicken embryos on day 12 of incubation at optimized doses (105 cfu egg-1 of probiotic, 2 mg egg-1 of prebiotic). Post hatching, 2,400 roosters were reared (600 individuals group-1 divided into eight replicate pens). Microbial communities were analyzed in ileal and cecal digesta on day 21 using FISH. Gene expression analysis (IL1beta, IL4, IL6, IL8, IL12, IL18, IFNbeta, and IFNgamma) was performed on days 7, 14, 21, and 42 for the spleen and cecal tonsils with RT-qPCR. Body weight and feed intake of the roosters did not differ by the treatments. Microbial populations of Lactobacillus spp. and Enterococcus spp. in the ileum were higher in S1 and S2 than in the control. In the cecum, the control had the highest bacterial counts. S1 caused significant up-regulation of IL6, IL18, IL1beta, IFNgamma, and IFNbeta in the spleen on day 21 and IL1beta on day 7 ($P < 0.05$). In cecal tonsils, S1 caused significant down-regulation of IL12, IL8, and IL1beta on day 42 and IFNbeta on day 14 ($P < 0.05$). S2 did not elicit such patterns in any tissues investigated. Thus, we demonstrate that divergent effects of synbiotics in broiler chickens were reflected in in vitro tests.

Eales, J., Gibson, P., Whorwell, P., Kellow, J., Yellowlees, A., Perry, R. H., Edwards, M., King, S., Wood, H., and Glanville, J. Systematic review and meta-analysis: the effects of fermented milk with Bifidobacterium lactis CNCM I-2494 and lactic acid bacteria on gastrointestinal discomfort in the general adult population. Therap.Adv.Gastroenterol. 2017; 10(1):74-88; PM: 28286561

ABSTRACT: BACKGROUND: It has been suggested that probiotics may improve gastrointestinal discomfort. Not all probiotics exhibit the same effects and consequently meta-analyses on probiotics should be confined to well-defined strains or strain combinations. The aim of this study was to evaluate the effectiveness of a probiotic fermented milk (PFM) that includes Bifidobacterium lactis (B. lactis) CNCM I-2494 and lactic acid bacteria on gastrointestinal discomfort in the general adult population. *METHODS*: Double-blind randomized controlled trials in the general adult population comparing PFM with a control dairy product for at least 4 weeks were searched from multiple literature databases (up to February 2015). Meta-analyses using random-effects models, with individual participant data were undertaken to calculate an odds ratio (OR) or standard mean difference (SMD), with a 95% confidence interval (CI). *RESULTS*: The search strategy identified 12,439 documents. Overall, three trials with a total of 598 adults (female = 96.5%) met the inclusion criteria. Consumption of the PFM product was associated with a significant improvement in overall gastrointestinal discomfort compared with the control product (OR = 1.48; 95% CI 1.07-2.05), with a number needed to treat (NNT) of 10.24 (95% CI 5.64-55.93). PFM was also superior to the control in

reducing digestive symptoms, as measured using a composite score (SMD = -0.21; 95% CI -0.37 to -0.05). Sensitivity analyses produced similar results, and the heterogeneity between studies was minimal. *CONCLUSIONS*: This meta-analysis shows that the consumption of PFM with B. lactis CNCM I-2494 and lactic acid bacteria is associated with a modest but consistent and significant improvement of outcomes related to gastrointestinal discomfort in healthy adults.

Eggers, S., Barker, A., Valentine, S., Hess, T., Duster, M., and Safdar, N. Impact of Probiotics for Reducing Infections in Veterans (IMPROVE): Study protocol for a double-blind, randomized controlled trial to reduce carriage of Staphylococcus aureus. Contemp.Clin.Trials. 2017; 52:39-45; PM: 27836508

ABSTRACT: BACKGROUND: Staphylococcus aureus (S. aureus) is an organism of great public health importance, causing 20,000 deaths annually. Decolonization of patients with S. aureus may prevent infections, yet current options are limited to antimicrobials that promote antibiotic resistance and can cause adverse side effects. Probiotics have potential to reduce colonization of pathogenic bacteria, representing a promising alternative for S. aureus decolonization, but thus far lack rigorous evaluation. *METHODS*: Potential subjects were recruited from inpatient and outpatient settings within a VA medical center and screened for S. aureus gastrointestinal (GI) or extra-GI colonization using swabs at multiple body sites. Positive, eligible, consenting participants were stratified by colonization site and randomized in a 1:1 ratio to 4-weeks of daily placebo or Lactobacillus rhamnosus (L. rhamnosus) HN001 probiotic treatment. Blood and stool samples, and treatment adherence reports were collected from each subject throughout the study, along with a final set of swabs at study completion to detect S. aureus carriage. The outcomes of this study are GI or extra-GI carriage by S. aureus at the end of 4weeks of therapy, change in phagocytic activity of polymorphonuclear cells from pre-intervention to post-intervention, and symptomatic S. aureus infection at any site during the study period. *CONCLUSION*: 114 participants have been recruited for this study. Analysis of outcomes is underway. This is the first clinical trial to examine the efficacy of L. rhamnosus HN001 for decolonization of S. aureus, and investigates the mechanism by which L. rhamnosus HN001 mediates its effect on S. aureus colonization. ClinicalTrials.govIdentifier NCT01321606.

Ekmekciu, I., Fiebiger, U., Stingl, K., Bereswill, S., and Heimesaat, M. M. Amelioration of intestinal and systemic sequelae of murine Campylobacter jejuni infection by probiotic VSL#3 treatment. Gut Pathog. 2017; 9:17; PM: 28413453

ABSTRACT: BACKGROUND: The incidence of human Campylobacter jejuni infections is progressively increasing worldwide. Probiotic compounds might open up valuable tools to decrease pathogen burden and subsequent pro-inflammatory immune responses, but in vivo data are scarce. *METHODS AND RESULTS*: Secondary abiotic mice generated by broad-spectrum antibiotic treatment were perorally challenged with the commercial probiotic compound VSL#3 consisting of Streptococcus thermophilus, Bifidobacterium breve, Bifidobacterium longum, Bifidobacterium infantis, Lactobacillus acidophilus, Lactobacillus plantarum, Lactobacillus paracasei, and Lactobacillus delbrueckii ssp. bulgaricus) either 5 days before (i.e. prophylactic regimen) or after (i.e. therapeutic regimen) peroral C. jejuni strain 81-176 infection, and analyzed 3 weeks following the initial bacterial re-association. Upon challenge, mice were colonized with the probiotic bacteria and/or C. jejuni at comparable intestinal loads, but co-colonization did not

result in reduction of the pathogen burden. Remarkably, prophylactic as well as therapeutic VSL#3 treatment of C. jejuni infected mice ameliorated intestinal apoptosis and pro-inflammatory immune responses as indicated by lower numbers of innate and adaptive immune cell populations in the murine colon upon probiotic prophylaxis or treatment and reduced colonic concentrations of pro-inflammatory mediators including IL-6 and MCP-1. Importantly, concentrations of anti-inflammatory mediators such as IL-10 were significantly elevated in the colon of probiotics treated mice as compared to untreated controls. Strikingly, prophylactic VSL#3 treatment attenuated C. jejuni induced systemic pro-inflammatory responses as indicated by less TNF and IL-12p70 secretion in the spleen of VSL#3 pre-treated as compared to non-treated mice. *CONCLUSION*: Administration of probiotic formulations such as VSL#3 might open up valuable strategies for prophylaxis and/or treatment of C. jejuni induced intestinal and systemic sequelae in vivo by the suppression of pro-inflammatory and induction of anti-inflammatory responses.

Enujiugha, V. N. and Badejo, A. A. Probiotic potentials of cereal-based beverages. Crit Rev.Food Sci.Nutr. 3-4-2017; 57(4):790-804; PM: 26558644

ABSTRACT: Probiotics offer remarkable potential for the prevention and management of various infective and noninfective disorders. They are reported to play key roles in the suppression of gastrointestinal infections, antimicrobial activity, improvement in lactose metabolism, reduction in serum cholesterol, immune system stimulation, antimutagenic properties, anticarcinogenic properties, anti-diarrheal properties, and improvement in inflammatory bowel disease. Although probiotic foods are classically confined to beverages and cheese, containing live organisms of the lactic acid bacteria family, such health-promoting foods are traditionally dairy-based, comprising milk and its fermented products. However, recent research focuses on the probiotic potentials of fermented cereal-based beverages which are especially consumed in developing countries characterized by low nutritional security and high incidence of gut pathogen infections. Moreover, lactose intolerance and cholesterol content associated with dairy products, coupled with the vegetarian tendencies of diverse populations in the third world, tend to enforce the recent recourse to nondairy beverages. Probiotic microorganisms are mostly of human or animal origin; however, strains recognized as probiotics are also found in nondairy fermented substrates. This review examines the potentials of some traditional cereal-based beverages to serve as probiotic foods, their microbial and functional properties, as well as their process optimization and storage for enhanced utilization.

Esmaeili, S. A., Mahmoudi, M., Momtazi, A. A., Sahebkar, A., Doulabi, H., and Rastin, M. Tolerogenic probiotics: potential immunoregulators in Systemic Lupus Erythematosus. J.Cell Physiol. 2017; 232(8):1994-2007; PM: 27996081

ABSTRACT: Probiotics are commensal or nonpathogenic microbes that colonize the gastrointestinal tract and confer beneficial effects on the host through several mechanisms such as competitive exclusion, anti-bacterial effects, and modulation of immune responses. There is growing evidence supporting the immunomodulatory ability of some probiotics. Several experimental and clinical studies have been shown beneficial effect of some probiotic bacteria, particularly Lactobacillus and Bifidobacteria strains, on inflammatory and autoimmune diseases. Systemic lupus erythematosus (SLE) is an autoimmune disease that is mainly characterized by immune intolerance towards self-antigens. Some immunomodulatory probiotics have been found

to regulate immune responses via tolerogenic mechanisms. Dendritic and T regulatory (Treg) cells, IL-6, IFN-gamma, IL-17, and IL-23 can be considered as the most determinant dysregulated mediators in tolerogenic status. As demonstrated by documented experimental and clinical trials on inflammatory and autoimmune diseases, a number of probiotic bacterial strains can restore tolerance in host through modification of such dysregulated mediators. Since there are limited reports regarding to impact of probiotic supplementation in SLE patients, the preset review was aimed to suggest a number of probiotics bacteria, mainly from Bifidobacteria and Lactobacillus strains that are able to ameliorate immune responses. The aim was followed through literature survey on immunoregulatory probiotics that can restore tolerance and also modulate the important dysregulated pro/anti-inflammatory cytokines contributing to the pathogenesis of SLE.

Fabersani, E., beijon-Mukdsi, M. C., Ross, R., Medina, R., Gonzalez, S., and Gauffin-Cano, P. Specific Strains of Lactic Acid Bacteria Differentially Modulate the Profile of Adipokines In Vitro. Front Immunol. 2017; 8:266; PM: 28348560

ABSTRACT: Obesity induces local/systemic inflammation accompanied by increases in macrophage infiltration into adipose tissue and production of inflammatory cytokines, chemokines, and hormones. Previous studies have shown that probiotics could improve the intestinal dysbiosis induced by metabolic diseases such as obesity, diabetes, and metabolic syndrome. Microorganisms could (directly or indirectly) affect adipokine levels due to their capacity to induce translocation of several intestinal microbial antigens into systemic circulation, which could lead to metabolic endotoxemia or produce immunomodulation in different organs. The aim of the present study was to select non-inflammatory lactic acid bacteria (LAB) strains with the capacity to modulate adipokine secretion by the adipose tissue. We wish to elucidate the role of potential probiotic strains in the regulation of the cross talking between immune cells such as macrophages and adipose cells. Mouse macrophage cell line RAW 264.7 was used for evaluating the ability of 14 LAB strains to induce cytokine production. The LAB strains were chosen based on their previously studied beneficial properties in health. Then, in murine adipocyte culture and macrophage-adipocyte coculture, we determined the ability of these strains to induce cytokines and leptin secretion. Tumor necrosis factor alpha, interleukin 6 (IL-6), IL-10, monocyte chemoattractant protein-1, and leptin levels were measured in cell supernatants. We also performed the detection and quantification of leptin receptor (Ob-Rb) expression in macrophage cell lines stimulated by these LAB strains. Differential secretion profile of cytokines in macrophage cells induced by LAB strains was observed. Also, the levels of Ob-Rb expression diverged among different LAB strains. In LAB-stimulated coculture cells (adipocytes and macrophages), we observed differential production of leptin and cytokines. Furthermore, we detected lower production levels in single culture than cocultured cells. The principal component analysis showed an association between the four clusters of strains established according to their inflammatory profiles and leptin adipocyte production and leptin receptor expression in macrophages. We conclude that coculture is the most appropriate system for selecting strains with the ability to modulate adipokine secretion. The use of microorganisms with low and medium inflammatory properties and ability to modulate leptin levels could be a strategy for the treatment of some metabolic diseases associated with dysregulation of immune response.

Famouri, F., Shariat, Z., Hashemipour, M., Keikha, M., and Kelishadi, R. Effects of Probiotics on Nonalcoholic Fatty Liver Disease in Obese Children and Adolescents. J.Pediatr.Gastroenterol.Nutr. 2017; 64(3):413-417; PM: 28230607

ABSTRACT: OBJECTIVES: This study aims to evaluate the effects of some probiotics on sonographic and biochemical nonalcoholic fatty liver disease (NAFLD). *METHODS*: This randomized triple-blind trial was conducted among 64 obese children with sonographic NAFLD. They were randomly allocated to receive probiotic capsule (containing Lactobacillus acidophilus ATCC B3208, 3 x 10 colony forming units [CFU]; Bifidobacterium lactis DSMZ 32269, 6 x 10 CFU; Bifidobacterium bifidum ATCC SD6576, 2 x 10 CFU; Lactobacillus rhamnosus DSMZ 21690, 2 x 10 CFU) or placebo for 12 weeks. *RESULTS*: After intervention, in the probiotic group the mean levels of alanine aminotransferase decreased from 32.8 (19.6) to 23.1 (9.9) U/L (P = 0.02) and mean aspartate aminotransferase decreased from 32.2 (15.7) to 24.3 (7.7) U/L (P = 0.02). Likewise the mean cholesterol, low-density lipoprotein-C, and triglycerides as well as waist circumference decreased in the intervention group, without significant change in weight, body mass index, and body mass index z score. After the trial, normal liver sonography was reported in 17 (53.1%) and 5 (16.5%) of patients in the intervention and placebo groups, respectively. *CONCLUSIONS*: The present findings suggest that a course of the abovementioned probiotic compound can be effective in improving pediatric NAFLD.

Fareez, I. M., Lim, S. M., Zulkefli, N. A. A., Mishra, R. K., and Ramasamy, K. Cellulose Derivatives Enhanced Stability of Alginate-Based Beads Loaded with Lactobacillus plantarum LAB12 against Low pH, High Temperature and Prolonged Storage. Probiotics.Antimicrob.Proteins. 5-10-2017; PM: 28493103

ABSTRACT: The susceptibility of probiotics to low pH and high temperature has limited their use as nutraceuticals. In this study, enhanced protection of probiotics via microencapsulation was achieved. Lactobacillus plantarum LAB12 were immobilised within polymeric matrix comprised of alginate (Alg) with supplementation of cellulose derivatives (methylcellulose (MC), sodium carboxymethyl cellulose (NaCMC) or hydroxypropyl methylcellulose (HPMC)). L. plantarum LAB12 encapsulated in Alg-HPMC(1.0) and Alg-MC(1.0) elicited improved survivability (91%) in simulated gastric conditions and facilitated maximal release (approximately 100%) in simulated intestinal condition. Alg-HPMC(1.0) and Alg-MC(1.0) significantly reduced (P < 0.05) the viability loss of LAB12 (viability loss <7%) when compared to Alg alone (viability loss <13%) under extreme temperatures (75 and 90 degrees C). Four-week storage of encapsulated LAB12 at 4 degrees C yielded viable counts >7 log CFU g-1. Alg-MC and Alg-HPMC improved the survival of LAB12 against simulated gastric condition (9.24 and 9.55 log CFU g-1, respectively), temperature up to 90 degrees C (9.54 and 9.86 log CFU g-1, respectively) and 4-week of storage at 4 degrees C (8.61 and 9.23 log CFU g-1, respectively) with sustained release of probiotic in intestinal condition (>9 log CFU g-1). These findings strongly suggest the potential of cellulose derivatives supplemented Alg bead as protective micro-transport for probiotic strains. They can be safely incorporated into new functional food or nutraceutical products.

Feizollahzadeh, S., Ghiasvand, R., Rezaei, A., Khanahmad, H., Sadeghi, A., and Hariri, M. Effect of Probiotic Soy Milk on Serum Levels of Adiponectin, Inflammatory Mediators, Lipid Profile,

and Fasting Blood Glucose Among Patients with Type II Diabetes Mellitus. Probiotics.Antimicrob.Proteins. 2017; 9(1):41-47; PM: 27757829

ABSTRACT: Probiotic therapies are going to be an effective alternative therapeutic strategy in the treatment and management of diabetes. The mechanism behind the essential effects of probiotic therapies in diabetic patients was not fully understood. The objective of this study was to evaluate the effects of probiotic soy milk containing Lactobacillus planetarum A7 on inflammation, lipid profile, fasting blood glucose, and serum adiponectin among patients with type 2 diabetes mellitus. Forty patients with type 2 diabetes, at the age of 35-68 years old, were assigned to two groups in this randomized, double-blind, controlled clinical trial. The patients in the intervention group consumed 200 ml/day of probiotic soy milk containing L. planetarum A7 and those in control group consumed 200 ml/day of pure soy milk for 8 weeks. Serum TNF-alpha, C reactive protein, adiponectin, lipid profile, and fasting blood glucose were determined before and after intervention. In intervention group, serum adiponectin in pre- and post-treatment did not show any significant changes (2.52 +/- 0.74 vs 2.84 +/- 0.61, P = 0.658), as well as changes in serum TNF-alpha and C reactive protein (172.44 +/- 5.7 vs 172.83 +/- 7.6, P = 0.278, 4.2 +/- 1.4 vs 4.5 +/- 1.9, P = 0.765, respectively). Low-density cholesterol and high-density cholesterol changed significantly (P = 0.023, P = 0.017, respectively), but fasting blood glucose did not show any significant changes. The results of this study showed that consumption of probiotic soy milk and soy milk has no effect on serum adiponectin and inflammation, but it can change lipid profile among type 2 diabetic patients.

Feria, M. G., Taborda, N. A., Hernandez, J. C., and Rugeles, M. T. [Effects of prebiotics and probiotics on gastrointestinal tract lymphoid tissue in hiv infected patients]. Rev.Med.Chil. 2017; 145(2):219-229; PM: 28453589

ABSTRACT: HIV infection induces alterations in almost all immune cell populations, mainly in CD4+ T cells, leading to the development of opportunistic infections. The gut-associated lymphoid tissue (GALT) constitutes the most important site for viral replication, because the main target cells, memory T-cells, reside in this tissue. It is currently known that alterations in GALT are critical during the course of the infection, as HIV-1 induces loss of tissue integrity and promotes translocation of microbial products from the intestinal lumen to the systemic circulation, leading to a persistent immune activation state and immune exhaustion. Although antiretroviral treatment decreases viral load and substantially improves the prognosis of the infection, the alterations in GALT remains, having a great impact on the ability to establish effective immune responses. This emphasizes the importance of developing new therapeutic alternatives that may promote structural and functional integrity of this tissue. In this regard, therapy with probiotics/prebiotics has beneficial effects in GALT, mainly in syndromes characterized by intestinal dysbiosis, including the HIV-1 infection. In these patients, the consumption of probiotics/prebiotics decreased microbial products in plasma and CD4+ T cell activation, increased CD4+ T cell frequency, in particular Th17, and improved the intestinal flora. In this review, the most important findings on the potential impact of the probiotics/prebiotics therapy are discussed.

Ferm, S., Varadi, N., Fisher, C., and Gutkin, E. Serum-Derived Bovine Immunoglobulin as Novel Adjunct in Complicated Clostridium difficile Colitis Treatment. ACG.Case.Rep.J. 2017; 4:e64; PM: 28516109

ABSTRACT: Clostridium difficile infection (CDI) is a well-known complication of antibiotic therapy. It is associated with significant morbidity, mortality, and cost in the hospital setting. The main symptoms include watery diarrhea, abdominal pain, and distension, but CDI can also present as toxic megacolon, bowel perforation with peritonitis, sepsis and renal failure. Therapy includes metronidazole and oral vancomycin, with rectal vancomycin and fecal transplant reserved for more complicated cases. Adjunctive treatments such as probiotics have been tried with mixed results. We present a patient with complicated CDI treated with adjuvant serum-derived bovine immunoglobulin, a novel approach in this context.

Fernandez-Alarcon, M. F., Trottier, N., Steibel, J. P., Lunedo, R., Campos, D. M., Santana, A. M., Pizauro, J. M., Jr., Furlan, R. L., and Furlan, L. R. Interference of age and supplementation of direct-fed microbial and essential oil in the activity of digestive enzymes and expression of genes related to transport and digestion of carbohydrates and proteins in the small intestine of broilers. Poult.Sci. 2-23-2017; PM: 28339792

ABSTRACT: The objectives of this study were to describe alterations that age and dietary inclusion of direct-fed microbial (DFM) Bacillus subtilis (BS) and a specific essential oil (EO) blend (carvacrol, cinnamaldehyde, cineol, and pepper extract) causes in the activity of digestive enzymes (maltase: MALT; aminopeptidase-N: APN; intestinal alkaline phosphate: IAP) and expression patterns of genes related to transport (oligopeptide transporter gene: SLC15A1; Na+-dependent glucose and galactose transporter gene: SLC5A1; Na+-independent glucose, galactose, and fructose transporter gene: SLC2A2; ATPase, Na+/K+ transporting gene: ATP1A1) and digestion (aminopeptidase-N gene: ANPEP; maltase-glucoamylase gene: MGAM; Sucrase-isomaltase gene: SI) of carbohydrates and proteins in the small intestine of broilers. Also, the objective was to analyze if growth performance of broilers is affected by supplementation (BS and EO blend). Day-old male broiler chicks (n = 1,320) were assigned to 5 treatments. Diets included a basal diet (BD) as a negative control (CON); experimental diets were BD + BS; BD + BS + EO; BD + EO; BD + antibiotic growth promoter (AGP) avilamycin was the positive control. Performance was evaluated between 1 to 42 d. Transcript abundance of transport-related genes and digestion-related genes were assayed by RT-qPCR and determined at d 7, 21, and 42. MALT-, APN-, and IAP-specific activities were determined at d 7, 21, and 42. Broilers fed BS had greater SLC15A1 mRNA abundance compared to CON, while EO and AGP were related to higher activities of IAP and APN. Analysis over time revealed higher abundance of MGAM, SLC2A2, SLC15A1, SLC5A1 and SI mRNA at d 42 when compared to d 7. Activity of IAP decreased after d 7 and activity of MALT increased with age. The current study suggests that age had effect over carbohydrate and protein transport and carbohydrate digestion. The supplementation of BS DFM hade evident effect over protein transport and that the use of EO in the diet enhanced the activities of carbohydrate and protein digestion, reflecting improvement in digestive and transport physiology of birds. Changes performed by BS DFM and EO did not favor performance.

Fernandez-Duarte, K. P., Olaya-Galan, N. N., Salas-Cardenas, S. P., Lopez-Rozo, J., and Gutierrez-Fernandez, M. F. Bifidobacterium adolescentis (DSM 20083) and Lactobacillus

casei (Lafti L26-DSL): Probiotics Able to Block the In Vitro Adherence of Rotavirus in MA104 Cells. Probiotics.Antimicrob.Proteins. 4-21-2017; PM: 28432676

ABSTRACT: Rotavirus is the leading worldwide cause of gastroenteritis in children under five years of age. Even though there are some available vaccines to prevent the disease, there are limited strategies for challenging diarrhea induced by rotavirus infection. For this reason, researchers are constantly searching for other approaches to control diarrhea by means of probiotics. In order to demonstrate the ability of some probiotic bacteria to interfere with the in vitro rotavirus infection in MA104 cells, strains of Lactobacillus sp. and Bifidobacterium sp. were tested in MA104 cells before the viral infection. As a preliminary assay, a blocking effect treatment was performed with viable bacteria. In this screening assay, four of initial ten bacteria showed a slight reduction of the viral infection (measured by percentage of infection). L. casei (Lafti L26-DSL), L. fermentum(ATCC 9338), B. adolescentis (DSM 20083), and B. bifidum (ATCC 11863) were used in further experiments. Three different treatments were tested in order to evaluate protein-based metabolites obtained from mentioned bacteria: (i) cell exposure to the protein-based metabolites before viral infection, (ii) exposure to protein-based metabolites after viral infection, and (iii) co-incubation of the virus and protein-based metabolites before viral infection to the cell culture. The best effect performed by protein-based metabolites was observed during the co-incubation assay of the virus and protein-based metabolites before adding them into the cell culture. The results showed 25 and 37% of infection in the presence of L. casei and B. adolescentis respectively. These results suggest that the antiviral effect may be occurring directly with the viral particle instead of making a blocking effect of the cellular receptors that are needed for the viral entrance.

Fernandez, M. A. and Marette, A. Potential Health Benefits of Combining Yogurt and Fruits Based on Their Probiotic and Prebiotic Properties. Adv.Nutr. 2017; 8(1):155S-164S; PM: 28096139

ABSTRACT: Fruit and yogurt have been identified individually as indicators of healthy dietary patterns. Fruits are relatively low in energy density and are an excellent source of antioxidants and prebiotic fibers and polyphenols, which can promote digestive health. Yogurt, on the other hand, is a nutrient-dense food that is a good source of dairy protein, calcium, magnesium, vitamin B-12, conjugated linoleic acid, and other key fatty acids. In addition, it contains beneficial bacterial cultures, making it a potential source of probiotics. Yogurt's unique fermented food matrix provides added health benefits by enhancing nutrient absorption and digestion. Combining the intake of yogurt and fruit could provide probiotics, prebiotics, high-quality protein, important fatty acids, and a mixture of vitamins and minerals that have the potential to exert synergistic effects on health. Yogurt consumption has been associated with reduced weight gain and a lower incidence of type 2 diabetes, whereas fruits have established effects on reducing the risk of cardiovascular disease. Yogurt and fruits can be eaten together and may exert combined health benefits through potential prebiotic and probiotic effects. Furthermore, substituting high-energy, nutrient-deficient snacks with fruit and yogurt could reduce the intake of high-calorie obesogenic foods. In light of the positive cardiometabolic impacts of fruit and yogurt and their association with healthy dietary patterns, there is sufficient evidence to warrant further exploration into the potential synergistic health benefits of a combined intake of fruit and yogurt.

Finamore, A., Palmery, M., Bensehaila, S., and Peluso, I. Antioxidant, Immunomodulating, and Microbial-Modulating Activities of the Sustainable and Ecofriendly Spirulina. Oxid.Med.Cell Longev. 2017; 2017:3247528; PM: 28182098

ABSTRACT: The highly nutritional and ecofriendly Spirulina (Arthrospira platensis) has hypolipidemic, hypoglycemic, and antihypertensive properties. Spirulina contains functional compounds, such as phenolics, phycocyanins, and polysaccharides, with antioxidant, anti-inflammatory, and immunostimulating effects. Studies conducted on Spirulina suggest that it is safe in healthy subjects, but attitude to eating probably affects the acceptability of Spirulina containing foods. Although the antioxidant effect of Spirulina is confirmed by the intervention studies, the concerted modulation of antioxidant and inflammatory responses, suggested by in vitro and animal studies, requires more confirmation in humans. Spirulina supplements seem to affect more effectively the innate immunity, promoting the activity of natural killer cells. The effects on cytokines and on lymphocytes' proliferation depend on age, gender, and body weight differences. In this context, ageing and obesity are both associated with chronic low grade inflammation, immune impairment, and intestinal dysbiosis. Microbial-modulating activities have been reported in vitro, suggesting that the association of Spirulina and probiotics could represent a new strategy to improve the growth of beneficial intestinal microbiota. Although Spirulina might represent a functional food with potential beneficial effects on human health, the human interventions used only supplements. Therefore, the effect of food containing Spirulina should be evaluated in the future.

Fisher, L. and Fisher, A. Acid-Suppressive Therapy and Risk of Infections: Pros and Cons. Clin.Drug Investig. 3-30-2017; PM: 28361440

ABSTRACT: This narrative review summarises the benefits, risks and appropriate use of acid-suppressing drugs (ASDs), proton pump inhibitors and histamine-2 receptor antagonists, advocating a rationale balanced and individualised approach aimed to minimise any serious adverse consequences. It focuses on current controversies on the potential of ASDs to contribute to infections-bacterial, parasitic, fungal, protozoan and viral, particularly in the elderly, comprehensively and critically discusses the growing body of observational literature linking ASD use to a variety of enteric, respiratory, skin and systemic infectious diseases and complications (Clostridium difficile diarrhoea, pneumonia, spontaneous bacterial peritonitis, septicaemia and other). The proposed pathogenic mechanisms of ASD-associated infections (related and unrelated to the inhibition of gastric acid secretion, alterations of the gut microbiome and immunity), and drug-drug interactions are also described. Both probiotics use and correcting vitamin D status may have a significant protective effect decreasing the incidence of ASD-associated infections, especially in the elderly. Despite the limitations of the existing data, the importance of individualised therapy and caution in long-term ASD use considering the balance of benefits and potential harms, factors that may predispose to and actions that may prevent/attenuate adverse effects is evident. A six-step practical algorithm for ASD therapy based on the best available evidence is presented.

Fleury, M. A., Le, Goff O., Denis, S., Chaucheyras-Durand, F., Jouy, E., Kempf, I., Alric, M., and Blanquet-Diot, S. Development and validation of a new dynamic in vitro model of the piglet colon (PigutIVM): application to the study of probiotics. Appl.Microbiol.Biotechnol. 2017; 101(6):2533-2547; PM: 28188340

ABSTRACT: For ethical, technical, regulatory, and cost reasons, in vitro methods are increasingly used as an alternative to in vivo experimentations. The aim of the present study was to validate, according to in vivo data in living animals, a new in vitro model of the piglet colon, the PigutIVM, under both control conditions and antibiotic disturbance by the widely used colistin. The PigutIVM reproduces the main biotic and abiotic parameters of the piglet colon: temperature, pH, retention time, supply of ileal effluents, complex, and metabolically active microbiota and self-maintained anaerobiosis. Under both control and antibiotic-treated conditions, qPCR analyses showed that the main bacterial populations of piglet gut microbiota were similar in vitro and in vivo, with Pearson correlation coefficient higher than 0.9. During colistin administration, both in piglets and in the in vitro model, a significant decrease in Escherichia coli populations was observed together with changes in microbial composition of subdominant populations. SCFA concentrations were similar in vitro and in vivo and were not modified by colistin. Interestingly, the administration of the probiotic Saccharomyces cerevisiae var. boulardii CNCM I-1079 led in vitro to a decrease in E. coli levels, as previously observed when the antibiotic treatment was applied. This new in vitro model of the piglet colon provides a flexible, reproducible, and cost-effective tool for the screening of drugs or new dietary compounds, such as pre- or probiotics. It will be helpful for researchers, feed producers, or veterinarians when developing innovative non-antibiotic strategies.

Fluxa, D. and Quera, R. [Diverticular disease: myths and realities]. Rev.Med.Chil. 2017; 145(2):201-208; PM: 28453588

ABSTRACT: Diverticulosis and diverticular disease of the colon are common conditions in Western countries. The incidence and prevalence of these diseases are increasing and becoming significant for health systems. A growing body of knowledge is shifting the paradigm of the pathogenesis and treatment of diverticular disease. Low-grade inflammation, altered intestinal microbiota, visceral hypersensitivity, and abnormal colonic motility have been identified as factors leading to diverticular disease. The risk of developing diverticulitis among individuals with diverticulosis is lower than 10 to 25%. Studies indicate that diverticular disease may become a chronic disorder in some patients, not merely an acute illness. Contrary to the advice from international guidelines, studies have not shown that a high-fiber diet protects against diverticulosis. The evidence about the use of antibiotics in uncomplicated diverticulitis is sparse and of low quality. In relation to surgery, studies support a more conservative approach to prophylactic surgery in patients with recurrent disease or chronic symptoms. Finally, new pathophysiological knowledge suggests that other treatments may be useful (mesalamine, rifaximin and probiotics). However, more research is necessary to validate the safety, effectiveness and cost-effectiveness of these strategies.

Fonseca, V. M., Milani, T. M., Prado, R., Bonato, V. L., Ramos, S. G., Martins, F. S., Vianna, E. O., and Borges, M. C. Oral administration of Saccharomyces cerevisiae UFMG A-905 prevents allergic asthma in mice. Respirology. 2-6-2017; PM: 28166610

ABSTRACT: BACKGROUND AND OBJECTIVE: The prevalence of asthma has increased in communities that adopt a Western lifestyle and become more urbanized. Probiotics may be effective in the prevention of allergic diseases, such as asthma. The aim of the current study was to examine the effects of Saccharomyces cerevisiae UFMG A-905 in an allergic model of asthma. *METHODS*: Balb/c mice were sensitized twice with ovalbumin (OVA) intraperitoneally, 1 week apart and challenged with OVA intranasally for 3 days.

Mice were daily treated with S. cerevisiae UFMG A-905 via gavaging needle 10 days before OVA sensitization and during challenges. After challenge, in vivo lung function was measured, and bronchoalveolar lavage (BAL) and lung inflammation were assessed. *RESULTS*: Oral treatment with S. cerevisiae UFMG A-905 significantly decreased airway hyperresponsiveness, total cell number and the influx of eosinophils to the airway, inflammatory cell in the lung, mucus expression in epithelial cells and the levels of IL-4, IL-5 and IL-13. Additionally, S. cerevisiae UFMG A-905 restored the levels of IL-10 and interferon (IFN)-gamma, and increased the levels of IL-17A. *CONCLUSION*: Oral administration of S. cerevisiae UFMG A-905 prevented the development of major asthma-like characteristics in a mouse model.

Forbes, A., Escher, J., Hebuterne, X., Klek, S., Krznaric, Z., Schneider, S., Shamir, R., Stardelova, K., Wierdsma, N., Wiskin, A. E., and Bischoff, S. C. ESPEN guideline: Clinical nutrition in inflammatory bowel disease. Clin.Nutr. 2017; 36(2):321-347 PM: 28131521

ABSTRACT: INTRODUCTION: The ESPEN guideline presents a multidisciplinary focus on clinical nutrition in inflammatory bowel disease (IBD). *METHODOLOGY*: The guideline is based on extensive systematic review of the literature, but relies on expert opinion when objective data were lacking or inconclusive. The conclusions and 64 recommendations have been subject to full peer review and a Delphi process in which uniformly positive responses (agree or strongly agree) were required. *RESULTS*: IBD is increasingly common and potential dietary factors in its aetiology are briefly reviewed. Malnutrition is highly prevalent in IBD - especially in Crohn's disease. Increased energy and protein requirements are observed in some patients. The management of malnutrition in IBD is considered within the general context of support for malnourished patients. Treatment of iron deficiency (parenterally if necessary) is strongly recommended. Routine provision of a special diet in IBD is not however supported. Parenteral nutrition is indicated only when enteral nutrition has failed or is impossible. The recommended perioperative management of patients with IBD undergoing surgery accords with general ESPEN guidance for patients having abdominal surgery. Probiotics may be helpful in UC but not Crohn's disease. Primary therapy using nutrition to treat IBD is not supported in ulcerative colitis, but is moderately well supported in Crohn's disease, especially in children where the adverse consequences of steroid therapy are proportionally greater. However, exclusion diets are generally not recommended and there is little evidence to support any particular formula feed when nutritional regimens are constructed. *CONCLUSIONS*: Available objective data to guide nutritional support and primary nutritional therapy in IBD are presented as 64 recommendations, of which 9 are very strong recommendations (grade A), 22 are strong recommendations (grade B) and 12 are based only on sparse evidence (grade 0); 21 recommendations are good practice points (GPP).

Forkus, B., Ritter, S., Vlysidis, M., Geldart, K., and Kaznessis, Y. N. Antimicrobial Probiotics Reduce Salmonella enterica in Turkey Gastrointestinal Tracts. Sci.Rep. 1-17-2017; 7:40695; PM: 28094807

ABSTRACT: Despite the arsenal of technologies employed to control foodborne nontyphoidal Salmonella (NTS), infections have not declined in decades. Poultry is the primary source of NTS outbreaks, as well as the fastest growing meat sector worldwide. With recent FDA rules for phasing-out antibiotics in animal production, pressure is mounting to develop new pathogen reduction strategies. We report on a technology to reduce Salmonella enteritidis in poultry. We engineered probiotic E. coli Nissle 1917, to

express and secrete the antimicrobial peptide, Microcin J25. Using in vitro experiments and an animal model of 300 turkeys, we establish the efficacy of this technology. Salmonella more rapidly clear the ceca of birds administered the modified probiotic than other treatment groups. Approximately 97% lower Salmonella carriage is measured in a treated group, 14 days post-Salmonella challenge. Probiotic bacteria are generally regarded as safe to consume, are bile-resistant and can plausibly be modified to produce a panoply of antimicrobial peptides now known. The reported systems may provide a foundation for platforms to launch antimicrobials against gastrointestinal tract pathogens, including ones that are multi-drug resistant.

Foschi, C., Laghi, L., Parolin, C., Giordani, B., Compri, M., Cevenini, R., Marangoni, A., and Vitali, B. Novel approaches for the taxonomic and metabolic characterization of lactobacilli: Integration of 16S rRNA gene sequencing with MALDI-TOF MS and 1H-NMR. PLoS.One. 2017; 12(2):e0172483; PM: 28207855

ABSTRACT: Lactobacilli represent a wide range of bacterial species with several implications for the human host. They play a crucial role in maintaining the ecological equilibrium of different biological niches and are essential for fermented food production and probiotic formulation. Despite the consensus about the 'health-promoting' significance of Lactobacillus genus, its genotypic and phenotypic characterization still poses several difficulties. The aim of this study was to assess the integration of different approaches, genotypic (16S rRNA gene sequencing), proteomic (MALDI-TOF MS) and metabolomic (1H-NMR), for the taxonomic and metabolic characterization of Lactobacillus species. For this purpose we analyzed 40 strains of various origin (intestinal, vaginal, food, probiotics), belonging to different species. The high discriminatory power of MALDI-TOF for species identification was underlined by the excellent agreement with the genotypic analysis. Indeed, MALDI-TOF allowed to correctly identify 39 out of 40 Lactobacillus strains at the species level, with an overall concordance of 97.5%. In the perspective to simplify the MALDI TOF sample preparation, especially for routine practice, we demonstrated the perfect agreement of the colony-picking from agar plates with the protein extraction protocol. 1H-NMR analysis, applied to both culture supernatants and bacterial lysates, identified a panel of metabolites whose variations in concentration were associated with the taxonomy, but also revealed a high intra-species variability that did not allow a species-level identification. Therefore, despite not suitable for mere taxonomic purposes, metabolomics can be useful to correlate particular biological activities with taxonomy and to understand the mechanisms related to the antimicrobial effect shown by some Lactobacillus species.

Franca, K. and Lotti, T. The gut-brain connection and the use of probiotics for the treatment of depression, anxiety and obsessive-compulsive disorders in dermatology. Dermatol.Ther. 5-16-2017; PM: 28508447

No Abstract Available.

Francavilla, R., De, Angelis M., Rizzello, C. G., Cavallo, N., Dal, Bello F., and Gobbetti, M. Selected Probiotic Lactobacilli Have the Capacity to Hydrolyze Gluten Peptides During Simulated Gastro-Intestinal Digestion. Appl.Environ.Microbiol. 5-12-2017; PM: 28500039

ABSTRACT: The aim of this study was to demonstrate the capacity of probiotic lactobacilli to hydrolyze immunogenic gluten peptides. Eighteen commercial strains of probiotic

lactobacilli with highly variable peptidase activity (i.e., aminopeptidase N, iminopeptidase, prolyl endopeptidyl peptidase, tripeptidase, prolidase, prolinase and dipeptidase), including towards Pro-rich peptides, were tested in this study. Ten probiotic strains were selected based on their specific enzyme activity. When pooled, these ten strains provide the peptidase portfolio that is required to completely degrade the immunogenic gluten peptides involved in celiac disease (CD). The selected probiotic mixture was able to completely hydrolyze well-known immunogenic epitopes, including the gliadin 33-mer, alpha9-gliadin peptide 57-68, A-gliadin peptide 62-75, and gamma-gliadin peptide 62-75. During digestion under simulated gastrointestinal conditions, the pool of 10 selected probiotic lactobacilli strongly hydrolyzed the wheat bread gluten (ca. 18.000 ppm) to less than 10 ppm after 360 min of treatment. As determined by multidimensional chromatography (MDLC) coupled to nanoelectrospray (ESI)-mass spectrometry (MS/MS), no known immunogenic peptides were detected in wheat bread that was digested in the presence of the probiotics. Accordingly, the level of cytokines (IL-2, IL-10 and IFN-gamma) produced by duodenal biopsies of CD patients who consumed wheat bread digested by probiotics was similar to the baseline value (negative control). Probiotics that specifically hydrolyze gluten polypeptides could also be used to hydrolyze immunogenic peptides that contaminate gluten-free products. This could provide a new and safe adjunctive therapy alternative to the gluten-free diet.IMPORTANCE This study confirmed that probiotic Lactobacillus strains have different enzymatic abilities for hydrolyzing polypeptides, including the Pro-rich epitopes involved in CD pathology. Ten lactobacilli with complementary peptidase activities that hydrolyze gluten peptides during simulated gastrointestinal digestion were selected and tested. The results collected showed the potential of probiotic formulas as novel dietary treatments for CD patients.

Fredua-Agyeman, M., Stapleton, P., Basit, A. W., Beezer, A. E., and Gaisford, S. In vitro inhibition of Clostridium difficile by commercial probiotics: A microcalorimetric study. Int.J.Pharm. 1-30-2017; 517(1-2):96-103; PM: 27923699

ABSTRACT: The aim of the study was to investigate the influence of some commercial probiotics on the growth of Clostridium difficile using isothermal microcalorimetry, a technique which can monitor the real time growth of bacteria. Commercial probiotic strains and products, Lactobacillus acidophilus LA-5(R), Bifidobacterium lactis BB-12(R), Probio 7(R) and Symprove were co-cultured with C. difficile in Brain Heart Infusion (BHI) broth supplemented with 0.1% (w/v) l-cysteine hydrochloride and 0.1% (w/v) sodium taurocholate and monitored in the microcalorimeter. Pseudomonas aeruginosa NCIMB 8628 was also co-cultured with C. difficile and studied. The results indicated inhibition of C. difficile by the probiotics. The inhibition of C. difficile was shown to be pH-dependent using neutralized and unmodified cell free supernatant (CFS) produced by the probiotic strains. However, concentrated CFS of the probiotics also inhibited the intestinal pathogen in a non pH-dependent manner, likely due to specific antimicrobial substances produced. The results also indicated that C. difficile growth was greatly influenced by the presence of sodium taurocholate and by the pH of the medium. A medium pH of between 6.45 and 6.9 demonstrated maximum growth of the organism in the microcalorimeter.

Freedberg, D. E., Kim, L. S., and Yang, Y. X. The Risks and Benefits of Long-term Use of Proton Pump Inhibitors: Expert Review and Best Practice Advice From the American Gastroenterological Association. Gastroenterology. 2017; 152(4):706-715; PM: 28257716

ABSTRACT: BACKGROUND & AIMS: The purpose of this review is to evaluate the risks associated with long-term use of proton pump inhibitors (PPIs), focusing on long-term use of PPIs for three common indications: gastroesophageal reflux disease (GERD), Barrett's esophagus (BE), and non-steroidal anti-inflammatory drug (NSAID) bleeding prophylaxis. *METHODS*: The recommendations outlined in this review are based on expert opinion and on relevant publications from PubMed, EMbase, and the Cochrane library (through July 2016). To identify relevant ongoing trials, we queried clinicaltrials.gov. To assess the quality of evidence, we used a modified approach based on the GRADE Working Group. The Clinical Practice Updates Committee of the American Gastroenterological Association has reviewed these recommendations. *Best Practice Advice 1*: Patients with GERD and acid-related complications (ie, erosive esophagitis or peptic stricture) should take a PPI for short-term healing, maintenance of healing, and long-term symptom control. *Best Practice Advice 2*: Patients with uncomplicated GERD who respond to short-term PPIs should subsequently attempt to stop or reduce them. Patients who cannot reduce PPIs should consider ambulatory esophageal pH/impedance monitoring before committing to lifelong PPIs to help distinguish GERD from a functional syndrome. The best candidates for this strategy may be patients with predominantly atypical symptoms or those who lack an obvious predisposition to GERD (eg, central obesity, large hiatal hernia). *Best Practice Advice 3*: Patients with Barrett's esophagus and symptomatic GERD should take a long-term PPI. *Best Practice Advice 4*: Asymptomatic patients with Barrett's esophagus should consider a long-term PPI. *Best Practice Advice 5*: Patients at high risk for ulcer-related bleeding from NSAIDs should take a PPI if they continue to take NSAIDs. *Best Practice Advice 6*: The dose of long-term PPIs should be periodically reevaluated so that the lowest effective PPI dose can be prescribed to manage the condition. *Best Practice Advice 7*: Long-term PPI users should not routinely use probiotics to prevent infection. Best *Practice Advice 8*: Long-term PPI users should not routinely raise their intake of calcium, vitamin B12, or magnesium beyond the Recommended Dietary Allowance (RDA). Best *Practice Advice 9:* Long-term PPI users should not routinely screen or monitor bone mineral density, serum creatinine, magnesium, or vitamin B12. *Best Practice Advice 10*: Specific PPI formulations should not be selected based on potential risks.

Frost, B. L., Modi, B. P., Jaksic, T., and Caplan, M. S. New Medical and Surgical Insights Into Neonatal Necrotizing Enterocolitis: A Review. JAMA Pediatr. 1-1-2017; 171(1):83-88; PM: 27893069

ABSTRACT: Importance: Necrotizing enterocolitis (NEC) has long remained a significant cause of morbidity and mortality in neonatal intensive care units. While the mainstay of treatment for this devastating condition remains largely supportive, research efforts continue to be directed toward understanding pathophysiology as well as how best to approach surgical management when indicated. Observations: In this review, we first examine recent medical observations, including overviews on the microbiome and a brief review of the use of probiotics. Next, we discuss the use of biomarkers and how clinicians may be able to use them in the future to predict the course of disease and, perhaps, the need for surgical intervention. We then provide an overview on the use of exclusive human milk feeding and the utility of this approach in preventing NEC. Finally, we discuss recent developments in the surgical management of NEC, beginning with

indications for surgery and following with a section on technical surgical considerations, including peritoneal drain vs laparotomy. The review concludes with outcomes from infants with surgically treated NEC. Conclusions and Relevance: Although medical treatment options for NEC are largely unchanged, understanding of the disease continues to evolve. As new research methods are developed, NEC pathophysiology can be more completely understood. In time, it is hoped that data from ongoing and planned clinical trials will allow us to routinely add targeted preventive measures in addition to human milk, such as prebiotics and probiotics, to the management of high-risk infants. In addition, the discovery of novel biomarkers may not only prove useful in predicting severity of illness but also will hopefully allow for identification of the disease prior to onset of clinical signs. Finally, continued investigation into optimizing surgical outcomes is essential in this population of infants, many of whom require long-term parenteral therapy and intestinal rehabilitation.

Fu, L., Peng, J., Zhao, S., Zhang, Y., Su, X., and Wang, Y. Lactic acid bacteria-specific induction of CD4+Foxp3+T cells ameliorates shrimp tropomyosin-induced allergic response in mice via suppression of mTOR signaling. Sci.Rep. 5-16-2017; 7(1):1987; PM: 28512288

ABSTRACT: The beneficial effects of probiotics have been described in allergic sensitization and diseases; however, many questions remain unanswered, such as characteristics of the most effective strains in modulation of allergic responses and how orally administered probiotics affect the systemic immune system. In the present work, oral administration of five lactic acid bacteria strains showed variable effects on protection against the allergic reaction in a mouse model of food allergy to shrimp tropomyosin (ST). The most effective anti-allergic strain, Bacillus coagulans 09.712 (Bc), greatly improved epithelial barrier function and increased lymphocytes proliferation. Moreover, Bc suppresses ST sensitization by altering Th1/Th2/Treg balance as a result of strong induction of CD4+Foxp3+Tregs in combination with IL-10 producing. Bc-specific induction of CD4+Foxp3+ Tregs also suppresses Th17 pro-inflammatory response in this mouse model. Finally, the intake of Bc suppresses mTOR activation and thus the phosphorylation of downstream factors. Inhibition of mTOR signaling by Bc further results in FOXP3 up-regulation and GATA-3 down-regulation, which, in turn, facilitate to control Th2-predominant and Th17 pro-inflammatory responses caused by ST. Our work provides further characterization of the anti-allergic effects of probiotic LAB strains, and identifies new targets for preventive and curative treatment of food allergies.

Fu, L., Wang, C., and Wang, Y. Seafood allergen-induced hypersensitivity at the microbiota-mucosal site: implications for prospective probiotic use in allergic response regulation. Crit Rev.Food Sci.Nutr. 1-13-2017; 0; PM: 28084786

ABSTRACT: Food allergy is a serious disease worldwide; it can significantly lower the standard of living of affected individuals and may be life-threatening. In particular, hypersensitivity to seafood has been increasing in recent years owing to rising consumption. The mucosal immune system plays a critical role in the onset of seafood allergy and other allergic diseases. Recently, experimental and clinical evidence has shown that probiotics significantly modulate immune responses and thus suppress allergic reactions. Therefore, in this review, we summarized the basic knowledge of seafood allergy, the mucosal immune system and probiotic activities. We also reviewed the critical immune factors involved in allergic reactions, as well as the potential mechanism and the potential use of probiotics to ameliorate seafood allergy. The elucidation of

these topics may help us to develop preventive and therapeutic approaches for seafood allergy and other immune disorders in the future.

Gadde, U., Kim, W. H., Oh, S. T., and Lillehoj, H. S. Alternatives to antibiotics for maximizing growth performance and feed efficiency in poultry: a review. Anim Health Res.Rev. 5-9-2017; 1-20; PM: 28485263

ABSTRACT: With the increase in regulations regarding the use of antibiotic growth promoters and the rise in consumer demand for poultry products from 'Raised Without Antibiotics' or 'No Antibiotics Ever' flocks, the quest for alternative products or approaches has intensified in recent years. A great deal of research has focused on the development of antibiotic alternatives to maintain or improve poultry health and performance. This review describes the potential for the various alternatives available to increase animal productivity and help poultry perform to their genetic potential under existing commercial conditions. The classes of alternatives described include probiotics, prebiotics, synbiotics, organic acids, enzymes, phytogenics, antimicrobial peptides, hyperimmune egg antibodies, bacteriophages, clay, and metals. A brief description of the mechanism of action, efficacy, and advantages and disadvantages of their uses are also presented. Though the beneficial effects of many of the alternatives developed have been well demonstrated, the general consensus is that these products lack consistency and the results vary greatly from farm to farm. Furthermore, their mode of action needs to be better defined. Optimal combinations of various alternatives coupled with good management and husbandry practices will be the key to maximize performance and maintain animal productivity, while we move forward with the ultimate goal of reducing antibiotic use in the animal industry.

Gadde, U., Oh, S. T., Lee, Y. S., Davis, E., Zimmerman, N., Rehberger, T., and Lillehoj, H. S. The Effects of Direct-fed Microbial Supplementation, as an Alternative to Antibiotics, on Growth Performance, Intestinal Immune Status, and Epithelial Barrier Gene Expression in Broiler Chickens. Probiotics.Antimicrob.Proteins. 4-18-2017; PM: 28421423

ABSTRACT: The objective of this study was to investigate the effects of Bacillus subtilis-based probiotic supplementation in broiler chicken diets on growth performance, feed efficiency, intestinal cytokine, and tight junction (TJ) protein mRNA expression. Zero-day-old broiler chicks (n = 140) were randomly assigned to one of five dietary treatments: basal diet (CON); basal diet supplemented with either antibiotic bacitracin methylene disalicylate (BMD); or probiotics, namely, B. subtilis strain 1781 (PB1), a combination of B. subtilis strain 1104 + strain 747 (PB2), or B. subtilis strain 1781 + strain 747 (PB3). Body weight and feed intake were measured at 14 days of age, and the feed conversion ratio (FCR) was calculated. At 14 days of age, ileal samples were collected and used for intestinal cytokine, TJ protein, and mucin gene expression analysis using qRT-PCR. The chickens supplemented with antibiotic (BMD) and B. subtilis strain 1781 alone (PB1) had significantly higher body weights compared to controls of the same age. Dietary supplementation with antibiotic (BMD) or probiotics (PB1, PB2, PB3) significantly improved the feed efficiency as evidenced by decreased FCR compared to controls. No differences were observed in the expression of IL1beta, IL17F, IFNgamma, and MUC2 gene among the different treatment groups. However, elevated expression of IL6 (BMD, PB1, PB2), IL8 (PB2), and TNFSF15 (PB1, PB2, PB3) compared to controls was observed in the ileum. IL2 and IL10 expression was upregulated in chicks in the PB2 and PB3 groups, and IL4 was elevated in the PB1 group. IL13 was elevated in all probiotic-fed groups (PB1,

PB2, PB3). Probiotic supplementation was also shown to significantly increase the expression of TJ proteins JAM2, ZO1 (PB2, PB3), and occludin (PB1, PB2). Taken together, B. subtilis supplementation altered intestinal immune activity and influenced gut barrier integrity through increased tight junction gene expression.

Gadde, U. D., Oh, S., Lee, Y., Davis, E., Zimmerman, N., Rehberger, T., and Lillehoj, H. S. Dietary Bacillus subtilis-based direct-fed microbials alleviate LPS-induced intestinal immunological stress and improve intestinal barrier gene expression in commercial broiler chickens. Res.Vet.Sci. 5-6-2017; 114:236-243; PM: 28505587

ABSTRACT: This study investigated the effects of Bacillus subtilis-based probiotics on the performance, modulation of host inflammatory responses and intestinal barrier gene expression of broilers subjected to LPS challenge. Chickens were randomly allocated to one of the 3 dietary treatment groups - control, antibiotic, or probiotic. At 14days, half of the chickens in each treatment were injected with LPS (1mg/kg body weight), and the other half injected with sterile PBS. Chickens fed probiotics weighed significantly more than controls at 15days of age, irrespective of immune challenge. LPS challenge significantly reduced weight gain at 24h post-injection, and the probiotics did not alleviate the LPS-induced reduction of weight gain. Serum alpha-1-AGP levels were significantly higher in LPS-injected chickens, and probiotic supplementation significantly reduced their levels. The percentages of CD4+ lymphocytes were significantly increased in probiotic groups in the absence of immunological challenge but were reduced during LPS challenge compared to controls. CD8+ lymphocytes were significantly reduced in probiotic-fed birds. The LPS-induced increase in the expression of cytokines IL8 and TNFSF15 was reduced by probiotic supplementation, and IL17F, iNOS expression was found to be significantly elevated in probiotic-fed birds subjected to LPS challenge. The reduced gene expression of tight junction proteins (JAM2, occludin and ZO1) and MUC2 induced by LPS challenge was reversed by probiotic supplementation. The results indicate that B. subtilis-based probiotics differentially regulate intestinal immune and tight junction protein mRNA expression during states of LPS-mediated immunological challenge.

Gandhi, G. R., Santos, V. S., Denadai, M., da, Silva Calisto, V, de Souza Siqueira, Quintans J., de Oliveira E Silva AM, de Souza Araujo, A. A., Narain, N., Cuevas, L. E., Junior, L. J. Q., and Gurgel, R. Q. Cytokines in the management of rotavirus infection: A systematic review of in vivo studies. Cytokine. 4-14-2017; 96:152-160; PM: 28414969

ABSTRACT: OBJECTIVE: Rotavirus is a leading cause of childhood diarrhoea. Rotavirus vaccines are effective against severe rotavirus gastroenteritis, but have lower efficacy in low income countries in Africa. Anti-rotavirus treatment is not available. This study reviews the literature of animal studies evaluating whether cytokine mediated pathways of immune activation could improve rotavirus therapy. *METHODS*: We performed a systematic review of articles in English published from 2010 to 2016 reporting agents with in vivo antirotavirus activity for the management of rotavirus infection. The search was carried in PubMed, EMBASE, Scopus and Web of Science. Animal experiments where cytokines were investigated to assess the outcome of rotavirus therapy were included. *RESULTS*: A total of 869 publications were identified. Of these, 19 pertained the objectives of the review, and 11 articles described the effect of probiotics/commensals on rotavirus infection and immune responses in animals. Eight further in vivo studies evaluated the immunomodulating effects of herbs, secondary metabolites and food-derived products

on cytokine responses of rotavirus-infected animals. Studies extensively reported the regulatory roles for T-helper (Th)1 (interferon gamma (IFN-gamma), interleukin (IL)-2, IL-12) and Th2 (IL-4, IL-6, IL-10) cytokines responses to rotavirus pathogenesis and immunity, inhibiting rotavirus infection through suppression of inflammation by viral inhibition. *CONCLUSION*: Th1 and Th2 cytokines stimulate the immune system, inhibiting rotavirus binding and/or replication in animal models. Th1/Th2 cytokine responses have optimal immunomodulating effects to reduce rotavirus diarrhoea and enhance immune responses in experimental rotavirus infection.

Ganji-Arjenaki, M. and Rafieian-Kopaei, M. Probiotics are a good choice in remission of inflammatory bowel diseases: A meta analysis and systematic review. J.Cell Physiol. 3-15-2017; PM: 28294322

ABSTRACT: Altered gut bacteria and bacterial metabolic pathways are two important factors in initiation and progression of inflammatory bowel disease (IBD). However, efficacy of probiotics in remission of patients with IBD has not been characterized. This study was performed on the studies that specifically assessed the efficacy of probiotics in attaining clinical response on patients with various types of IBD. The efficacy of variant species of probiotics in different conditions and the influence of study quality in outcomes of randomized controlled trials (RCTs) were also assessed. The RCTs were collected by searching in MEDLINE Web of Science and Google scholar. Then all studies were abstracted in abstraction form and the outcomes were analyzed with fixed-effect and mixed-effect models for assessment of efficacy of variant species of probiotics in subgroups of IBDs. Analysis of 9 trials showed that probiotics had not significant effect on Crohn's disease (CD) ($p = 0.07$) but analysis of 3 trials in children with IBD revealed a significant advantage ($p < 0.01$). Analysis of 18 trials revealed that probiotics in patients with Ulcerative colitis (UC) in different conditions have significant effects ($p = 0.007$). VSL#3 probiotics in patients with UC had significant effect ($p < 0.01$). Combination of Lactobacillus probiotic, prebiotics had significant effect ($p = 0.03$) only in patients with UC. Combination of Saccharomyces boulardii, Lactobacillus, and VSL#3 probiotics in CD had also a trend for efficiency ($p = 0.057$). In children with IBD, the combination of Lactobacillus with VSL#3 probiotics had significant effect ($p < 0.01$). Probiotics are beneficial in IBD, especially the combination ones in UC.

Gao, X. Y., Liu, Y., Miao, L. L., Li, E. W., Hou, T. T., and Liu, Z. P. Mechanism of anti-Vibrio activity of marine probiotic strain Bacillus pumilus H2, and characterization of the active substance. AMB.Express. 2017; 7(1):23; PM: 28097594

ABSTRACT: Vibriosis is a major epizootic disease that impacts free-living and farmed fish species worldwide. Use of probiotics is a promising approach for prevention of Vibrio infections in aquaculture. A probiotic anti-Vibrio strain, Bacillus pumilus H2, was characterized, and the mechanism of its effect was investigated. All 29 Vibrio strains tested were growth-inhibited by H2. The anti-Vibrio substance present in cell-free supernatant of H2 was purified and characterized by reversed-phase HPLC. Minimum inhibitory concentrations of the purified substance, determined in liquid media for various Vibrio strains, ranged from 0.5 to 64 microg/ml. Addition of the purified substance to Vibrio vulnificus culture inhibited cell growth (estimated by OD600). Confocal microscopy and scanning electron microscopy analyses showed that surface structure of V. vulnificus cells was damaged by the purified substance, as reflected by presence of membrane holes, disappearance of cellular contents, and formation of cell cavities. The major mechanism of this anti-Vibrio activity appeared to involve disruption of cell membranes,

and consequent cell lysis. The purified anti-Vibrio substance was shown to be structurally identical to amicoumacin A by MS and NMR analysis. Our findings indicate that B. pumilus H2 has strong potential for prevention or treatment of fish vibriosis in the aquaculture industry.

Gao, X. Y., Liu, Y., Miao, L. L., Li, E. W., Sun, G. X., Liu, Y., and Liu, Z. P. Characterization and mechanism of anti-Aeromonas salmonicida activity of a marine probiotic strain, Bacillus velezensis V4. Appl.Microbiol.Biotechnol. 2017; 101(9):3759-3768; PM: 28074223

ABSTRACT: The bacterium Aeromonas salmonicida is the causative agent of furunculosis, a systemic, ubiquitous disease of fish in the salmon family, characterized by high mortality and morbidity. Probiotics are a promising approach for prevention of furunculosis in aquaculture. A bacterial strain with anti-A. salmonicida properties, Bacillus velezensis V4, was isolated and the mechanisms underlying these properties were investigated. Anti-A. salmonicida compounds present in cell-free supernatant of V4 were purified and structurally identified as members of the iturin, macrolactin, and difficidin groups. The compounds contributed jointly to inhibition of A. salmonicida, and the diversity of the compounds was related to the versatility of their mode of action. Addition of the compounds to A. salmonicida cell suspensions reduced cell density. Analyses by confocal microscopy and scanning electron microscopy revealed cell membrane disruption, deletion of cellular content, and cell lysis of A. salmonicida. The V4 genome was sequenced, and gene clusters involved in synthesis of anti-Aeromonas compounds were detected and identified. A possible probiotic effect on growth performance of Oncorhynchus mykiss (rainbow trout) was investigated by addition of 0, 1, and 3 % (v/w) V4. Relative to control, mortality was reduced 27.25 % in the 1 % addition group and 81.86 % in the 3 % addition group. Feed coefficient ratio was reduced 19.49 % and weight gain ratio was increased 71.22 % in the 1 % addition group. Our findings demonstrate that V4 is an effective probiotic strain in O. mykiss and has clear potential for both control of furunculosis and growth promotion of aquaculture animals.

Garay, R. P. Vaccinating against depression or anxiety: is it plausible? Expert.Opin.Biol.Ther. 2017; 17(5):525-528; PM: 28277809

No Abstract Available.

Garcia-Velasco, J. A., Menabrito, M., and Catalan, I. B. What fertility specialists should know about the vaginal microbiome: a review. Reprod.Biomed.Online. 4-19-2017; PM: 28479120

ABSTRACT: Our understanding of the composition of the microbial communities that inhabit the human body, known as the 'microbiome', is aided by the development of non-culture-dependent DNA sequencing. It is increasingly apparent that the balance of microbial species greatly affects the health of the host. Disturbances in the composition of bacterial communities have been shown to contribute to various disease states, and there is a growing body of evidence that the vaginal microbiota, which is unique to each woman, plays an important role in determining many facets of reproductive health. The purpose of this review is to investigate what is currently known about the composition of the vaginal microbiome, including what is considered 'normal' in terms of

bacterial species and abundance. We will investigate the impact of vaginal microbiome composition on reproductive outcomes within the context of infertility treatments, and the implications this has been shown to have on assisted reproductive technology procedures.

Garg, B. D., Balasubramanian, H., and Kabra, N. S. Physiological effects of prebiotics and its role in prevention of Necrotizing enterocolitis in preterm neonates. J.Matern.Fetal Neonatal Med. 5-17-2017; 1-22; PM: 28514886

ABSTRACT: Necrotizing enterocolitis (NEC) is one of the most serious gastrointestinal emergencies in very low birth weight (VLBW) preterm neonates, affecting 7% to 14% of these neonates. Due to seriousness of disease, prevention of NEC is the most important goal. Current evidence from systematic review and meta-analysis revealed probiotics are the most promising intervention in reduction of the incidence of NEC in VLBW neonates. As per the evidence, prebiotics modulate the composition of human intestine microflora to the benefit of the host by suppression of colonization of harmful microorganism and/or the stimulation of bifidobacterial growth, decreased stool viscosity, reduced gastrointestinal transit time and better feed tolerance. Prebiotics may be potential alternatives or adjunctive therapies to probiotics, despite a lack of evidence supporting its clinical efficacy in prevention of NEC. In this review article, we discuss evidence based physiological effects of prebiotics and its therapeutic role in prevention of NEC.

Genis, S., Sanchez-Chardi, A., Bach, A., Fabregas, F., and Aris, A. A combination of lactic acid bacteria regulates Escherichia coli infection and inflammation of the bovine endometrium. J.Dairy Sci. 2017; 100(1):479-492; PM: 27837977

ABSTRACT: Uterine function in cattle is compromised by bacterial contamination and inflammation after calving. The objective of this study was to select a combination of lactic acid bacteria (LAB) to decrease endometrium inflammation and Escherichia coli infection. Primary endometrial epithelial cells were cultured in vitro to select the most favorable LAB combination modulating basal tissue inflammation and E. coli infection. Supernatants were obtained to determine expression of pro-inflammatory cytokines, and E. coli infection was evaluated after harvesting the tissue and plate counting. The selected LAB combination was tested in uterus explants to assess its capacity to modulate basal and acute inflammation (associated with E. coli infection). The combination of Lactobacillus rhamnosus, Pediococcus acidilactici, and Lactobacillus reuteri at a ratio of 25:25:2, respectively, reduced E. coli infection in vitro with (89.77%) or without basal tissue inflammation (95.10%) compared with single LAB strains. Lactic acid bacteria treatment reduced CXCL8 and IL1B expression 4.7- and 2.2-fold, respectively, under acute inflammation. Ex vivo, the tested LAB combination reduced acute inflammation under E. coli infection, decreasing IL-8, IL-1beta, and IL-6 up to 2.2-, 2.5-, and 2.2-fold, respectively. In the total inflammation model, the LAB combination decreased IL-8 1.6-fold and IL-6 1.2-fold. Ultrastructural evaluation of the tissue suggested no direct interaction between the LAB and E. coli, although pathological effects of E. coli in endometrial cells were greatly diminished or even reversed by the LAB combination. This study shows the promising potential of LAB probiotics for therapeutic use against endometrial inflammation and infection.

Ghoshal, U. C., Shukla, R., and Ghoshal, U. Small Intestinal Bacterial Overgrowth and Irritable Bowel Syndrome: A Bridge between Functional Organic Dichotomy. Gut Liver. 3-15-2017; 11(2):196-208; PM: 28274108

ABSTRACT: The pathogenesis of irritable bowel syndrome (IBS), once thought to be largely psychogenic in origin, is now understood to be multifactorial. One of the reasons for this paradigm shift is the realization that gut dysbiosis, including small intestinal bacterial overgrowth (SIBO), causes IBS symptoms. Between 4% and 78% of patients with IBS and 1% and 40% of controls have SIBO; such wide variations in prevalence might result from population differences, IBS diagnostic criteria, and, most importantly, methods to diagnose SIBO. Although quantitative jejunal aspirate culture is considered the gold standard for the diagnosis of SIBO, noninvasive hydrogen breath tests have been popular. Although the glucose hydrogen breath test is highly specific, its sensitivity is low; in contrast, the early-peak criteria in the lactulose hydrogen breath test are highly nonspecific. Female gender, older age, diarrhea-predominant IBS, bloating and flatulence, proton pump inhibitor and narcotic intake, and low hemoglobin are associated with SIBO among IBS patients. Several therapeutic trials targeting gut microbes using antibiotics and probiotics have further demonstrated that not all symptoms in patients with IBS originate in the brain but rather in the gut, providing support for the micro-organic basis of IBS. A recent proof-of-concept study showing the high frequency of symptom improvement in patients with IBS with SIBO further supports this hypothesis.

Giannetti, E., Maglione, M., Sciorio, E., Coppola, V., Miele, E., and Staiano, A. Do Children Just Grow Out of Irritable Bowel Syndrome? J.Pediatr. 2017; 183:122-126; PM: 28108106

ABSTRACT: *OBJECTIVE*: Few data exist on natural history of irritable bowel syndrome (IBS) in children; therefore we investigated symptoms evolution over time in a cohort of children with IBS. *STUDY DESIGN*: In this observational, single-center study, we prospectively enrolled newly diagnosed children with IBS and reassessed them after 24 months. At both time points, patients completed a symptoms questionnaire, and a score of stool consistency was obtained. The therapeutic strategy adopted was also recorded. *RESULTS*: Eighty-three children (age 11 years, range, 4-16.6 years; 53 males) completed the study. Forty-seven (56.6%) patients received no medical treatment, whereas polyethylene glycol, probiotics, and trimebutine were prescribed to 9 (10.8%), 24 (28.9%), and 3 (3.6%) subjects, respectively. Twenty-four months after diagnosis, 48 children (57.8%) reported resolution of symptoms (P <.001), without differences between sexes (P = .35) or among IBS subtypes (P = .49). Of these, 30 (62.5%) had been only reassured and 18 (37.5%) had been prescribed medical treatment (P = .26). Despite not being statistically significant, symptoms resolution was more common in patients receiving no medical treatment than in those receiving probiotics (63.8% vs 41.6%, P = .08). Among patients with constipation-IBS, no difference was found in symptoms resolution between patients receiving polyethylene glycol and those receiving no medical treatment (67% and 40%, respectively, P = 1). *CONCLUSIONS*: Children with IBS are likely to show spontaneous symptoms resolution over a 24-month follow-up, regardless of sex, age, impact of symptoms on daily activities, and IBS subtypes.

Giannetti, E., Maglione, M., Alessandrella, A., Strisciuglio, C., De, Giovanni D., Campanozzi, A., Miele, E., and Staiano, A. A Mixture of 3 Bifidobacteria Decreases Abdominal Pain and Improves the Quality of Life in Children With Irritable Bowel Syndrome: A Multicenter,

Randomized, Double-Blind, Placebo-Controlled, Crossover Trial. J.Clin.Gastroenterol. 2017; 51(1):e5-e10; PM: 27306945

ABSTRACT: GOALS: We assessed the efficacy of a probiotic mixture of Bifidobacterium infantis M-63, breve M-16V, and longum BB536 in improving abdominal pain (AP) and quality of life (QoL) in children with irritable bowel syndrome (IBS) and functional dyspepsia (FD). *BACKGROUND*: AP-associated functional gastrointestinal disorders, particularly IBS and FD, are common in pediatrics, and no well-established treatment is currently available. Although probiotics have shown promising results in adults, data in children are heterogeneous. *STUDY*: Forty-eight children with IBS (median age, 11.2 y; range, 8 to 17.9 y) and 25 with FD (age, 11.6 y; range, 8 to 16.6 y) were randomized to receive either a mixture of 3 Bifidobacteria or a placebo for 6 weeks. After a 2-week "washout" period, each patient was switched to the other group and followed up for further 6 weeks. At baseline and follow-up, patients completed a symptom diary and a QoL questionnaire. AP resolution represented the primary outcome parameter. *RESULTS*: In IBS, but not in FD, Bifidobacteria determined a complete resolution of AP in a significantly higher proportion of children, when compared with placebo (P=0.006), and significantly improved AP frequency (P=0.02). The proportion of IBS children with an improvement in QoL was significantly higher after probiotics than after placebo (48% vs. 17%, P=0.001), but this finding was not confirmed in FD. *CONCLUSIONS*: In children with IBS a mixture of Bifidobacterium infantis M-63, breve M-16V, and longum BB536 is associated with improvement in AP and QoL. These findings were not confirmed in FD subjects. Trial identifier: NCT02566876 (http://www.clinicaltrial.gov).

Giarma, E., Amanetidou, E., Toufexi, A., and Touraki, M. Defense systems in developing Artemia franciscana nauplii and their modulation by probiotic bacteria offer protection against a Vibrio anguillarum challenge. Fish.Shellfish.Immunol. 5-4-2017; 66:163-172; PM: 28478257

ABSTRACT: The alterations of immune responses of Artemia franciscana nauplii as a function of culture time and after a challenge with the pathogen Vibrio anguillarum were studied. The effect of the administration of the probiotic bacteria Bacillus subtilis, Lactobacillus plantarum and Lactococcus lactis either alone or in combination with the pathogen was evaluated. The activity of the antioxidant enzymes superoxide dismutase (SOD), Glutathione reductase (GRed), Glutathione transferase (GST) and Phenoloxidase (PO) presented a significant increase as a function of culture time, appeared elevated following probiotic administration and were depleted 48 h following the experimental challenge. Lipid peroxidation reached peak levels at 48 h of culture, when nauplii start feeding and returned to lower values at 144 h, remaining however significantly higher than control ($P < 0.05$). The three probiotics significantly reduced lipid peroxidation in comparison with the corresponding control, while challenge with the pathogen resulted in its threefold increase. Survival of nauplii remained high throughout culture and was either increased or remained at control levels following the administration of the probiotics. The challenge with the pathogen resulted in a significantly decreased survival of 15.3% for the positive control, while in the probiotic treated series survival values were not significantly different from the negative control ($P > 0.05$). Following a combined administration of each probiotic and the pathogen the activities of all enzymes tested were significantly lower ($P < 0.001$) than the negative control (no treatment), but higher than the positive control (challenge, no probiotic). Lipid peroxidation was significantly lower in the probiotic treated series in comparison to the positive control ($P < 0.001$). The results of the present study provide evidence that major alterations take place as a function of culture time of Artemia nauplii. In addition the pathogen induces an

oxidative stress response. The probiotics B. subtilis, L. plantarum and L. lactis protect Artemia against a V. anguillarum challenge by enhancing its immune responses thus contributing to reduced oxidative damage and increased survival.

Gibson, P. S., Lang, S., Dhawan, A., Fitzpatrick, E., Blumfield, M. L., Truby, H., Hart, K. H., and Moore, J. B. Systematic Review: Nutrition and Physical Activity in the Management of Paediatric Non-alcoholic Fatty Liver Disease. J.Pediatr.Gastroenterol.Nutr. 5-9-2017; PM: 28489673

ABSTRACT: OBJECTIVES: To evaluate efficacy of nutrition and physical activity interventions in the clinical management of paediatric non-alcoholic fatty liver disease (NAFLD). The prevalence of paediatric NAFLD continues to rise alongside childhood obesity. Weight loss through lifestyle modification is currently first-line treatment, although supplementation of specific dietary components may be beneficial. *METHODS*: Medline, CINAHL, EMBASE, Scopus and Cochrane Libraries were systematically searched to identify randomised controlled trials (RCTs) assessing nutritional and physical activity interventions. Primary outcome measures were changes to liver biomarkers assessed by imaging, histology or serum liver function tests. Study quality was evaluated using the American Dietetic Association Quality Criteria Checklist. *RESULTS*: Fifteen articles met eligibility criteria investigating nutritional supplementation (vitamin E [n = 6], probiotics [n = 2], omega-3 fatty acids [n = 5]), dietary modification (low glycaemic load [n = 1] and reducing fructose intake [n = 1]). No RCTs examining physical activity interventions were identified. Vitamin E was ineffective at improving alanine transaminase levels, while omega-3 fatty acids decreased hepatic fat content. Probiotics gave mixed results while reduced fructose consumption did not improve primary outcome measures. A low glycaemic load diet and a low fat diet appeared equally effective in decreasing hepatic fat content and transaminases. Most studies were deemed neutral as assessed by the American Dietetic Association Quality Criteria Checklist. *CONCLUSION*: The limited evidence base inhibits the prescription of specific dietary and/or lifestyle strategies for clinical practice. General healthy eating and physical activity guidelines, promoting weight loss, should remain first-line treatment until high quality evidence emerges that support specific interventions that offer additional clinical benefit.

Girbovan, A., Sur, G., Samasca, G., and Lupan, I. Dysbiosis a risk factor for celiac disease. Med.Microbiol.Immunol. 2017; 206(2):83-91; PM: 28204873

ABSTRACT: Celiac disease remains one of the most challenging pathologies of the small intestine. It involves multiple pathogenic pathways and there are no disease-changing pharmacological agents available against it yet. The term microbiota refers to the community of microorganisms that inhabit a particular region of the body. Normal gut microbiota has a vital role in maintaining the intestinal homeostasis and promoting health. Celiac disease is associated with microbiota alteration, especially with an increase in the number of Gram-negative bacteria and a decrease in the number of Gram-positive bacteria. There is a strong relationship between intestinal dysbiosis and celiac disease, and recent studies are aimed at determining whether the celiac disease is a risk factor for dysbiosis or dysbiosis is for celiac disease. Therefore, the aim of this review was to assess the latest findings regarding the gut microbiota and its impact on the celiac disease, including therapeutic aspects.

Gisbert, J. P. and McNicholl, A. G. Optimization strategies aimed to increase the efficacy of H. pylori eradication therapies. Helicobacter. 5-2-2017; PM: 28464347

ABSTRACT: BACKGROUND: As with any other infectious disease, we should aim for treatments offering >/=90% Helicobacter pylori eradication rates in clinical practice. AIM: To summarize optimization strategies aimed to increase the efficacy of H. pylori eradication therapies. *METHODS*: A systematic bibliographic search (in PubMed up to August 2016) was designed to identify studies investigating optimization strategies aimed to increase the efficacy of H. pylori eradication therapies. *RESULTS*: The most direct way to optimize a treatment is using higher doses of drugs unless it has been shown that lower doses are equally effective. Similarly, prescriptions should use 14-day duration unless a shorter scheme has been shown locally to be equally effective. Double-dose proton-pump inhibitor therapy is recommended for triple therapy and may probably increase the efficacy of nonbismuth concomitant regimen as well. The efficacy of triple therapies in the presence of resistance can be significantly improved by the addition of bismuth salts, which offer an additive effect in combination with antibiotics. Overall, probiotics seem to reduce antibiotic side effects, but the increase in eradication rates is not so evident; therefore, they cannot be generally recommended for clinical practice yet. *CONCLUSIONS*: Using potent acid inhibition and/or higher antibiotic doses-especially by increasing the number of daily intakes-and lengthening treatments up to 14 days improves efficacy in most regimens and should be generally recommended. Triple therapies can be efficiently improved by the addition of bismuth salts, turning them into quadruple therapies. Finally, some treatments will require a combination of optimization strategies to significantly improve results.

Godfrey, K. M., Cutfield, W., Chan, S. Y., Baker, P. N., and Chong, Y. S. Nutritional Intervention Preconception and During Pregnancy to Maintain Healthy Glucose Metabolism and Offspring Health ("NiPPeR"): study protocol for a randomised controlled trial. Trials. 3-20-2017; 18(1):131; PM: 28320484

ABSTRACT: BACKGROUND: Improved maternal nutrition and glycaemic control before and during pregnancy are thought to benefit the health of the mother, with consequent benefits for infant body composition and later obesity risk. Maternal insulin resistance and glycaemia around conception and in early pregnancy may be key determinants of maternal physiology and placental function, affecting fetal nutrient supply and maternal-feto-placental communications throughout gestation, with implications for later postnatal health. *METHODS/DESIGN*: This double-blind randomised controlled trial will recruit up to 1800 women, aged 18-38 years, who are planning a pregnancy in the United Kingdom (UK), Singapore and New Zealand, with a view to studying 600 pregnancies. The primary outcome is maternal glucose tolerance at 28 weeks' gestation following an oral glucose tolerance test. Secondary outcomes include metabolic, molecular and health-related outcomes in the mother and offspring, notably infant body composition. Participants will be randomly allocated to receive a twice-daily control nutritional drink, enriched with standard micronutrients, or a twice-daily intervention nutritional drink enriched with additional micronutrients, myo-inositol and probiotics, both demonstrated previously to assist in maintaining healthy glucose metabolism during pregnancy. Myo-inositol is a nutrient that enhances cellular glucose uptake. The additional micronutrients seek to address deficiencies of some B-group vitamins and vitamin D that are both common during pregnancy and that have been associated with maternal dysglycaemia, epigenetic changes and greater offspring adiposity. Women who conceive within a year of starting the nutritional drinks will be followed through pregnancy and studied with their infants at six time points during the first year of life.

Blood, urine/stool, hair and cheek swabs will be collected from the mothers for genetic, epigenetic, hormone, nutrient and metabolite measurements, and assessments of the mother's body composition, anthropometry, health, diet and lifestyle will be made. Infants will also undergo hair, cheek swab, urine and stool sampling for similar biological measurements; infant body composition will be assessed and feeding recorded. *DISCUSSION*: There is an increasing focus on the need to optimise maternal nutrition starting prior to conception. This trial will provide evidence on the potential for nutritional interventions beginning prior to conception to promote healthy maternal and offspring outcomes. *TRIAL REGISTRATION*: ClinicalTrials.gov, identifier: NCT02509988 , Universal Trial Number U1111-1171-8056. Registered on 16 July 2015. This is an academic-led study by the EpiGen Global Research Consortium.

Goncalves, A. T. and Gallardo-Escarate, C. Microbiome dynamic modulation through functional diets based on pre- and probiotics (mannan-oligosaccharides and Saccharomyces cerevisiae) in juvenile rainbow trout (Oncorhynchus mykiss). J.Appl.Microbiol. 2017; 122(5):1333-1347; PM: 28256031

ABSTRACT: *AIMS*: This study used high-throughput sequencing to evaluate the intestinal microbiome dynamics in rainbow trout (Oncorhynchus mykiss) fed commercial diets supplemented with either pre- or probiotics (0.6% mannan-oligosaccharides and 0.5% Saccharomyces cerevisiae respectively) or the mixture of both. METHODS AND *RESULTS*: A total of 57 fish whole intestinal mucosa and contents bacterial communities were characterized by high-throughput sequencing and analysis of the V3-V4 region of the 16S rRNA gene, as well as the relationship between plasma biochemical health indicators and microbiome diversity. This was performed at 7, 14 and 30 days after start feeding functional diets, and microbiome diversity increased when fish fed functional diets after 7 days and it was positively correlated with plasma cholesterol levels. Dominant phyla were, in descending order, Proteobacteria, Firmicutes, Actinobacteria, Acidobacteria, Bacteroidetes and Fusobacteria. However, functional diets reduced the abundance of Gammaproteobacteria to favour abundances of organisms from Firmicutes and Fusobacteria, two phyla with members that confer beneficial effects. A dynamic shift of the microbiome composition was observed with changes after 7 days of feeding and the modulation by functional diets tend to cluster the corresponding groups apart from CTRL group. The core microbiome showed an overall stability with functional diets, except genus such as Escherichia-Shigella that suffered severe reductions on their abundances when feeding any of the functional diets. *CONCLUSIONS*: Functional diets based on pre- or probiotics dynamically modulate intestinal microbiota of juvenile trout engaging taxonomical abundance shifts that might impact fish physiological performance. *SIGNIFICANCE AND IMPACT OF THE STUDY*: This study shows for the first time the microbiome modulation dynamics by functional diets based on mannan-oligosaccharides and S. cerevisiae and their synergy using culture independent high-throughput sequencing technology, revealing the complexity behind the dietary modulation with functional feeds in aquatic organisms.

Goncalves, A. T., Valenzuela-Munoz, V., and Gallardo-Escarate, C. Intestinal transcriptome modulation by functional diets in rainbow trout: A high-throughput sequencing appraisal to highlight GALT immunomodulation. Fish.Shellfish.Immunol. 2017; 64:325-338; PM: 28300682

ABSTRACT: Functional ingredients such as pre- and probiotics are used in aquaculture to

improve fish condition, modulating microbiota and promoting a healthy intestinal functioning. They also exert an active effect on the gut associated lymphoid tissue (GALT), stimulating the immune system. However, the molecular underpinnings of pre- and probiotics effect on intestinal mucosa are still unknown. This study investigated the intestinal mucosa transcriptome modulation when fish were fed functional diets and kept at different stocking densities. Juvenile rainbow trout were kept at low (LD-3Kgm-3) and high density (HD-40 kgm-3) and fed for 30 days functional diets with the prebiotic mannanoligosaccharide (PRE-0.6%), the probiotic Saccharomyces cerevisiae (PRO-0.5%), the mixture of both (MIX) and a control diet (CTRL). Intestinal transcriptome was evaluated by high-throughput sequencing and blood plasma for biochemical parameters. Fish fed functional diets presented better condition regardless density, and that functional diets modulate intestinal transcriptome in different manner depending on the stocking density. At LD, fish from PRO presented stronger modulation with the majority of transcripts being down-regulated, including the immune related ones, whereas at HD both PRO and MIX groups were more modulated, when comparing to the respective CTRL groups. Density had an overwhelming suppressive effect on the immune-related genes, but this effect was counteracted by feeding functional diets, especially in fish fed with probiotics. This study shows for the first time the intestinal transcriptomic modulation when fish are fed functional diets at different stocking densities, and it shows the mitigating effect of these diets against deleterious conditions such as high density.

Gonzalez, A., Galvez, N., Martin, J., Reyes, F., Perez-Victoria, I., and Dominguez-Vera, J. M. Identification of the key excreted molecule by Lactobacillus fermentum related to host iron absorption. Food Chem. 8-1-2017; 228:374-380; PM: 28317737

ABSTRACT: We have taken a vital step towards understanding why probiotic bacteria increase iron absorption in the gastrointestinal tract. We show here that Lactobacillus fermentum, one of the main probiotics of the microbiota, exhibits an extraordinary ferric-reducing activity. This activity is predominantly due to an excreted molecule: p-hydroxyphenyllactic acid (HPLA). Reduction of Fe(III) to Fe(II) is essential for iron absorption in the gastrointestinal tract. By reducing Fe(III), HPLA boosts Fe(II) absorption through the DMT1 channels of enterocytes. An in vitro experiment tested and confirmed this hypothesis. This discovery opens new avenues for the treatment of iron deficiency in humans, one of the most common and widespread nutritional disorders in the world.

Gorshein, E., Wei, C., Ambrosy, S., Budney, S., Vivas, J., Shenkerman, A., Manago, J., McGrath, M. K., Tyno, A., Lin, Y., Patel, V., Gharibo, M., Schaar, D., Jenq, R. R., Khiabanian, H., and Strair, R. Lactobacillus rhamnosus GG probiotic enteric regimen does not appreciably alter the gut microbiome or provide protection against GVHD after allogeneic hematopoietic stem cell transplantation. Clin.Transplant. 2017; 31(5); PM: 28256022

ABSTRACT: Graft-versus-host disease (GVHD) is a major adverse effect associated with allogeneic stem cell transplant. Previous studies in mice indicated that administration of the probiotic Lactobacillus rhamnosus GG can reduce the incidence of GVHD after hematopoietic stem cell transplant. Here we report results from the first randomized probiotic enteric regimen trial in which allogenic hematopoietic stem cell patients were supplemented with Lactobacillus rhamnosus GG. Gut microbiome analysis confirmed a previously reported gut microbiome association with GVHD. However, the clinical trial was terminated when interim analysis did not detect an appreciable probiotic-related change in the gut microbiome or incidence of GVHD. Additional studies are necessary

to determine whether probiotics can alter the incidence of GVHD after allogeneic stem cell transplant.

Graham, K., Rea, R., Simpson, P., and Stack, H. Development of a rapid, one-step screening method for the isolation of presumptive proteolytic enterococci. J.Microbiol.Methods. 2017; 132:99-105; PM: 27894832

ABSTRACT: Enterococci show higher proteolytic activities than other lactic acid bacteria and thus have received considerable attention in scientific literature in recent years. Proteolytic enzymes of enterococci have warranted the use of some species as starter, adjuncts or protective cultures and as probiotics, while in some strains they have also been linked with virulence. Consequently, the isolation and identification of proteolytic enterococci is becoming of increasing interest and importance. However, current screening methods for proteolytic enterococci can be time consuming, requiring a two-step procedure which may take up to 96h. This study describes a method, utilising Kanamycin Skim Milk Aesculin Azide (KSMEA) agar, for the isolation of proteolytic enterococci in one-step, thereby significantly reducing screening time. KSMEA combines the selective properties of Kanamycin Aesculin Azide Agar (KAA) with skim milk powder for the detection of proteolytic enterococci. Enterococci produced colonies with a black halo on KSMEA which were accompanied by a zone of clearing in the media when enterococci were proteolytic. KSMEA medium retained the selectivity of KAA, while proteolytic enterococci were easily distinguished from non-proteolytic enterococci when two known strains were propagated on KSMEA. KSMEA also proved effective at isolating and detecting enterococci in raw milk, faeces and soil. Isolates recovered from the screen were confirmed as enterococci using genus-specific primers. Proteolytic enterococci were present in the raw milk sample only and were easily distinguishable from non-proteolytic enterococci and other microorganisms. Therefore, KSMEA provides a rapid, one-step screening method for the isolation of presumptive proteolytic enterococci.

Grat, M., Wronka, K. M., Lewandowski, Z., Grat, K., Krasnodebski, M., Stypulkowski, J., Holowko, W., Masior, L., Kosinska, I., Wasilewicz, M., Raszeja-Wyszomirska, J., Rejowski, S., Bik, E., Patkowski, W., and Krawczyk, M. Effects of continuous use of probiotics before liver transplantation: A randomized, double-blind, placebo-controlled trial. Clin.Nutr. 5-4-2017; PM: 28506447

ABSTRACT: BACKGROUND & AIMS: Although there is increasing evidence for the benefits of probiotics in patients with liver diseases, data on the benefits of pre-LT administration of probiotics are lacking. The aim of this study was to evaluate the effects of continuous administration of probiotics before liver transplantation (LT) on pre- and post-transplant patient outcomes. *METHODS*: In this randomized, double-blind, and placebo-controlled trial adult cirrhotic patients listed for LT received a 4-strain probiotic preparation or placebo daily from enrollment until LT. The primary outcome measures were postoperative mortality and infection rates. The secondary outcome measures were 5-day post-transplant aspartate and alanine aminotransferase activities, bilirubin concentration, and international normalized ratio; waiting-list mortality; pre-transplant Model for End-stage Liver Disease score and Child-Turcotte-Pugh class changes; and pre-transplant infections. *RESULTS*: A total of 55 patients were randomized. The 90-day postoperative mortality rates were 0% and 4.3% in the probiotic and placebo groups, respectively ($p > 0.99$). Patients receiving probiotics had significantly reduced 30-day

(4.8% versus 34.8%, p = 0.02) and 90-day (4.8% versus 47.8%, p = 0.002) infection rates, lower post-LT bilirubin concentration (p = 0.02), and more rapid decrease of aspartate (p = 0.03) and alanine (p = 0.03) aminotransferase activities. Probiotics did not have significant effects on other secondary outcome measures. *CONCLUSIONS*: Although continuous administration of probiotics before LT does not appear to affect postoperative mortality, it effectively prevents postoperative infections and improves early biochemical parameters of allograft function. *CLINICALTRIALS. GOV IDENTIFIER*: NCT01735591.

Grau, T., Vilcinskas, A., and Joop, G. Sustainable farming of the mealworm Tenebrio molitor for the production of food and feed. Z.Naturforsch.C. 5-17-2017; PM: 28525347

ABSTRACT: The farming of edible insects is an alternative strategy for the production of protein-rich food and feed with a low ecological footprint. The industrial production of insect-derived protein is more cost-effective and energy-efficient than livestock farming or aquaculture. The mealworm Tenebrio molitor is economically among the most important species used for the large-scale conversion of plant biomass into protein. Here, we review the mass rearing of this species and its conversion into food and feed, focusing on challenges such as the contamination of food/feed products with bacteria from the insect gut and the risk of rapidly spreading pathogens and parasites. We propose solutions to prevent the outbreak of infections among farmed insects without reliance on antibiotics. Transgenerational immune priming and probiotic bacteria may provide alternative strategies for sustainable insect farming.

Grenov, B., Namusoke, H., Lanyero, B., Nabukeera-Barungi, N., Ritz, C., Molgaard, C., Friis, H., and Michaelsen, K. F. Effect of Probiotics on Diarrhea in Children With Severe Acute Malnutrition: A Randomized Controlled Study in Uganda. J.Pediatr.Gastroenterol.Nutr. 2017; 64(3):396-403; PM: 28079729

ABSTRACT: OBJECTIVES: The aim of the study was to assess the effect of probiotics on diarrhea during in- and outpatient treatment of children with severe acute malnutrition (SAM). *METHODS*: A randomized, double-blind, placebo-controlled study was conducted involving 400 children admitted with SAM. Patients received 1 daily dose of a blend of Bifidobacterium animalis subsp lactis and Lactobacillus rhamnosus (10 billion colony-forming units, 50:50) or placebo during hospitalization followed by an 8- to 12-week outpatient treatment period, depending on patients' recovery rate. All outcomes were reported for in- and outpatient treatment separately. The primary outcome was number of days with diarrhea during hospitalization. Secondary outcomes included other diarrhea outcomes, pneumonia, weight gain, and recovery. *RESULTS*: There was no difference in number of days with diarrhea between the probiotic (n = 200) and placebo (n = 200) groups during inpatient treatment (adjusted difference +0.2 days, 95% confidence interval -0.8 to 1.2, P = 0.69); however, during outpatient treatment, probiotics reduced days with diarrhea (adjusted difference -2.2 days 95% confidence interval -3.5 to -0.3, P = 0.025). There were no effects of probiotics on diarrhea incidence and severity or pneumonia, weight gain or recovery during in- or outpatient treatment. Twenty-six patients died in the probiotic versus 20 in the placebo group (P = 0.38). *CONCLUSIONS*: Bifidobacterium animalis subsp lactis and Lactobacillus rhamnosus had no effect on diarrhea in children with SAM during hospitalization, but reduced the number of days with diarrhea in outpatient treatment by 26%. Probiotics may have a role

in follow-up of hospitalized children with SAM or in community-based treatment of malnourished children, but further studies are needed to confirm this.

Greppi, A., Saubade, F., Botta, C., Humblot, C., Guyot, J. P., and Cocolin, L. Potential probiotic Pichia kudriavzevii strains and their ability to enhance folate content of traditional cereal-based African fermented food. Food Microbiol. 2017; 62:169-177; PM: 27889145

ABSTRACT: With the aim of selecting starter cultures with interesting probiotic potential and with the ability to produce folate in a food matrix, yeast strains isolated from fermented cereal-based African foods were investigated. A total of 93 yeast strains were screened for their tolerance to pH 2 and 0.3% of bile salts. Pichia kudriavzevii isolates gave the best results. Selected P. kudriavzevii strains were tested for survival to the simulated human digestion and for adhesion to Caco-2 cells. Moreover, presence of folate biosynthesis genes was verified and production of extra and intra-cellular folate determined during growth in culture medium. 31% of yeast strains could tolerate pH 2, while 99% bile salts. Survival rate after simulated digestion ranged between 11 and 45%, while adhesion rate between 12 and 40%. Folate production was mainly intracellular, maximum after 24 h of growth. To be closer to traditional cereal-based fermentations, a P. kudriavzevii strain with good probiotic potential was co-inoculated with Lactobacillus fermentum strains in a pearl millet gruel. This resulted in in situ folate production that peaked after 4 h. The use of strains with both probiotic and nutritional enrichment properties may have a greater impact for the consumers.

Grimshaw, K., Logan, K., O'Donovan, S., Kiely, M., Patient, K., van, Bilsen J., Beyer, K., Campbell, D. E., Garcia-Larsen, V., Grabenhenrich, L., Lack, G., Mills, C., Wal, J. M., and Roberts, G. Modifying the infant's diet to prevent food allergy. Arch.Dis.Child. 2017; 102(2):179-186; PM: 27530541

ABSTRACT: Recommendations and guidelines on the prevention of food allergy have changed in recent decades. The aim of this review of the current evidence and ongoing studies is to provide a comprehensive and up to date picture of prevention of food allergy for healthcare professionals. The review was undertaken as part of the European Union funded Integrated Approaches to Food Allergy and Allergen Management (iFAAM) study. This is a wide ranging project bringing together expertise across the breadth of food allergy research. Specifically, the review discusses dietary manipulation in food allergy prevention, and covers the possible preventive strategies of allergen avoidance, early allergen introduction, general nutrition and supplements, as well as other strategies, such as prebiotics and probiotics. The review concludes that despite agreement that allergen avoidance strategies should not be undertaken for allergy prevention, there is currently no consensus regarding what actions should be recommended beyond exclusive breastfeeding for the first 4-6 months of life. Recent and upcoming trial results, which are detailed in this review, should help inform the debate and add clarity to the topic.

Guardiola, F. A., Bahi, A., Messina, C. M., Mahdhi, A., Santulli, A., Arena, R., Bakhrouf, A., and Esteban, M. A. Quality and antioxidant response of gilthead seabream (Sparus aurata L.) to dietary supplements of fenugreek (Trigonella foenum graecum) alone or combined with probiotic strains. Fish.Shellfish.Immunol. 2017; 63:277-284; PM: 28232283

ABSTRACT: The present study was conducted to determine the potential effect of the

dietary intake of fenugreek (Trigonella foenum graecum) seeds alone or in combination with Bacillus licheniformis, Lactobacillus plantarum or B. subtilis on gilthead seabream quality and antioxidant response after 2 and 3 weeks of experimental feeding. The results showed that the supplements did not affect the percentage of the fatty acid profiles of muscle, demonstrating that all the additives tested can be administrated without any negative effect on biochemical composition and quality of gilthead seabream. The quantification of thiobarbituric acid reactive substances in muscle demonstrated the significant beneficial effect of the experimental diets compared with the control one. Besides, an increase in superoxide dismutase and catalase in liver was recorded after 3 weeks of administration of experimental diets. Furthermore, real time qPCR revealed that dietary supplementation with FEBS significantly enhances the expression of scavenging enzymes, such as cat and gr genes in the liver after 3 weeks. The findings suggest that the administration of fenugreek supplement alone or combined with probiotic strains could be considered as a good source of natural antioxidants and as a functional aquafeed ingredient for gilthead seabream.

Guardiola, F. A., Bahi, A., Bakhrouf, A., and Esteban, M. A. Effects of dietary supplementation with fenugreek seeds, alone or in combination with probiotics, on gilthead seabream (Sparus aurata L.) skin mucosal immunity. Fish.Shellfish.Immunol. 2017; 65:169-178; PM: 28433714

ABSTRACT: Despite increasing interest in modulating the immune response of fish, providing a combination of probiotics and herbal immunostimulants in aquafeed has rarely has been studied. The effects on gilthead seabream (Sparus aurata L.) of the dietary administration of fenugreek (Trigonella foenum graecum) seeds alone (FE), or combined with one of the following probiotic strains: Bacillus licheniformis (FEBL), Lactobacillus plantarum (FELP) or Bacillus subtilis (FEBS) were evaluated. Fish were fed a control or one of the supplemented diets for 3 weeks. After 2 and 3 weeks of the feeding trial, the abundance of terminal carbohydrates, IgM levels, enzymatic activities (proteases, alkaline phosphatase, esterase and ceruloplasmin) and bactericidal activity were determined in skin mucus. Our results demonstrated that the dietary administration of FE in combination with L. plantarum, particularly, increased carbohydrate abundance, the activity of certain enzymes such as ceruloplasmin, and bactericidal activity against the pathogenic bacterium Photobacterium damselae and the non-pathogenic bacterium B. subtilis in skin mucus at the end of the trial. The carbohydrates most affected by the FELP diet were mannose/glucose, N-acetyl-d-galactosamine and N-acetyl-beta-d-glucosamine. Interestingly, IgM levels were significantly higher in fish fed the FELP and FEBS diets whilst protease activity generally increased in all supplemented diets, which could suggests that the main effect in this activity was to the result of FE supplementation although that fact cannot be confirmed because the effects of probiotics addition alone were not studied. These results suggest that the combined dietary administration of fenugreek and L. plantarum will best enhance the skin mucosal immunity response of gilthead seabream.

Guo, H., Pan, L., Li, L., Lu, J., Kwok, L., Menghe, B., Zhang, H., and Zhang, W. Characterization of Antibiotic Resistance Genes from Lactobacillus Isolated from Traditional Dairy Products. J.Food Sci. 2017; 82(3):724-730; PM: 28182844

ABSTRACT: Lactobacilli are widely used as starter cultures or probiotics in yoghurt, cheese, beer, wine, pickles, preserved food, and silage. They are generally recognized as safe (GRAS). However, recent studies have shown that some lactic acid bacteria

(LAB) strains carry antibiotic resistance genes and are resistant to antibiotics. Some of them may even transfer their intrinsic antibiotic resistance genes to other LAB or pathogens via horizontal gene transfer, thus threatening human health. A total of 33 Lactobacillus strains was isolated from fermented milk collected from different areas of China. We analyzed (1) their levels of antibiotic resistance using a standardized dilution method, (2) their antibiotic resistance gene profiles by polymerase chain reaction (PCR) using gene-specific primers, and (3) the transferability of some of the detected resistance markers by a filter mating assay. All Lactobacillus strains were found to be resistant to vancomycin, but susceptible to gentamicin, linezolid, neomycin, erythromycin, and clindamycin. Their susceptibilities to tetracycline, kanamycin, ciprofloxacin, streptomycin, quinupristin/dalfopristin, trimethoprim, ampicillin, rifampicin, and chloramphenicol was different. Results from our PCR analysis revealed 19 vancomycin, 10 ciprofloxacin, and 1 tetracycline-resistant bacteria that carried the van(X), van(E), gyr(A), and tet(M) genes, respectively. Finally, no transferal of the monitored antibiotic resistance genes was observed in the filter mating assay. Taken together, our study generated the antibiotic resistance profiles of some milk-originated lactobacilli isolates and preliminarily assessed their risk of transferring antibiotic gene to other bacteria. The study may provide important data concerning the safe use of LAB.

Guo, M., Wu, F., Hao, G., Qi, Q., Li, R., Li, N., Wei, L., and Chai, T. Bacillus subtilis Improves Immunity and Disease Resistance in Rabbits. Front Immunol. 2017; 8:354; PM: 28424690

ABSTRACT: Probiotics such as Lactobacillus and Bifidobacterium have been successfully used to promote growth and prevent diseases. Previous reports have demonstrated that Bacillus subtilis (B. subtilis) was a potential probiotic for animals. In this research, 180 B. subtilis were isolated from the soil, identified, and investigated in vitro. Furthermore, five B. subtilis were selected and mixed to investigate their effect on growth performance, immune response, intestine microbiota, and disease resistance in rabbits. Rabbits with a diet of 106 CFU g-1 mixed B. subtilis exhibited the best growth performance and higher serum IgG and IgA than controls ($P < 0.05$). Moreover, dairy with B. subtilis can promote the balance of intestinal flora. The major proinflammatory factor and beta-defensin were upregulated compared with the controls. After 7 weeks of feeding, the survival rate of the rabbits fed with B. subtilis was significantly higher than those in the control groups postinfected with Escherichia coli. At the same time, this study detected higher expression of beta-defensin and reduced bacteria contents of the heart and cecal contents from the diet mixed with B. subtilis compared with the control groups. In conclusion, dietary supplementation with B. subtilis for rabbits could improve growth performance, intestinal homeostasis, and immune organ index and enhance innate immune response as well as disease resistance. These findings showed that the induction of beta-defensin by B. subtilis might be an interesting new therapeutic strategy to strengthen innate defense mechanisms.

Guo, Q., Li, S., Xie, Y., Zhang, Q., Liu, M., Xu, Z., Sun, H., and Yang, Y. The NAD+-dependent deacetylase, Bifidobacterium longum Sir2 in response to oxidative stress by deacetylating FOXO3a and SigH (sigmaH) in Bifidobacterium longum and HEK293T cells respectively. Free Radic.Biol.Med. 5-12-2017; 108:929-939; PM: 28506746

ABSTRACT: Silent information regulator 2 (Sir2) enzymes which catalyze NAD+-dependent protein/histone deacetylation. The mammalian sirtuin family SIRT1, SIRT2, SIRT3 and SIRT6 can regulate oxidative stress. The probiotics (Bifidobacterium longum(B.longum) and

Lactobacillus acidophilus(L. acidophilus)) have Sir2 gene family and have antioxidant activity in human body. it remains unknown whether probiotics Sir2 has a direct role in regulating oxidative stress. To this end, we knockout BL-sir2(sir2 B. longum) and LA-sir2(sir2 L.acidophilus) in low oxygen level. The antioxidant activities of two sir2 deficient strains was decreased, while when reintroduction of BL-sir2 and LA-sir2, the antioxidant activities were recoveried. In order to understand the regulation mechanism of probiotics Sir2 oxidation response. Then, we screened 65 acetylated protein, and found that SigH (sigmaH) was a substrate of BL-Sir2. In addition, the acetylation level of sigmaH decreased with the increase of BL-Sir2 level in B. longum. Thus, BL-Sir2 deacetylated sigmaH in response to oxidative stress. Next, we transfected BL-Sir2 into H2O2-induced oxidative damage of 293T cells, BL-Sir2 increased the activity of manganese superoxide dismutase (MnSOD/SOD2) and catalase (CAT) and reduced reactive oxygen species(ROS). Then, we analyzed the differential gene by RNA sequencing and Gene ontology (GO) and found that BL-Sir2 regulated forkhead transcription factor (FOXO3a) mediated antioxidant genes in overexpressed BL-Sir2 HEK293T cells. Our study is the first to link probiotics Sir2 with oxidative stress and uncover the antioxidant mechanism of BL-Sir2 in B. longum itself and human body.

Guo, S., Gillingham, T., Guo, Y., Meng, D., Zhu, W., Walker, W. A., and Ganguli, K. Secretions of Bifidobacterium infantis and Lactobacillus acidophilus Protect Intestinal Epithelial Barrier Function. J.Pediatr.Gastroenterol.Nutr. 2017; 64(3):404-412; PM: 28230606

ABSTRACT: OBJECTIVES: The secreted metabolites of probiotics are cytoprotective to intestinal epithelium and have been shown to attenuate inflammation and reduce gut permeability. The present study was designed to determine the protective effects of probiotic conditioned media (PCM) from Bifidobacterium infantis (BCM) and Lactobacillus acidophilus (LCM) on interleukin (IL)-1beta-induced intestinal barrier compromise. *METHODS*: The epithelial barrier was determined by measuring the transepithelial electrical resistance (TER) across a Caco-2 cell monolayer using a Transwell model. The paracellular permeability was determined by fluorescein isothiocyanate-labeled dextran flux. The expression of tight junction (TJ) proteins and nuclear factor-kappa B (NF-kappaB) p65 were determined using Western blot and the distribution of NF-kappaB p65 was determined by immunofluorescence staining. *RESULTS*: BCM and LCM induced a dose-dependent increase in Caco-2 TER after 4 and 24 hours of incubation ($P < 0.05$). The maximal increase of Caco-2 TER occurred at 4 hours of treatment with a PCM concentration of 15%. Preincubation with BCM and LCM for 4 hours significantly prevented the decrease of Caco-2 TER induced by 24 hours of stimulation with 10 ng/mL IL-1beta. BCM and LCM decreased paracellular permeability in both stimulated and unstimulated Caco-2 monolayers ($P < 0.05$). IL-1beta stimulation decreased occludin expression and increased claudin-1 expression in Caco-2 cells ($P < 0.05$), which was prevented in cells treated with BCM or LCM. The changes of claudin-1 expression in H4 cells were similar to Caco-2 cells in response to PCM treatment and IL-1beta stimulation; however, a similar response in occludin was not demonstrated. The IL-1beta-induced nuclear translocation of NF-kappaB p65 in Caco-2 cells was prevented by pretreatment with both PCMs. *CONCLUSIONS*: BCM and LCM protected the intestinal barrier against IL-1beta stimulation by normalizing the protein expression of occludin and claudin-1 and preventing IL-1beta-induced NF-kappaB activation in Caco-2 cells, which may be partly responsible for the preservation of intestinal permeability.

Gupta, N. D., Sharma, S., and Sharma, V. K. Probiotic - An emerging therapy in recolonizing periodontal pocket. J.Oral Biol.Craniofac.Res. 2017; 7(1):72-73; PM: 28316927

ABSTRACT: One of the etiological factors in the pathogenesis of periodontitis is reduction or the absence of the so-called "beneficial bacteria". Most of the globally applied treatment approach is based on subgingival bacterial elimination but recolonization with less pathogenic bacteria is seen within weeks. Therefore, researchers have started focusing on shifting the current treatment approach from specific bacterial elimination to restoring periodontal pocket with beneficial bacteria. This alteration in the ecology of niches from the one with the pathological plaque to the one with the biofilm of commensals can be achieved via subgingival application of probiotics. This article suggests the important prospects of subgingival delivery of probiotics in guiding periodontal recolonization with beneficial bacteria and emphasizes research in this study field.

Gutierrez, S., Moran, A., Martinez-Blanco, H., Ferrero, M. A., and Rodriguez-Aparicio, L. B. The Usefulness of Non-Toxic Plant Metabolites in the Control of Bacterial Proliferation. Probiotics.Antimicrob.Proteins. 3-29-2017; PM: 28357646

ABSTRACT: The effect of generally recognised as safe (GRAS) plant metabolites in regulating the growth of human pathogenic and probiotic bacteria and in the formation of biofilm was investigated. Thymol, carvacrol and eugenol showed the strongest antibacterial action against both pathogenic and probiotic microorganisms, at a subinhibitory concentration (SIC) of </=50 mug ml-1. Genistein, hydroquinone, p-hydroxybenzoic acid and resveratrol also showed antibacterial effects but at a wide concentration range (SIC = 50-1000 mug ml-1). Catechin, gallic acid, protocatechuic acid and cranberry extracts were the most biologically compatible molecules (SIC >/= 1000 mug ml-1). Regarding the effect on biofilm, it was observed that thymol, carvacrol and eugenol showed antibiofilm activity against all potential pathogenic bacteria tested whilst specifically enhancing probiotic aggregation. Catechin, genistein and cranberry extracts did not inhibit the pathogenic aggregation but they stimulated probiotic biofilm formation, whilst gallic acid, protocateuchic acid, hydroquinone, p-hydroxybenzoic acid and resveratrol did not show opposite effect on biofilm formation between pathogenic and probiotic microorganisms. These results indicate that an appropriate combination of GRAS plant metabolites, which have traditionally been used as dietary constituents due to their health-promoting characteristics, can also be extremely useful in the regulation of bacterial proliferation in the intestinal microbiota. Hence, it is suggested to apply these natural GRAS molecules as dietary supplements in the food industry in order to promote probiotic viability and to prevent or reduce colonisation or proliferation of intestinal pathogens.

Haak, B. W., Levi, M., and Wiersinga, W. J. Microbiota-targeted therapies on the intensive care unit. Curr.Opin.Crit Care. 2017; 23(2):167-174; PM: 28092309

ABSTRACT: PURPOSE OF REVIEW: The composition and diversity of the microbiota of the human gut, skin, and several other sites is severely deranged in critically ill patients on the ICU, and it is likely that these disruptions can negatively affect outcome. We here review new and ongoing studies that investigate the use of microbiota-targeted therapeutics in the ICU, and provide recommendations for future research. *RECENT FINDINGS*: Practically every intervention in the ICU as well as the physiological effects of critical illness itself can

have a profound impact on the gut microbiota. Therapeutic modulation of the microbiota, aimed at restoring the balance between 'pathogenic' and 'health-promoting' microbes is therefore of significant interest. Probiotics have shown to be effective in the treatment of ventilator-associated pneumonia, and the first fecal microbiota transplantations have recently been safely and successfully performed in the ICU. However, all-encompassing data in this vulnerable patient group remain sparse, and only a handful of novel studies that study microbiota-targeted therapies in the ICU are currently ongoing. *SUMMARY*: Enormous strides have been made in characterizing the gut microbiome of critically ill patients in the ICU, and an increasing amount of preclinical data reveals the huge potential of microbiota-targeted therapies. Further understanding of the causes and consequences of dysbiosis on ICU-related outcomes are warranted to push the field forward.

Halmos, E. P. When the low FODMAP diet does not work. J.Gastroenterol.Hepatol. 2017; 32 Suppl 1:69-72; PM: 28244666

ABSTRACT: Irritable bowel syndrome (IBS) is heterogeneous. Patients need proper assessment and explanation of IBS pathophysiology and appropriate therapies. A low FODMAP (fermentable oligosaccharides, disaccharides, monosaccharides, and polyols) diet effectively reduces symptoms in 75% of patients. Best treatment for those nonresponsive will depend on the pathophysiological basis for symptom genesis, with the following possible abnormalities: (i) Visceral hypersensitivity and/or enhanced gut-brain communication: a low FODMAP diet is mainly targeted for this patient group. A dietitian may also recommend antispasmodic agents, including peppermint oil. Another dietary treatment is a low food chemical diet, although this diet is often extremely limited, and therefore, not suited for some populations. Psychological therapies are also clinically beneficial. (ii) Altered motility: in patients with fast transit, a dietitian may recommend a reduction in all FODMAPs or targeted monosaccharides and disaccharides, which are more osmotic in nature. If not effective, patients may benefit from psyllium, which has an exceptional water-holding capacity aimed to promote more formed stools. Patients with slow or uncoordinated transit are often more difficult to treat. Dietary interventions have some success and usually comprise a combination of adequate fiber and fluid, osmotic laxatives, and stimulating agents such as caffeine, senna, and exercise. (iii) Altered microbiome: supplementary probiotics and prebiotics have weak evidence of efficacy with some notable exceptions. A dietitian may trial supplementary Bifidobacterium infantis or oligosaccharides, usually as an adjunct therapy. Guidance from a dietitian will encompass dietary methods to treat IBS but additionally identify where dietary treatment is not indicated to ensure that diet is correctly used and patients are not nutritionally or psychologically compromised.

Halnes, I., Baines, K. J., Berthon, B. S., Donald-Wicks, L. K., Gibson, P. G., and Wood, L. G. Soluble Fibre Meal Challenge Reduces Airway Inflammation and Expression of GPR43 and GPR41 in Asthma. Nutrients. 1-10-2017; 9(1); PM: 28075383

ABSTRACT: Short chain fatty acids (SCFAs) are produced following the fermentation of soluble fibre by gut bacteria. In animal models, both dietary fibre and SCFAs have demonstrated anti-inflammatory effects via the activation of free fatty acid receptors, such as G protein-coupled receptor 41 and 43 (GPR41 and GPR43). This pilot study examined the acute effect of a single dose of soluble fibre on airway inflammation-including changes in gene expression of free fatty acid receptors-in asthma. Adults with

stable asthma consumed a soluble fibre meal (n = 17) containing 3.5 g inulin and probiotics, or a control meal (n = 12) of simple carbohydrates. Exhaled nitric oxide (eNO) was measured and induced sputum was collected at 0 and 4 h for differential cell counts, measurement of interleukin-8 (IL-8) protein concentration, and GPR41 and GPR43 gene expression. At 4 h after meal consumption, airway inflammation biomarkers, including sputum total cell count, neutrophils, macrophages, lymphocytes, sputum IL-8, and eNO significantly decreased compared to baseline in the soluble fibre group only. This corresponded with upregulated GPR41 and GPR43 sputum gene expression and improved lung function in the soluble fibre group alone. Soluble fibre has acute anti-inflammatory effects in asthmatic airways. Long-term effects of soluble fibre as an anti-inflammatory therapy in asthma warrants further investigation.

Hamad, A. and Burks, W. A. Emerging Approaches to Food Desensitization in Children. Curr.Allergy Asthma Rep. 2017; 17(5):32; PM: 28429307

ABSTRACT: PURPOSE OF REVIEW: The purpose of this review is to highlight the recent advances in food desensitization in children with food allergy. *RECENT FINDINGS*: Recent advancements in epicutaneous, sublingual, and oral immunotherapy for food allergy in the future may offer children with food allergy and their families a viable option to reduce risk or severity of anaphylaxis with phase III trials ongoing for two of these treatment modalities. Food allergy prevalence in children is estimated to be up to 8%. These children are at risk of significant allergic reactions and anaphylaxis. Food avoidance and use of antihistamines or epinephrine has been the standard of care for these patients. This approach also has a significant socioeconomic effects on patients and their families. Recent advancements in understanding food allergy have allowed for exploring new methods of treatment. There is an increasing interest in oral immunotherapy, epicutaneous immunotherapy, or sublingual immunotherapy for food allergy. There have been also innovative approaches to immunotherapy by modification of food allergens (to make them less allergenic while maintain their immunogenicity) or adding adjunctive treatments (probiotics, anti-IgE, etc.) to increase efficacy or safety.

Han, G. G., Song, A. A., Kim, E. B., Yoon, S. H., Bok, J. D., Cho, C. S., Kil, D. Y., Kang, S. K., and Choi, Y. J. Improved antimicrobial activity of Pediococcus acidilactici against Salmonella Gallinarum by UV mutagenesis and genome shuffling. Appl.Microbiol.Biotechnol. 5-3-2017; PM: 28470335

ABSTRACT: Pediococcus acidilactici is a widely used probiotic, and Salmonella enterica serovar Gallinarum (SG) is a significant pathogen in the poultry industry. In this study, we improved the antimicrobial activity of P. acidilactici against SG using UV mutation and genome shuffling (GS). To improve antimicrobial activity against SG, UV mutagenesis was performed against wild-type P. acidilactici (WT), and five mutants showed improved antimicrobial activity. To further improve antimicrobial activity, GS was performed on five UV mutants. Following GS, four mutants showed improved antimicrobial activity compared with the UV mutants and WT. The antimicrobial activity of GS1 was highest among the mutants; however, the activity was reduced when the culture supernatant was treated with proteinase K, suggesting that the improved antimicrobial activity is due to a proteinous substance such as bacteriocin. To validate the activity of GS1 in vivo, we designed multi-species probiotics and performed broiler feeding experiments. Groups consisted of no treatment (NC), avilamycin-treated (PC), probiotic group 1 containing WT (T1), and probiotic group 2 containing GS1 (T2). In broiler feeding experiments,

coliform bacteria were significantly reduced in T2 compared with NC, PC, and T1. The cecal microbiota was modulated and pathogenic bacteria were reduced by GS1 oral administration. In this study, GS1 showed improved antimicrobial activity against SG in vitro and reduced pathogenic bacteria in a broiler feeding experiment. These results suggest that GS1 can serve as an efficient probiotic, as an alternative to antibiotics in the poultry industry.

Han, K., Wang, J., Seo, J. G., and Kim, H. Efficacy of double-coated probiotics for irritable bowel syndrome: a randomized double-blind controlled trial. J.Gastroenterol. 2017; 52(4):432-443; PM: 27178566

ABSTRACT: BACKGROUND: The purpose of this study was to elucidate the effects of a dual-coated probiotic supplement (Duolac Care) on symptoms of diarrhea-predominant irritable bowel syndrome in a randomized double-blind clinical trial. *METHODS*: Fifty subjects with diarrhea-predominant irritable bowel syndrome were randomly assigned to either the non-coating group or the dual-coating group in order to receive two capsules per day of multi-species probiotics containing 5 billion bacteria per capsule for 4 weeks. Data from an adequate relief questionnaire were used in assessment of primary outcome. Daily records of stool frequencies and the Bristol stool scale, a weekly symptom diary using 100-mm visual analog scale, and Beck depression inventories were collected. Blood tests including blood cell counts, interleukin-10, tumor necrosis factor-alpha and inducible nitric oxide synthase, and regulatory T cells-CD4 + CD25high T cells, CD4 + LAP + T cells and CD25high + LAP + T cells-were analyzed before and after the study. The shift of gut microbiota was investigated using a quantitative real-time polymerase chain reaction assay. *RESULTS*: Responses to the adequate relief questionnaire indicated significant improvement in overall discomfort in the dual-coating group and the ratio of normal stools to hard or watery stools had a better effect from dual-coated probiotics compared to non-coated probiotics. This may be due to a shift of intestinal microbiota, as our correlation analysis showed significant negative correlation between Bifidobacterium and urgency of defecation. *CONCLUSIONS*: Our result implies that dual-coating layers of probiotic supplement can be a candidate for treatment of diarrhea-predominant irritable bowel syndrome.

Han, X., Zhang, J., Tan, Y., and Zhou, G. Probiotics: A non-conventional therapy for oral lichen planus. Arch.Oral Biol. 4-26-2017; 81:90-96; PM: 28499235

ABSTRACT: Oral lichen planus (OLP) is a common T-cell mediated chronic inflammatory disease. Although the etiology is still unclear, present studies suggest that the composition of the oral microbiota and psychological problems are implicated in the etiology of OLP. The pathogenesis of OLP includes mainly antigen-specific and non-specific mechanisms. Antigen-specific mechanisms involve T-cell activation following antigen presentation and apoptosis of basal keratinocytes triggered by CD8+ cytotoxic T cells, while non-specific mechanisms consist of matrix metalloproteinase over-expression and mast cell degranulation in OLP lesions. Therapies for OLP are mainly used to control symptoms and a specific cure is not yet available. Probiotics are capable of modulating the immune response in a strain-specific manner. They are able to alleviate microbial infection and suppress T-cell activation, infiltration and proliferation, as well as suppress keratinocyte apoptosis and nuclear factor-kappa B signaling. Furthermore, probiotics can also modulate the production of inflammatory cytokines and microRNAs, inhibit MMP-9 expression and mast cell degranulation, and ameliorate psychological problems, all of which are involved in the pathogenesis of OLP. Therefore, we hypothesize that

probiotics may be applicable to OLP as a safe, inexpensive and non-conventional therapy.

Hao, K., Wu, Z. Q., Li, D. L., Yu, X. B., Wang, G. X., and Ling, F. Effects of Dietary Administration of Shewanella xiamenensis A-1, Aeromonas veronii A-7, and Bacillus subtilis, Single or Combined, on the Grass Carp (Ctenopharyngodon idella) Intestinal Microbiota. Probiotics.Antimicrob.Proteins. 3-21-2017; PM: 28321827

ABSTRACT: Gut microbiota of grass carp plays an important role in host. However, detailed information regarding the changes of microbiota after probiotics administration in relation to the gastrointestinal microbiota is absent. In the present study, dietary administration of putative probiotics Shewanella xiamenensis A-1, Aeromonas veronii A-7, and Bacillus subtilisstrains was conducted in grass carp to investigate if there is a discernible alteration in intestinal microbiota and whether the alteration is associated with previous study about the immunity regulation in grass carp. Bacterial 16S rRNA gene sequence-based comparisons of the bacterial communities in the grass carp intestine were detected after 28 days feeding by five diets, and results demonstrated the changes of microbial community composition at genus level. The abundance of Cetobacterium genus with potential immunity function increased. Potential pathogens and probiotics are important constitutions of the intestinal microbiota. Orally taken probiotics considerably reduced the abundance of the potential pathogenic bacteria (e.g., Pseudomonas and Flavobacterium genus) in the intestine. Meanwhile, putative probiotics used in this study were favorable to the reproduction of potential probiotics in THE intestine of grass carp (e.g., Vibrio, Streptococcus, and Enterococcus genus). Moreover, modulation of intestinal environment by the probiotics could impact the abundance of cellulose-degrading bacteria (e.g., Citrobacter genus). Those results suggested that oral probiotics administration can positively improve the composition of intestinal microbial community in grass carp, and this was associated with regulation of immunity in grass carp. Probiotics-induced alteration of microbiota may potentially lower the risk of disease outbreaks during cultivation stage of grass carp.

Happel, A. U., Jaumdally, S. Z., Pidwell, T., Cornelius, T., Jaspan, H. B., Froissart, R., Barnabas, S. L., and Passmore, J. S. Probiotics for vaginal health in South Africa: what is on retailers' shelves? BMC.Womens Health. 1-19-2017; 17(1):7; PM: 28103868

ABSTRACT: BACKGROUND: Probiotics are widely used to improve gastrointestinal (GI) health, but they may also be useful to prevent or treat gynaecological disorders, including bacterial vaginosis (BV) and candidiasis. BV prevalence is high in South Africa and is associated with increased HIV risk and pregnancy complications. We aimed to assess the availability of probiotics for vaginal health in retail stores (pharmacies, supermarkets and health stores) in two major cities in South Africa. *METHODS*: A two-stage cluster sampling strategy was used in the Durban and Cape Town metropoles. Instructions for use, microbial composition, dose, storage and manufacturers' details were recorded. *RESULTS*: A total of 104 unique probiotics were identified in Cape Town and Durban (66.4% manufactured locally). Cape Town had more products than Durban (94 versus 59 probiotics), although 47% were common between cities (49/104). Only four products were explicitly for vaginal health. The remainder were for GI health in adults (51.0%) or infants (17.3%). The predominant species seen overall included Lactobacillus acidophilus (53.5%), L. rhamnosus (37.6%), Bifidobacterium longum ssp. longum (35.6%)

and B. animalis ssp. lactis (33.7%). Products for vaginal health contained only common GI probiotic species, with a combination of L. acidophilus/B. longum ssp. longum/B. bifidum, L. rhamnosus/L. reuteri or L. rhamnosus alone, despite L. crispatus, L. gasseri, and L. jensenii being the most common commensals found in the lower female reproductive tract. *CONCLUSION*: This survey highlights the paucity of vaginal probiotics available in South Africa, where vaginal dysbiosis is common. Most vaginal products contained organisms other than female genital tract commensals.

Harlow, B. E., Lawrence, L. M., Harris, P. A., Aiken, G. E., and Flythe, M. D. Exogenous lactobacilli mitigate microbial changes associated with grain fermentation (corn, oats, and wheat) by equine fecal microflora ex vivo. PLoS.One. 2017; 12(3):e0174059; PM: 28358885

ABSTRACT: Cereal grains are often included in equine diets. When starch intake exceeds foregut digestion starch will reach the hindgut, impacting microbial ecology. Probiotics (e.g., lactobacilli) are reported to mitigate GI dysbioses in other species. This study was conducted to determine the effect of exogenous lactobacilli on pH and the growth of amylolytic and lactate-utilizing bacteria. Feces were collected from 3 mature geldings fed grass hay with access to pasture. Fecal microbes were harvested by differential centrifugation, washed, and re-suspended in anaerobic media containing ground corn, wheat, or oats at 1.6% (w/v) starch and one of five treatments: Control (substrate only), L. acidophilus, L. buchneri, L. reuteri, or an equal mixture of all three (107 cells/mL, final concentration). After 24 h of incubation (37 degrees C, 160 rpm), samples were collected for pH and enumerations of total amylolytics, Group D Gram-positive cocci (GPC; Enterococci, Streptococci), lactobacilli, and lactate-utilizing bacteria. Enumeration data were log transformed prior to ANOVA (SAS, v. 9.3). Lactobacilli inhibited pH decline in corn and wheat fermentations ($P < 0.0001$). Specifically, addition of either L. reuteri or L. acidophilus was most effective at mitigating pH decline with both corn and wheat fermentation, in which the greatest acidification occurred ($P < 0.05$). Exogenous lactobacilli decreased amylolytics, while increasing lactate-utilizers in corn and wheat fermentations ($P < 0.0001$). In oat fermentations, L. acidophilus and L. reuteri inhibited pH decline and increased lactate-utilizers while decreasing amylolytics ($P < 0.0001$). For all substrates, L. reuteri additions (regardless of viability) had the lowest number of GPC and the highest number of lactobacilli and lactate-utilizers ($P < 0.05$). There were no additive effects when lactobacilli were mixed. Exogenous lactobacilli decreased the initial (first 8 h) rate of starch catalysis when wheat was the substrate, but did not decrease total (24 h) starch utilization in any case. These results indicate that exogenous lactobacilli can impact the microbial community and pH of cereal grain fermentations by equine fecal microflora ex vivo. Additionally, dead (autoclaved) exogenous lactobacilli had similar effects as live lactobacilli on fermentation. This latter result indicates that the mechanism by which lactobacilli impact other amylolytic bacteria is not simple resource competition.

Hasegawa, S., Jao, T. M., and Inagi, R. Dietary Metabolites and Chronic Kidney Disease. Nutrients. 4-4-2017; 9(4); PM: 28375181

ABSTRACT: Dietary contents and their metabolites are closely related to chronic kidney disease (CKD) progression. Advanced glycated end products (AGEs) are a type of uremic toxin produced by glycation. AGE accumulation is not only the result of elevated glucose levels or reduced renal clearance capacity, but it also promotes CKD

progression. Indoxyl sulfate, another uremic toxin derived from amino acid metabolism, accumulates as CKD progresses and induces tubulointerstitial fibrosis and glomerular sclerosis. Specific types of amino acids (d-serine) or fatty acids (palmitate) are reported to be closely associated with CKD progression. Promising therapeutic targets associated with nutrition include uremic toxin absorbents and inhibitors of AGEs or the receptor for AGEs (RAGE). Probiotics and prebiotics maintain gut flora balance and also prevent CKD progression by enhancing gut barriers and reducing uremic toxin formation. Nrf2 signaling not only ameliorates oxidative stress but also reduces elevated AGE levels. Bardoxolone methyl, an Nrf2 activator and NF-kappaB suppressor, has been tested as a therapeutic agent, but the phase 3 clinical trial was terminated owing to the high rate of cardiovascular events. However, a phase 2 trial has been initiated in Japan, and the preliminary analysis reveals promising results without an increase in cardiovascular events.

Hashizume, N., Yagi, M., Ushijima, K., Seki, Y., Fukahori, S., Muto, M., Matsufuji, H., and Taguchi, T. Pharmacotherapy for pediatric chronic intestinal pseudo-obstruction: Nationwide survey in Japan. Pediatr.Int. 2017; 59(4):467-472; PM: 27862707

ABSTRACT: BACKGROUND: Chronic intestinal pseudo-obstruction (CIPO) is a rare disabling and life-threatening disorder characterized by severe impairment of gastrointestinal peristalsis. While a number of pharmacotherapeutics have been developed, only a few trials have been carried out for improvement of the pathological condition of CIPO patients. This report describes the results of a nationwide survey on the pharmacotherapy used in pediatric CIPO in Japan. *METHODS*: In 2012, a nationwide survey was conducted to identify the clinical presentation of CIPO in Japan. Information was gathered on pharmacotherapy. Four categories were created for medicines used in pharmacotherapy: "probiotics", "Japanese herbal medicines (Kampo medicines)", "laxatives", and "prokinetics". *RESULTS*: Ninety-two responses were collected from 47 facilities. Of the 62 patients who met the diagnostic criteria, 52 were treated with medications, while the remaining 10 were not. Thirty-four patients were given a total of 49 probiotics; 39 were treated with a total of 50 Kampo medicines; 20 were treated with a total of 28 laxatives; and 26 were given a total of 30 prokinetics, 70% of whom were treated specifically with mosapride. *CONCLUSION*: Traditional Japanese medicines such as Kampo medicines and mosapride are often used to treat CIPO in Japan. Two combinations, that is, probiotics and Kampo medicines; and Kampo medicines and prokinetics, were often used for pediatric CIPO in Japan.

Hastings, C. N., Sheridan, H., Pariante, C. M., and Mondelli, V. Does Diet Matter? The Use of Polyunsaturated Fatty Acids (PUFAs) and Other Dietary Supplements in Inflammation-Associated Depression. Curr.Top.Behav.Neurosci. 2017; 31:321-338 PM: 27431396

ABSTRACT: An increasingly pertinent issue in psychiatry in recent years is that of the limitations of conventional antidepressants, which are not effective in a large number of patients with major depressive disorder (MDD). Coupled with emerging hypotheses about the role of inflammation in depression, it would appear that it is time to look for alternative treatments for these symptoms.This review will examine an emerging area in psychiatry, that of dietary supplements and the diet in general to treat depressive symptoms, and inflammation in depression. In particular, polyunsaturated fatty acids (PUFAs), probiotics and folic acid are three supplements that demonstrate the ability to

target inflammation and other underlying systems in depression. While there is a definite need for more research in all these supplements to determine true efficacy, dosage and target populations, they can be used as mono- or adjunctive therapies to good effect, and show superior safety profiles when compared with more traditional alternatives.

Hendijani, F. and Akbari, V. Probiotic supplementation for management of cardiovascular risk factors in adults with type II diabetes: A systematic review and meta-analysis. Clin.Nutr. 2-24-2017; PM: 28318686

ABSTRACT: BACKGROUND & AIMS: The effectiveness of probiotics in control of hypertension and dyslipidemia in diabetic patients remains unclear. Therefore, we systematically reviewed relevant data to elucidate the effects of probiotics on blood pressure and lipid profile of type 2 diabetic patients. *METHODS*: We searched PubMed, ISI Web of Knowledge, Scopus, The Cochrane Library, ClinicalTrials.gov, ProQuest Dissertations and Theses databases until May 2016. The primary outcomes were systolic blood pressure (SBP) and diastolic blood pressure (DBP), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C) and triglycerides (TG). Other biochemical response and adverse effects were considered as secondary outcomes. Data was extracted from included studies and pooled in meta-analysis whenever possible (both standardized mean difference (SMD) analysis and weighted mean difference (WMD) analysis were performed). *RESULTS*: Eleven eligible randomized controlled trial (n = 641) were identified. Pooling data from these trials demonstrated probiotic consumption significantly decreased SBP (WMD, -3.28 mmHg; 95% confidence interval [CI], -5.38 to -1.18), DBP (WMD, -2.13 mmHg; 95% CI, -4.5 to 0.24), LDL-C (WMD, 8.32 mg/dl; 95% CI, -15.24 to -1.4), TC (WMD, -12.19 mg/dl; 955 CI -17.62 to -6.75) and TG (WMD, -24.48 mg/dl; 95% CI, -33.77 to -11.18) in type 2 diabetic patients compared with placebo. The methodological quality varied across trials included in this study. *CONCLUSION*: This systematic review suggests probiotics supplementation may be helpful for control of dyslipidemia and hypertension in type 2 diabetic patients. Conducting more trails with large sample size and long follow-up time still is necessary to develop clinical practice guidelines for management of cardiovascular risk factors in patient with type 2 diabetes.

Hiergeist, A. and Gessner, A. Clinical implications of the microbiome in urinary tract diseases. Curr.Opin.Urol. 2017; 27(2):93-98; PM: 27898455

ABSTRACT: PURPOSE OF REVIEW: The purpose of this review is to outline and evaluate the most recent literature on the role of the microbiome in urinary tract diseases. *RECENT FINDINGS*: High throughput molecular DNA sequencing of bacterial 16S rRNA genes enabled the analysis of complex microbial communities inhabiting the human urinary tract. Several recent studies have identified bacterial taxa of the urinary microbiome to impact urinary tract diseases including interstitial cystitis, urgency urinary incontinence or calcium oxalate stone formation. Furthermore, treatment of urinary tract infections by antibiotics globally impacts community profiles of the intestinal microbiota and might indirectly influence human health. Alternative treatment options like application of probiotics for the treatment of urinary tract infections are currently under investigation. *SUMMARY*: The urinary microbiome and its relationship to urinary tract diseases is currently under comprehensive investigation. Further studies are needed to shed light on the role of commensal microbiota for urinary tract infections.

Hijova, E., Kuzma, J., Strojny, L., Bomba, A., Bertkova, I., Chmelarova, A., Hertelyova, Z., Benetinova, V., Stofilova, J., and Ambro, L. Ability of Lactobacillus plantarum LS/07 to modify intestinal enzymes activity in chronic diseases prevention. Acta Biochim.Pol. 2017; 64(1):113-116; PM: 27824363

ABSTRACT: The ability of probiotic strain Lactobacillus plantarum LS/07 to modify the activity of intestinal bacterial enzymes - beta-glucuronidase (beta-GLUCUR), beta-galactosidase (beta-GAL), and beta-glucosidase (beta-GLU) in prevention of chronic diseases - cancer, atherosclerosis and dysbiosis was investigated. The male Sprague-Dawley rats were randomly divided into 12 experimental groups: controls groups - C (control), AT (atherosclerotic), CC (carcinogenic), dysbiotic groups - each group in combination with antibiotics (ATB), probiotics groups - in combinatioan with probiotic (PRO) alone, and each group with combination of antibiotic and probiotic (ATB+PRO). In the control group the beta-glucuronidase activity did not change throughout the experiment. High fat diet in atherosclerotic group significantly increased the activity of beta-glucuronidase ($P<0.001$) and beta-glucosidase ($P<0.01$). Azoxymethane application in carcinogenic group significantly increased beta-glucuronidase ($P<0.01$), but reduced beta-glucosidase ($P<0.01$) activity. Daily application of probiotics alone and in combination with antibiotic increased beta-galactosidase, of beta-glucosidase, and decreased beta-glucuronidase activity. In control antibiotic group we observed significant increase in beta-glucuronidase ($P<0.05$) and decreased beta-glucosidase ($P<0.01$) activity which can be caused by the change of microflora in favor of coliform bacteria. These findings indicate the positive effects of probiotic Lactobacillus plantarum LS/07 and suggest its use in disease prevention in human medicine and some animal species.

Hlaing, M. M., Wood, B. R., McNaughton, D., Ying, D., Dumsday, G., and Augustin, M. A. Effect of Drying Methods on Protein and DNA Conformation Changes in Lactobacillus rhamnosus GG Cells by Fourier Transform Infrared Spectroscopy. J.Agric.Food Chem. 3-1-2017; 65(8):1724-1731; PM: 28132503

ABSTRACT: Microencapsulation protects cells against environmental stress encountered during the production of probiotics, which are used as live microbial food ingredients. Freeze-drying and spray-drying are used in the preparation of powdered microencapsulated probiotics. This study examines the ability of Fourier transform infrared (FTIR) spectroscopy to detect differences in cells exposed to freeze-drying and spray-drying of encapsulated Lactobacillus rhamnosus GG cells. The FTIR analysis clearly demonstrated there were more significant molecular changes in lipid, fatty acid content, protein, and DNA conformation of nonencapsulated compared to encapsulated bacterial cells. The technique was also able to differentiate between spray-dried and freeze-dried cells. The results also revealed the extent of protection from a protein-carbohydrate-based encapsulant matrix on the cells depending on the type drying process. The extent of this protection to the dehydration stress was shown to be less in spray-dried cells than in freeze-dried cells. This suggests that FTIR could be used as a rapid, noninvasive, and real-time measurement technique to detect detrimental drying effects on cells.

Ho, Y. H., Huang, Y. T., Lu, Y. C., Lee, S. Y., Tsai, M. F., Hung, S. P., and Hsu, T. Y. Effects of Gender and Age on Immune Responses of Human Peripheral Blood Mononuclear Cells to

Probiotics: A Large Scale Pilot Study. J.Nutr.Health Aging. 2017; 21(5):521-526; PM: 28448082

ABSTRACT: BACKGROUND: Despite the widely accepted concept that probiotics confer miscellaneous benefits to hosts, the controversies surrounding these health-promoting claims cannot be ignored. These controversies hinder development and innovation in this field. *RESULTS*: To clarify the effects of age and gender on probiotic-induced immune responses, we recruited 1613 Taiwanese individuals and calculated the ratio of IFN-gamma to IL-10 production after each individual's PBMCs were stimulated by six probiotic strains (L. paracasei BRAP01, L. acidophilus AD300, B. longum BA100, E. faecium BR0085, L. rhamnosus AD500 and L. reuteri BR101). Our results indicated that gender and age have only minor effects on the immune modulation of probiotics. Additionally, we showed that L. paracasei BRAP01 and L. acidophilus AD300 are the two dominant strains inducing IFN-gamma/IL-10 production in Taiwanese individuals and that L. reuteri BR101 was the most effective stimulator of IL-10/IFN-gamma. Additionally, a significant inverse relationship between the ability of L. paracasei BRAP01 and L. rhamnosus AD500 to stimulate IFN-gamma/IL-10 or IL-10/IFN-gamma production was also observed. *CONCLUSIONS*: Our results indicated that age and gender have only minor effects on the immune modulation abilities of probiotics.

Hod, K., Sperber, A. D., Ron, Y., Boaz, M., Dickman, R., Berliner, S., Halpern, Z., Maharshak, N., and Dekel, R. A double-blind, placebo-controlled study to assess the effect of a probiotic mixture on symptoms and inflammatory markers in women with diarrhea-predominant IBS. Neurogastroenterol.Motil. 3-8-2017; PM: 28271623

ABSTRACT: BACKGROUND: Micro-inflammation is considered an element in the pathogenesis of irritable bowel syndrome (IBS). High-sensitivity C reactive protein (hs-CRP) was previously shown to be higher in IBS compared to healthy controls, albeit within the normal range. Since probiotics may suppress micro-inflammation in the gut, we tested if they reduce symptoms and inflammatory markers (hs-CRP and fecal calprotectin (FC) in diarrhea-predominant IBS (IBS-D). The aim of this study was to assess the clinical and laboratory effects of BIO-25, a multispecies probiotic, in women with IBS-D. *METHODS*: A double-blind, placebo-controlled study. Following a 2-week run-in, eligible women were assigned at random to a probiotic capsule or an indistinguishable placebo, twice daily for 8 weeks. IBS symptoms and stool consistency were rated daily by Visual Analogue Scales (VAS) and the Bristol Stool Scale (BSS). High-sensitivity C reactive protein was tested at baseline, 4 and 8 weeks. FC was tested at baseline and 8 weeks. *KEY RESULTS*: One hundred and seventy-two IBS-D patients were recruited and 107 eligible patients were allocated to the intervention (n=54) or placebo (n=53) group. All symptoms improved in both groups with no significant difference between them in symptom improvement, hs-CRP or FC levels. *CONCLUSIONS & INFERENCES*: An 8-week treatment with BIO-25 improved symptoms in women with IBS-D, but was not superior to placebo. This rigorously designed and executed study supports the findings of other studies that did not demonstrate superiority of probiotics over placebo in IBS. High quality clinical studies are necessary to examine the efficacy of other specific probiotics in IBS-D patients since data are still conflicting.

Holleran, G., Lopetuso, L. R., Ianiro, G., Pecere, S., Pizzoferrato, M., Petito, V., Graziani, C., Mc, Namara D., Gasbarrini, A., and Scaldaferri, F. Gut microbiota and inflammatory bowel disease: an update. Minerva Gastroenterol.Dietol. 3-14-2017; PM: 28293937

ABSTRACT: Major advances have occurred in the knowledge of the pathogenesis of Inflammatory Bowel Disease (IBD) over the last decade, and perhaps the most major, and clinically advantageous of these advances has been the discovery of the microbiome as a key multifaceted component of inflammation. The Gut microbiome is the largest known group of cells in the body, and is now recognised as an organ in its own right. Initial studies looking at a possible role of bacterial manipulation of the immune system in IBD, looked at identifying a specific bacterial species, and were not representative of a feasible model of inflammation in IBD overall. More recently there has been a shift towards the concept of dysbiosis, and the acceptance that a number of bacterial factors interact with the immune system in order for inflammation to occur. In the present review we will focus on past perspective of the role of microbiota in IBD, current evidences about dysbiosis in IBD and also the main therapeutic modalities to affect IBD by affecting gut microbiota: probiotics, prebiotics, faecal Microbiota Transplantation and emerging dietary intervention.

Homayouni-Rad, A., Soroush, A. R., Khalili, L., Norouzi-Panahi, L., Kasaie, Z., and Ejtahed, H. S. Diabetes Management by Probiotics: Current Knowledge and Future Pespective. Int.J.Vitam.Nutr.Res. 4-24-2017; 1-13; PM: 28436760

ABSTRACT: Diabetes mellitus, a multifactorial disorder, is related to the intestinal microbiota via numerous molecular mechanisms. The vast increase in the prevalence of diabetes and its associated complications requires a natural and safe solution. There is a growing evidence of gut microbiota effi ciency in improving insulin resistance, impaired insulin secretion, and metabolic complications in diabetic patients. Probiotics are defi ned as live microorganisms that, when ingested in adequate amounts, exert health benefi ts to the host. Probiotics can increase insulin sensitivity and reduce autoimmune responses by modulating intestinal microbiota and decreasing the infl ammatory reactions and oxidative stress. Recent evidences show that the intestinal microbiota infl uences the host through modulating intestinal permeability and mucosal immune response, manipulating eating behaviors by appetite-regulating hormones, including agouti related protein (AgRP), glucagon like peptide-1 (GLP-1) and neuropeptide Y, and controlling gut endocannabinoid (eCB) system which is now believed to be associated with infl ammation and diabetes. Moreover, intestinal microbiota control the host metabolism by affecting energy extraction from food and by biochemically converting molecules derived from the host or from gut microbes themselves. Experimental studies and clinical trials support the hypothesis that the modulation of the intestinal microbiota by probiotics, especially Lactobacillus and Bifidobacterium strains may be effective in prevention and management of diabetes. This review will highlight the current evidences in probiotic effectiveness and future prospects for exploring probiotic therapy in prevention and control of diabetes.

Hsu, T. C., Huang, C. Y., Liu, C. H., Hsu, K. C., Chen, Y. H., and Tzang, B. S. Lactobacillus paracasei GMNL-32, Lactobacillus reuteri GMNL-89 and L. reuteri GMNL-263 ameliorate hepatic injuries in lupus-prone mice. Br.J.Nutr. 5-15-2017; 1-9; PM: 28502277

ABSTRACT: Probiotics are known to regulate host immunity by interacting with systemic and mucosal immune cells as well as intestinal epithelial cells. Supplementation with certain probiotics has been reported to be effective against various disorders, including immune-related diseases. However, little is known about the effectiveness of

Lactobacillus paracasei GMNL-32 (GMNL-32), Lactobacillus reuteri GMNL-89 (GMNL-89) and L. reuteri GMNL-263 (GMNL-263) in the management of autoimmune diseases, especially systemic lupus erythematosus (SLE). NZB/W F1 mice, which are a lupus-prone animal model, were orally gavaged with GMNL-32, GMNL-89 or GMNL-263 to investigate the effects of these Lactobacillus strains on liver injuries in NZB/W F1 mice. The results thus obtained reveal that supplementary GMNL-32, GMNL-89 or GMNL-263 in NZB/W F1 mice ameliorates hepatic apoptosis and inflammatory indicators, such as matrix metalloproteinase-9 activity and C-reactive protein and inducible nitric oxide synthase expressions. In addition, supplementation with GMNL-32, GMNL-89 or GMNL-263 in NZB/W F1 mice reduced the expressions of hepatic IL-1beta, IL-6 and TNF-alpha proteins by suppressing the mitogen-activated protein kinase and NF-kappaB signalling pathways. These findings, presented here for the first time, reveal that GMNL-32, GMNL-89 and GMNL-263 mitigate hepatic inflammation and apoptosis in lupus-prone mice and may support an alternative remedy for liver disorders in cases of SLE.

Hu, H. J., Zhang, G. Q., Zhang, Q., Shakya, S., and Li, Z. Y. Probiotics Prevent Candida Colonization and Invasive Fungal Sepsis in Preterm Neonates: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Pediatr.Neonatol. 2017; 58(2):103-110; PM: 27793494

ABSTRACT: To investigate whether probiotic supplementation could reduce the risk of fungal infection in preterm neonates in neonatal intensive care units (NICUs), we systematically searched PubMed, EMBASE, and the Cochrane Central Register of Controlled Trials databases for randomized controlled trials (RCTs) focusing on the effect of probiotics on fungal infection in preterm neonates. The outcomes of interest were Candida colonization and invasive fungal sepsis. Seven trials involving 1371 preterm neonates were included. Meta-analysis (fixed-effects model) showed that probiotic supplementation was significantly associated with a lower risk of Candida colonization (2 RCTs, n = 329; relative risk (RR), 0.43; 95% confidence interval (CI), 0.27-0.67; p = 0.0002; I2 = 0%), and invasive fungal sepsis (7 RCTs, n = 1371; RR, 0.64; 95% CI, 0.46-0.88; p = 0.006; I2 = 13%). After excluding one study with a high baseline incidence (75%) of fungal sepsis, the effect of probiotics on invasive fungal sepsis became statistically insignificant (RR, 0.88; 95% CI, 0.44-1.78; p = 0.72; I2 = 15%). When using the random-effects model, the effect of probiotics remained favorable for Candida colonization (RR, 0.43; 95% CI 0.27-0.68; p = 0.0002; I2 = 0%) but not for fungal sepsis (RR, 0.64; 95% CI 0.38-1.08; p = 0.10; I2 = 13%). Current evidence indicates that probiotics can reduce the risk of Candida colonization in preterm neonates in NICUs. Limited data support that probiotic supplementation prevents invasive fungal sepsis in preterm neonates. High-quality and adequately powered RCTs are warranted.

Hu, S., Wang, L., and Jiang, Z. Dietary additive probiotics modulation of the intestinal microbiota. Protein Pept.Lett. 2-23-2017; PM: 28240160

ABSTRACT: The importance of the intestinal microbiota of animals is widely acknowledged because of its vital role in the health of animals. There are complex communities of microbiota, which colonize the gastrointestinal tract. Intestinal microbiota are conductive to animal health and the development of the host immune system. Probiotics are commonly used dietary additives where they provide the host with many beneficial functions, such as modulating intestinal homeostasis and promoting gut health. These beneficial effects of probiotics may accrue from the inhibiting the growth

of pathogenic bacteria and promoting the growth of beneficial flora in the gastrointestinal tract. Probiotics colonization and its impact on gut microbiota members are highly species specific. Different probiotics have been shown to have dramatically different capacities of modulation physiological function. This review summarizes existing studies of the influence of dietary additive probiotics on the gut microbiota in different animals, such as humans, mice, pigs and chickens, to clarify the contribution of different kinds of probiotics to the intestinal microbiota. Moreover, the probable mechanism for the benefits of dietary supplementation with probiotics will be discussed.

Hu, Y. M., Zhou, F., Yuan, Y., and Xu, Y. C. Effects of probiotics supplement in patients with type 2 diabetes mellitus: A meta-analysis of randomized trials. Med.Clin.(Barc.). 4-21-2017; 148(8):362-370; PM: 28237613

ABSTRACT: BACKGROUND AND OBJECTIVE: To objectively evaluate the effects of probiotics supplement on glycemic control and lipid metabolism in patients with type 2 diabetes mellitus (T2DM). *MATERIAL AND METHODS*: The randomized controlled trials (RCTs) with regard to the probiotics or synbiotics for the treatment of T2DM were collected through retrieving 5 databases from their establishment to March 2016. After study selection, quality assessment and data extraction were performed by 2 authors independently; and STATA software was used for statistical analysis. The level of evidence was evaluated by applying the GRADE system. *RESULTS*: Twelve RCTs involving 770 participants were enrolled. The results of the meta-analysis showed that probiotics could significantly reduce fasting blood glucose by -11.27mg/dL (95% CI -21.76 to -0.79; P<.001) and serum insulin concentration by -2.36muU/mL (95% CI -4.01 to -0.72; P=.005), but with no significant reduction on HbA1c (-0.19%; 95% CI -0.49 to 0.12; P=.23). Probiotics could significantly reduce HOMA-IR of T2DM patients (-1.05; 95% CI -1.52 to -0.59; P<.001). Nevertheless, the effect on QUICKI was negligible (0.00; 95% CI -0.00 to 0.01; P=.27). Results also confirmed the significant lowering effect of probiotics on total cholesterol (-8.49mg/dL; 95% CI -15.24 to -1.73; P=.014) and triglycerides (TG; -23.66mg/dL; 95% CI -40.26 to -7.05; P<.001), as well as the elevating effect on HDL-c (3.92mg/dL; 95% CI 2.14 to5.7; P<.01). However, there was no significant change on LDL-c (-0.84mg/dL; 95% CI -5.84 to 4.17; P=.75). Subgroup analysis was conducted for 2 outcomes, that is, serum insulin concentration and TG, whose heterogeneity was too high. The results showed multiple species of probiotics had stronger reduction effect on serum insulin concentration (-3.32muU/mL; 95% CI -5.89 to-0.75; P=.001) and TG (-25.94mg/dL; 95% CI -65.33 to 13.44; P<.001). In addition, it also suggested that only the duration of treatment for>/=8 weeks could significantly reduce TG by -24.47mg/dL (95% CI -40.15 to -8.78; P=.001). The duration of treatment for<8 weeks didn't result in significant reduction on TG (-4.31mg/dL; 95% CI -37.69 to 29.06; P=.8). Finally, all the evidences were at moderate and low levels according to the GRADE system. *CONCLUSION*: As a kind of the potential biotherapeutics in the management of T2DM, probiotics can improve glucose control and lipid metabolism.

Huang, R. and Hu, J. Positive Effect of Probiotics on Constipation in Children: A Systematic Review and Meta-Analysis of Six Randomized Controlled Trials. Front Cell Infect.Microbiol. 2017; 7:153; PM: 28503492

ABSTRACT: Context: Constipation in children is a prevalent, burdensome, and psychologically important pediatric issue, the treatment of which remains a global challenge. The use of probiotics has been reported for management of the

gastrointestinal microbiota. Objective: This study reviewed the existing literatures of 6 Randomized Control Trials (RCTs) to ascertain some baseline understanding and available information for the effects of probiotics on stool frequency and consistency in children with constipation. Data Sources: PubMed, Springer, Elsevier Science, Cochrane Library, Scopus, Ovid (Medline, EMBASE, PsycINFO), Orbis, and Web of Science from the earliest record in each database to 15 September, 2016. Study selection: Eligible studies were randomized controlled trials that compared the effect of probiotics interventions to any control intervention on stool frequency and consistency. Data Extraction: Studies were identified by searching electronic databases. The meta-analysis was performed by Review Manager 5.3 software using a randomized model. Results: Six studies were identified. The use of probiotics significantly increased the stool frequency [mean difference (MD), 0.73; 95% confidence interval (CI), 0.14-1.31; P = 0.02]. Subgroup assessment showed a significantly increased stool frequency in Asian patients (MD, 1.18; 95% CI, 0.33-2.02; P = 0.006), but no significant difference in stool consistency (MD, -0.07; 95% CI, -0.21-0.06; P = 0.27). Limitations: Only six RCTs met the criteria and were included. Each RCT in this study was performed in a different country, and some of the included studies had a small sample size, which might have influenced the reliability and validity of the conclusions. Conclusion: The present study shows that probiotics increase stool frequency and have beneficial effects in Asian children. However, caution is needed when interpreting these outcomes because of the existence of heterogeneity. Evidence from larger samples and more adequately powered RCTs with results obtained by standardized measurements are necessary to determine which species and dosage of probiotics and what length of treatment are most efficacious for constipation in children.

Huang, X., Nie, S., and Xie, M. Interaction between gut immunity and polysaccharides. Crit Rev.Food Sci.Nutr. 9-22-2017; 57(14):2943-2955; PM: 26479888

ABSTRACT: The human gut is colonized with a vast and diverse microbial ecosystem, and these bacteria play fundamental roles in the well being of our bodies. Gut-associated lymphoid tissues, the largest mucosal immune system, should never be overlooked for their profound effect in maintaining the host immunity. Therefore, we discussed the relationship between gut immunity and host health, primarily from two aspects: the homeostasis of gut microbiota, and the function of gut-associated lymphoid tissues. Polysaccharides, widely concerned as bioactive macromolecules in recent centuries, have been proved to benefit the intestinal health. Dietary polysaccharides can improve the ratio of probiotics, regulate the intestinal microenvironment like decreasing the gut pH, and stimulate the macrophages or lymphocytes in gut tissues to fight against diseases like cancer. Based on various experimental and clinical evidence, the impacts of dietary polysaccharides on intestinal health are summarized, in order to reveal the possible immunomodulatory mechanisms of polysaccharides.

Hudson, L. E., Anderson, S. E., Corbett, A. H., and Lamb, T. J. Gleaning Insights from Fecal Microbiota Transplantation and Probiotic Studies for the Rational Design of Combination Microbial Therapies. Clin.Microbiol.Rev. 2017; 30(1):191-231; PM: 27856521

ABSTRACT: Beneficial microorganisms hold promise for the treatment of numerous gastrointestinal diseases. The transfer of whole microbiota via fecal transplantation has already been shown to ameliorate the severity of diseases such as Clostridium difficile infection, inflammatory bowel disease, and others. However, the exact mechanisms of fecal microbiota transplant efficacy and the particular strains conferring this benefit are

still unclear. Rationally designed combinations of microbial preparations may enable more efficient and effective treatment approaches tailored to particular diseases. Here we use an infectious disease, C. difficile infection, and an inflammatory disorder, the inflammatory bowel disease ulcerative colitis, as examples to facilitate the discussion of how microbial therapy might be rationally designed for specific gastrointestinal diseases. Fecal microbiota transplantation has already shown some efficacy in the treatment of both these disorders; detailed comparisons of studies evaluating commensal and probiotic organisms in the context of these disparate gastrointestinal diseases may shed light on potential protective mechanisms and elucidate how future microbial therapies can be tailored to particular diseases.

Hugo, A. A., Rolny, I. S., Romanin, D., and Perez, P. F. Lactobacillus delbrueckii subsp. lactis (strain CIDCA 133) stimulates murine macrophages infected with Citrobacter rodentium. World J.Microbiol.Biotechnol. 2017; 33(3):48; PM: 28176201

ABSTRACT: Citrobacter rodentium is a specific murine enteropathogen which causes diarrheal disease characterized by colonic hyperplasia and intestinal inflammation. Recruitment of neutrophils and macrophages constitute a key step to control the infection. Since modulation of the activity of professional phagocytic cells could contribute to improve host s defences against C. rodentium, we investigated the effect of Lactobacillus delbrueckii subsp. lactis (strain CIDCA 133) on the interaction between murine macrophages (RAW 264.7) and C. rodentium. Phagocytosis, surface molecules and inducible nitric oxide synthase (iNOs) expression were determined by flow cytometry. Reactive oxygen species (ROS) were assessed by fluorescence microscopy. The presence of lactobacilli increased phagocytosis of C. rodentium whereas C. rodentium had no effect on lactobacilli internalization. Survival of internalized C. rodentium diminished when strain CIDCA 133 was present. CD-86, MHCII, iNOs expression and nitrite production were increased when C. rodentium and lactobacilli were present even though strain CIDCA 133 alone had no effect. Strain CIDCA 133 led to a strong induction of ROS activity which was not modified by C. rodentium. Lactobacillus delbrueckii subsp. lactis (strain CIDCA 133) is able to increase the activation of murine macrophages infected with C. rodentium. The sole presence of lactobacilli is enough to modify some stimulation markers (e.g. ROS induction) whereas other markers require the presence of both bacteria; thus, indicating a synergistic effect.

Hussain, S. A., Patil, G. R., Reddi, S., Yadav, V., Pothuraju, R., Singh, R. R., and Kapila, S. Aloe vera (Aloe barbadensis Miller) supplemented probiotic lassi prevents Shigella infiltration from epithelial barrier into systemic blood flow in mice model. Microb.Pathog. 2017; 102:143-147; PM: 27914960

ABSTRACT: The aim of present work was to investigate preventive role of orally administered Aloe vera supplemented probiotic lassi (APL) on Shigella dysenteriae infection in mice. At the end of experimental period (2, 5 and 7 days of challenging), different organs such as spleen, liver, small intestine, large intestine, and peritoneal fluid were collected and assessed for Shigella colonization. Secretary IgA was estimated in intestinal fluid. Blood was collected in heparinized tubes for various haematological studies. Oral administration of APL showed a significant ($p < 0.05$) reduction in the Shigella counts (log cfu/mL) in all organs as compared to other treatment groups at different intervals after post feeding. Similarly, secretary IgA antibody levels (mug/mL) in intestinal fluid were significantly ($p < 0.05$) increased in case of APL fed mice. Further,

feeding of APL also demonstrated a positive effect on different haematological parameters viz. Hb (gm %), RBC and WBC count. The results indicated the immunoprotective effects of APL against Shigella dysenteriae induced infection in mice.

Huynh, T. G., Shiu, Y. L., Nguyen, T. P., Truong, Q. P., Chen, J. C., and Liu, C. H. Current applications, selection, and possible mechanisms of actions of synbiotics in improving the growth and health status in aquaculture: A review. Fish.Shellfish.Immunol. 2017; 64:367-382; PM: 28336489

ABSTRACT: Synbiotics, a conjunction between prebiotics and probiotics, have been used in aquaculture for over 10 years. However, the mechanisms of how synbiotics work as growth and immunity promoters are far from being unraveled. Here, we show that a prebiotic as part of a synbiotic is hydrolyzed to mono- or disaccharides as the sole carbon source with diverse mechanisms, thereby increasing biomass and colonization that is established by specific crosstalk between probiotic bacteria and the surface of intestinal epithelial cells of the host. Synbiotics may indirectly and directly promote the growth of aquatic animals through releasing extracellular bacterial enzymes and bioactive products from synbiotic metabolic processes. These compounds may activate precursors of digestive enzymes of the host and augment the nutritional absorptive ability that contributes to the efficacy of food utilization. In fish immune systems, synbiotics cause intestinal epithelial cells to secrete cytokines which modulate immune functional cells as of dendritic cells, T cells, and B cells, and induce the ability of lipopolysaccharides to trigger tumor necrosis factor-alpha and Toll-like receptor 2 gene transcription leading to increased respiratory burst activity, phagocytosis, and nitric oxide production. In shellfish, synbiotics stimulate the proliferation and degranulation of hemocytes of shrimp due to the presence of bacterial cell walls. Pathogen-associated molecular patterns are subsequently recognized and bound by specific pattern-recognition proteins, triggering melanization and phagocytosis processes.

Hyung, K. E., Kim, S. J., Jang, Y. W., Lee, D. K., Hyun, K. H., Moon, B. S., Kim, B., Ahn, H., Park, S. Y., Sohn, U. D., Park, E. S., and Hwang, K. W. Therapeutic effects of orally administered CJLP55 for atopic dermatitis via the regulation of immune response. Korean J.Physiol Pharmacol. 2017; 21(3):335-343; PM: 28461776

ABSTRACT: Atopic dermatitis (AD) is an inflammatory skin condition accompanied by symptoms such as edema and hemorrhage. Kimchi is a traditional fermented Korean dish consisting of various probiotics. In this study, the therapeutic effect of Lactobacillus plantarum CJLP55 isolated from Kimchi was studied in AD-induced mice. Orally administered Lactobacillus strain, CJLP55, suppressed AD symptoms and high serum IgE levels. CJLP55 administration reduced the thickness of the epidermis, infiltration of mast cells and eosinophils into the skin lesion, enlargement of axillary lymph nodes, and increase in cell population in axillary lymph nodes. CJLP55 treatment decreased the production of type 2 cytokines, such as interleukin (IL)-4, IL-5, IL-10, IL-12, interferon (IFN)-gamma, and IL-6,which were stimulated by house dust mite extracts, in the axillary lymph node cells. Orally administered CJLP55 exhibited a therapeutic effect on house dust mite-induced AD in NC/Nga mice after onset of the disease by altering immune cell activation. The Lactobacillus strain, CJLP55, isolated from Kimchi, suppressed AD. Our results suggest its possible use as a potential candidate for management of AD.

Irecta-Najera, C. A., Del, Rosario Huizar-Lopez, Casas-Solis, J., Castro-Felix, P., and Santerre, A. Protective Effect of Lactobacillus casei on DMH-Induced Colon Carcinogenesis in Mice. Probiotics.Antimicrob.Proteins. 2017; 9(2):163-171; PM: 28316010

ABSTRACT: The administration of probiotics is a promising approach to reduce the prevalence of colon cancer, a multifactorial disease, with hereditary factors, as well as environmental lifestyle-related risk factors. Biogenic polyamines, putrescine, spermidine, and spermine are small cationic molecules with great roles in cell proliferation and differentiation as well as regulation of gene expression. Ornithine decarboxylase is the first rate-limiting enzyme for polyamine synthesis, and upregulation of ornithine decarboxylase activity and polyamine metabolism has been associated with abnormal cell proliferation. This paper is focused on studying the protective role of Lactobacillus casei ATCC 393 in a chemically induced mouse model of colon carcinogenesis, directing our attention on aberrant crypt foci as preneoplastic markers, and on polyamine metabolism as a possible key player in carcinogenesis. BALB/c mice were administered 1,2-dimethylhydrazine dihydrochloride (DMH) to induce colon cancer (20 mg/kg body weight, subcutaneous, twice a week for 24 weeks). L. casei ATCC 393 was given orally (106 CFU, twice a week), 2 weeks before DMH administration. Hematoxylin and eosin staining, high-performance liquid chromatography, and Western blotting were used to evaluate aberrant crypt foci, urinary polyamines, and ornithine decarboxylase expression in the colon. The experimental data showed that the preventive administration of L. casei ATCC 393 may delay the onset of cancer as it significantly reduced the number of DMH-induced aberrant crypt foci, the levels of putrescine, and the expression of ornithine decarboxylase. Hence, this probiotic strain has a prospective role in protection against colon carcinogenesis, and its antimutagenic activity may be associated with the maintenance of polyamine metabolism.

Irwin, C., Khalesi, S., Cox, A. J., Grant, G., Davey, A. K., Bulmer, A. C., and Desbrow, B. Effect of 8-weeks prebiotics/probiotics supplementation on alcohol metabolism and blood biomarkers of healthy adults: a pilot study. Eur.J.Nutr. 3-19-2017; PM: 28317073

ABSTRACT: PURPOSE: Modulating gut bacteria via regular prebiotics/probiotics consumption may improve the metabolism of acute alcohol ingestion. This study investigated the impact of 8-weeks prebiotics/probiotics supplementation on microbiome changes and responses to acute alcohol consumption. *METHODS*: 38 participants (21 females, 23.6 +/- 3.4 kg m-2, mean +/- SD) attended the laboratory on two occasions separated by an 8-week intervention period. On each of these visits, a dose of alcohol (0.40 +/- 0.04 g kg-1, Vodka + Soda-Water) was consumed over 10 min. Breath alcohol concentration was sampled over 5 h and alcohol pharmacokinetics was analysed using WinNonlin non-compartmental modelling (C max, t max, AUClast). For the intervention, participants were randomised to receive Placebo + Placebo (PLA), Placebo + Prebiotics (PRE), Probiotics + Placebo (PRO), or Probiotics + Prebiotics (SYN) in a double-blinded manner. Probiotics were a commercially available source of Lactobacillus acidophilus (NCFM(R)) and Bifidobacterium lactis (Bi-07). Prebiotics were a commercially available source of Larch Gum (from Larix occidentalis). Placebo was microcrystalline cellulose. Each visit, participants provided a stool sample, which was analysed to determine the presence of L. acidophilus and B. lactis. Differences between trials were analysed using paired samples t tests. *RESULTS*: Increased counts for at least one bacterial strain (L. acidophilus or B. lactis) were observed for all participants on SYN (n = 10) and PRO (n = 10) trials. No difference in C max or t max was observed between trials when analysed by treatment condition or microbiome outcome. A significant

decrease in AUClast was observed between trials for PLA (p = 0.039) and PRE (p = 0.030) treatments, and when increases in at least one bacterial strain (p = 0.003) and no microbiome changes (p = 0.016) were observed. *CONCLUSION*: Consumption of probiotics appears to alter faecal counts of supplemental bacterial strains in otherwise healthy individuals. However, translation to any possible beneficial impact on alcohol metabolism remains to be elucidated.

Islam, M. M. and Yang, C. J. Efficacy of mealworm and super mealworm larvae probiotics as an alternative to antibiotics challenged orally with Salmonella and E. coli infection in broiler chicks. Poult.Sci. 1-1-2017; 96(1):27-34; PM: 27520069

ABSTRACT: This study was conducted to evaluate dry mealworm (Tenebrio molitor) (DMLP) and super mealworm (Zophobas morio) (DSMLP) larvae probiotics as alternatives to antibiotics in broiler chicks. A total of 240 one-day old Ross 308 male broiler chicks were randomly assigned to three dietary treatments consisting of ten replications with eight birds each in a completely randomized design. The dietary treatments were, (i) control (basal diet), (ii) 0.4% DMLP (basal diet + 0.4% DMLP, DM basis), and (iii) 0.4% DSMLP (basal diet + 0.4% DSMLP, DM basis). On day one, 1 mL of mixed broth agar consisting of 2.4 x 107 cfu Salmonella enteritidis KCTC 2021 and 3.7 x 107 cfu Escherichia coli KCTC 2571 was injected orally into each chick. After one week, growth performance, immunity, mortality, internal organ weight, and cecal and fecal microbiota were investigated. Average daily gain (ADG:) and average daily feed intake (ADFI) increased, while feed conversion ratio (FCR) (g intake/g gain per bird) decreased in response to DMLP and DSMLP supplementation ($P < 0.05$). Additionally, mortality decreased ($P < 0.05$), while IgG and IgA levels increased following DMLP and DSMLP supplementation ($P < 0.05$). Internal organs remained unaffected, except for a reduced bursa of Fabricius weight in DSMLP supplementation ($P < 0.05$). Cecal E. coli and Salmonella contents were reduced in DMLP and DSMLP supplementation ($P < 0.05$), while fecal microbiota contents and pH of cecal and fecal digesta remained unaffected. In conclusion, dietary supplementation with DMLP and DSMLP increased ADG and IgG and IgA levels, while reducing FCR, mortality and cecal E. coli and Salmonella spp. CONTENTS: Thus, DMLP and DSMLP can be utilized as an alternative to antibiotics in broiler diets.

Isokpehi, R. D., Simmons, S. S., Johnson, M. O., and Payton, M. Genomic Evidence for Bacterial Determinants Influencing Obesity Development. Int.J.Environ.Res.Public Health. 3-26-2017; 14(4); PM: 28346358

ABSTRACT: Obesity is a major global public health problem requiring multifaceted interventional approaches including dietary interventions with probiotic bacteria. High-throughput genome sequencing of microbial communities in the mammalian gastrointestinal system continues to present diverse protein function information to understand the bacterial determinants that influence obesity development. The goal of the research reported in this article was to identify biological processes in probiotic bacteria that could influence the mechanisms for the extraction of energy from diet in the human gastrointestinal system. Our research strategy of combining bioinformatics and visual analytics methods was based on the identification of operon gene arrangements in genomes of Lactobacillus species and Akkermansiamuciniphila that include at least a gene for a universal stress protein. The two major findings from this research study are related to Lactobacillus plantarum and Akkermansia muciniphila

bacteria species which are associated with weight-loss. The first finding is that Lactobacillus plantarum strains have a two-gene operon that encodes a universal stress protein for stress response and the membrane translocator protein (TSPO), known to function in mitochondrial fatty acid oxidation in humans. The second finding is the presence of a three-gene operon in Akkermansia muciniphila that includes a gene whose human mitochondrial homolog is associated with waist-hip ratio and fat distribution. From a public health perspective, elucidation of the bacterial determinants influencing obesity will help in educating the public on optimal probiotic use for anti-obesity effects.

Jang, S. H., Park, J., Kim, S. H., Choi, K. M., Ko, E. S., Cha, J. D., Lee, Y. R., Jang, H., and Jang, Y. S. Red ginseng powder fermented with probiotics exerts antidiabetic effects in the streptozotocin-induced mouse diabetes model. Pharm.Biol. 2017; 55(1):317-323; PM: 27927080

ABSTRACT: CONTEXT: Red ginseng (heat-processed Panax ginseng) is a well-known alternative medicine with pharmacological antidiabetic activity. It exerts pharmacological effects through the transformation of saponin into metabolites by the intestinal microbiota. Given that intestinal conditions and intestinal microflora vary among individuals, the pharmacological effects of orally administered red ginseng likely may vary among individuals. *OBJECTIVE*: To overcome this variation and produce homogeneously effective red ginseng, we evaluated the antidiabetic effects of probiotic-fermented red ginseng in a mouse model. *MATERIALS AND METHODS*: The antidiabetic efficacy of orally administered probiotic-fermented red ginseng was assessed in ICR mice after induction of diabetes using streptozotocin (170 mg/kg body weight). Samples were given orally for 8 weeks, and indicators involved in diabetic disorders such as body weight change, water intake, blood glucose, glucose tolerance and various biochemical parameters were determined. *RESULTS*: Oral administration of probiotic-fermented red ginseng significantly decreased the level of blood glucose of about 62.5% in the fasting state and induced a significant increase in glucose tolerance of about 10.2% compared to the control diabetic mice. Additionally, various indicators of diabetes and biochemical data (e.g., blood glycosylated haemoglobin level, serum concentrations of insulin, and alpha-amylase activity) showed a significant improvement in the diabetic conditions of the mice treated with probiotic-fermented red ginseng in comparison with those of control diabetic mice. *DISCUSSION AND CONCLUSION*: Our results demonstrate the antidiabetic effects of probiotic-fermented red ginseng in the streptozotocin-induced mouse diabetes model and suggest that probiotic-fermented red ginseng may be a uniformly effective red ginseng product.

Jang, S. H., Park, J., Kim, S. H., Choi, K. M., Ko, E. S., Cha, J. D., Lee, Y. R., Jang, H., and Jang, Y. S. Oral administration of red ginseng powder fermented with probiotic alleviates the severity of dextran-sulfate sodium-induced colitis in a mouse model. Chin J.Nat.Med. 2017; 15(3):192-201; PM: 28411687

ABSTRACT: Red ginseng is a well-known alternative medicine with anti-inflammatory activity. It exerts pharmacological effects through the transformation of saponin into metabolites by intestinal microbiota. Given that intestinal microflora vary among individuals, the pharmacological effects of red ginseng likely vary among individuals. In order to produce homogeneously effective red ginseng, we prepared probiotic-fermented red ginseng and evaluated its activity using a dextran sulfate sodium (DSS)-

induced colitis model in mice. Initial analysis of intestinal damage indicated that the administration of probiotic-fermented red ginseng significantly decreased the severity of colitis, compared with the control and the activity was higher than that induced by oral administration of ginseng powder or probiotics only. Subsequent analysis of the levels of serum IL-6 and TNF-alpha, inflammatory biomarkers that are increased at the initiation stage of colitis, were significantly decreased in probiotic-fermented red ginseng-treated groups in comparison to the control group. The levels of inflammatory cytokines and mRNAs for inflammatory factors in colorectal tissues were also significantly decreased in probiotic-fermented red ginseng-treated groups. Collectively, oral administration of probiotic-fermented red ginseng reduced the severity of colitis in a mouse model, suggesting that it can be used as a uniformly effective red ginseng product.

Jang, S. Y., Heo, J., Park, M. R., Song, M. H., Kim, J. N., Jo, S. H., Jeong, D. Y., Lee, H. K., Kim, Y., and Oh, S. Genome Characteristics of Lactobacillus fermentum strain JDFM216 for Application as Probiotic Bacteria. J.Microbiol.Biotechnol. 4-25-2017; PM: 28438015

ABSTRACT: Lactobacillus fermentum strain JDFM216, isolated from a Korean infant feces, possesses an enhancement of longevity and immune response on Caenorhabditis elegans host. To explore the molecular characteristics of strain JDFM216, we performed a whole-genome sequencing using PacBio system. The single circular DNA chromosome of 2,076,427 bp was completely assembled and 2,623 encoding sequences were predicted. Phylogenetically featured five genes possibly related to longevity and immune response of host were identified in L. fermentum strain JDFM216. These genes encode UDP-N-acetylglucosamine 1-carboxyvinyltransferase (EC 2.5.1.7), ErfK/YbiS/YcfS/YnhG family protein, site-specific recombinase XerD, homocysteine S-methyltransferase (EC 2.1.1.10), and aspartate-ammonia ligase (EC 6.3.1.1), which are peptidoglycan synthesis and amino acid metabolism in the gut environment. Our findings suggest that the genetic backgrounds of L. fermentum strain JDFM216 and its potential candidate genes for host longevity and immune response provide new insight for applying on food industry as newly isolated functional probiotics.

Jensen-Jarolim, E., Pali-Scholl, I., and Roth-Walter, F. Outstanding animal studies in allergy II. From atopic barrier and microbiome to allergen-specific immunotherapy. Curr.Opin.Allergy Clin.Immunol. 2017; 17(3):180-187; PM: 28375932

ABSTRACT: PURPOSE OF REVIEW: Animal studies published within the past 18 months were assessed, focusing on innate and specific immunomodulation, providing knowledge of high translational relevance for human atopic and allergic diseases. *RECENT FINDINGS*: Allergic companion animals represent alternative models, but most studies were done in mice. Atopic dermatitis mouse models were refined by the utilization of cytokines like IL-23 and relevant skin allergens or enzymes. A novel IL-6 reporter mouse allows biomonitoring of inflammation. Both skin pH and the (transferable) microflora have a pivotal role in modulating the skin barrier. The microflora of the gastrointestinal mucosa maintains tolerance to dietary compounds and can be disturbed by antiacid drugs. A key mouse study evidenced that dust from Amish households, but not from Hutterites protected mice against asthma. In studies on subcutaneous and sublingual allergen-specific immunotherapy, much focus was given on delivery and adjuvants, using poly-lacto-co-glycolic particles, CpGs, probiotics or Vitamin D3. The epicutaneous and intralymphatic routes showed promising results in mice and horses in terms of prophylactic and therapeutic allergy treatment. *SUMMARY*: In atopic dermatitis, food

allergies and asthma, environmental factors, together with the resident microflora and barrier status, decide on sensitization versus tolerance. Also allergen-specific immunotherapy operates with immunomodulatory principles.

Jers, C., Strube, M. L., Cantor, M. D., Nielsen, B. K. K., Sorensen, O. B., Boye, M., and Meyer, A. S. Selection of Bacillus species for targeted in situ release of prebiotic galacto-rhamnogalacturonan from potato pulp in piglets. Appl.Microbiol.Biotechnol. 2017; 101(9):3605-3615; PM: 28204884

ABSTRACT: We have previously shown that galacto-rhamnogalacturonan fibers can be enzymatically extracted from potato pulp and that these fibers have potential for exerting a prebiotic effect in piglets. The spore-forming Bacillus species are widely used as probiotics in feed supplements for pigs. In this study, we evaluated the option for further functionalizing Bacillus feed supplements by selecting strains possessing the enzymes required for extraction of the potentially prebiotic fibers. We established that it would require production and secretion of pectin lyase and/or polygalacturonase but no or limited secretion of galactanase and beta-galactosidase. By screening a library of 158 Bacillus species isolated from feces and soil, we demonstrated that especially strains of Bacillus amyloliquefaciens, Bacillus subtilis, and Bacillus mojavensis have the necessary enzyme profile and thus the capability to degrade polygalacturonan. Using an in vitro porcine gastrointestinal model system, we revealed that specifically strains of B. mojavensis were able to efficiently release galacto-rhamnogalacturonan from potato pulp under simulated gastrointestinal conditions. The work thus demonstrated the feasibility of producing prebiotic fibers via a feed containing Bacillus spores and potato pulp and identified candidates for future in vivo evaluation in piglets.

Jiang, C., Li, G., Huang, P., Liu, Z., and Zhao, B. The Gut Microbiota and Alzheimer's Disease. J.Alzheimers.Dis. 2017; 58(1):1-15; PM: 28372330

ABSTRACT: The gut microbiota comprises a complex community of microorganism species that resides in our gastrointestinal ecosystem and whose alterations influence not only various gut disorders but also central nervous system disorders such as Alzheimer's disease (AD). AD, the most common form of dementia, is a neurodegenerative disorder associated with impaired cognition and cerebral accumulation of amyloid-beta peptides (Abeta). Most notably, the microbiota-gut-brain axis is a bidirectional communication system that is not fully understood, but includes neural, immune, endocrine, and metabolic pathways. Studies in germ-free animals and in animals exposed to pathogenic microbial infections, antibiotics, probiotics, or fecal microbiota transplantation suggest a role for the gut microbiota in host cognition or AD-related pathogenesis. The increased permeability of the gut and blood-brain barrier induced by microbiota dysbiosis may mediate or affect AD pathogenesis and other neurodegenerative disorders, especially those associated with aging. In addition, bacteria populating the gut microbiota can secrete large amounts of amyloids and lipopolysaccharides, which might contribute to the modulation of signaling pathways and the production of proinflammatory cytokines associated with the pathogenesis of AD. Moreover, imbalances in the gut microbiota can induce inflammation that is associated with the pathogenesis of obesity, type 2 diabetes mellitus, and AD. The purpose of this review is to summarize and discuss the current findings that may elucidate the role of the gut microbiota in the development of AD. Understanding the underlying mechanisms may provide new insights into novel therapeutic strategies for AD.

Jiang, T., Li, H. S., Han, G. G., Singh, B., Kang, S. K., Bok, J. D., Kim, D. D., Hong, Z. S., Choi, Y. J., and Cho, C. S. Oral Delivery of Probiotics in Poultry Using pH-Sensitive Tablets. J.Microbiol.Biotechnol. 4-28-2017; 27(4):739-746; PM: 28081355

ABSTRACT: As alternatives to antibiotics in livestocks, probiotics have been used, although most of them in the form of liquid or semisolid formulations, which show low cell viability after oral administration. Therefore, suitable dry dosage forms should be developed for livestocks to protect probiotics against the low pH in the stomach such that the products have higher probiotics survivability. Here, in order to develop a dry dosage forms of probiotics for poultry, we used hydroxypropyl methylcellulose phthalate 55 (HPMCP 55) as a tablet-forming matrix to develop probiotics in a tablet form for poultry. Here, we made three different kinds of probiotics-loaded tablet under different compression forces and investigated their characteristics based on their survivability, morphology, disintegration time, and kinetics in simulated gastrointestinal fluid. The results indicated that the probiotics formulated in the tablets displayed higher survival rates in acidic gastric conditions than probiotics in solution. Rapid release of the probiotics from the tablets occurred in simulated intestinal fluid because of fast swelling of the tablets in neutral pH. As a matrix of tablet, HPMCP 55 provided good viability of probiotics after 6 months under refrigeration. Moreover, after oral administration of probiotics-loaded tablets to chicken, more viable probiotics were observed, than with solution type, through several digestive areas of chicken by the tablets.

Joerger, R. D. and Ganguly, A. Current Status of the Preharvest Application of Pro- and Prebiotics to Farm Animals to Enhance the Microbial Safety of Animal Products. Microbiol.Spectr. 2017; 5(1); PM: 28185614

ABSTRACT: The selection of microorganisms that act as probiotics and feed additives that act as prebiotics is an ongoing research effort, but a sizable range of commercial pro-, pre- and synbiotic (combining pro- and prebiotics) products are already available and being used on farms. A survey of the composition of commercial products available in the United States revealed that Lactobacillus acidophilus, Enterococcus faecium, and Bacillus subtilis were the three most common species in probiotic products. Of the nearly 130 probiotic products (also called direct-fed microbials) for which information was available, about 50 also contained yeasts or molds. The focus on these particular bacteria and eukaryotes is due to long-standing ideas about the benefits of such strains, research data on effectiveness primarily in laboratory or research farm settings, and regulations that dictate which microorganisms or feed additives can be administered to farm animals. Of the direct-fed microbials, only six made a claim relating to food safety or competitive exclusion of pathogens. None of the approximately 50 prebiotic products mentioned food safety in their descriptions. The remainder emphasized enhancement of animal performance such as weight gain or overall animal health. The reason why so few products carry food safety-related claims is the difficulties in establishing unambiguous cause and effect relationships between the application of such products in varied and constantly changing farm environments and improved food safety of the end product.

Johnson, T. J., Shank, J. M., and Johnson, J. G. Current and Potential Treatments for Reducing Campylobacter Colonization in Animal Hosts and Disease in Humans. Front Microbiol. 2017; 8:487; PM: 28386253

ABSTRACT: Campylobacter jejuni is the leading cause of bacteria-derived gastroenteritis worldwide. In the developed world, Campylobacter is usually acquired by consuming under-cooked poultry, while in the developing world it is often obtained through drinking contaminated water. Once consumed, the bacteria adhere to the intestinal epithelium or mucus layer, causing toxin-mediated inhibition of fluid reabsorption from the intestine and invasion-induced inflammation and diarrhea. Traditionally, severe or prolonged cases of campylobacteriosis have been treated with antibiotics; however, overuse of these antibiotics has led to the emergence of antibiotic-resistant strains. As the incidence of antibiotic resistance, emergence of post-infectious diseases, and economic burden associated with Campylobacter increases, it is becoming urgent that novel treatments are developed to reduce Campylobacter numbers in commercial poultry and campylobacteriosis in humans. The purpose of this review is to provide the current status of present and proposed treatments to combat Campylobacter infection in humans and colonization in animal reservoirs. These treatments include anti-Campylobacter compounds, probiotics, bacteriophage, vaccines, and anti-Campylobacter bacteriocins, all of which may be successful at reducing the incidence of campylobacteriosis in humans and/or colonization loads in poultry. In addition to reviewing treatments, we will also address several proposed targets that may be used in future development of novel anti-Campylobacter treatments.

Jones, R. M. and Neish, A. S. Redox signaling mediated by the gut microbiota. Free Radic.Biol.Med. 2017; 105:41-47; PM: 27989756

ABSTRACT: The microbiota that inhabits the mammalian intestine can influence a range of physiological functions, including the modulation of immune responses, enhancement epithelial barrier function, and the stimulation of cell proliferation. While the mechanisms by which commensal prokaryotes stimulate immune signaling networks are well-characterized, less is known about the mechanistic control over homeostatic pathways within tissues. Recent reports by our research group have demonstrated that contact between the gut epithelia and some groups of enteric commensal bacteria prompts the rapid generation of reactive oxygen species (ROS) within host cells. Whereas the bacterial-induced production of ROS in phagocytes in response to ligand binding to Formyl Peptide Receptors (FPRs) and ensuing activation of NADPH oxidase 2 (Nox2) is a well-defined mechanism, ROS generated by other cell types such as intestinal epithelia in response to microbial signals via FPRs and the NADPH oxidase 1 (Nox1) is less appreciated. Importantly, enzymatically generated ROS have been shown to function as second messengers in many signal transduction pathways via the transient oxidative activity on sensor proteins bearing oxidant-sensitive thiol groups. Examples of redox sensitive proteins include tyrosine phosphatases that serve as regulators of MAPK pathways, focal adhesion kinase, as well as components involved NF-kB activation. Here, we review the leading edge discoveries gleaned from investigations that focus on microbial-induced generation of ROS and their functional effects on host physiology. These studies identify the functional molecular elements and mechanistic events that mediate the established effects of the normal microbiota on intestinal physiology.

Jones, R. M., Mulle, J. G., and Pacifici, R. Osteomicrobiology: The influence of gut microbiota on bone in health and disease. Bone. 4-27-2017; PM: 28433758

No Abstract Available.

Juan, Z., Zhao-Ling, S., Ming-Hua, Z., Chun, W., Hai-Xia, W., Meng-Yun, L., Jian-Qiong, H., Yue-Jie, Z., and Xin, S. Oral administration of Clostridium butyricum CGMCC0313-1 reduces ovalbumin-induced allergic airway inflammation in mice. Respirology. 1-25-2017; PM: 28122397

ABSTRACT: BACKGROUND AND OBJECTIVE: Probiotic bacteria can induce immune regulation or immune tolerance in patients with allergic diseases, but the underlying mechanisms are still unclear. There has been a growing interest in the use of beneficial bacteria for allergic diseases recently. This study aimed at exploring whether Clostridium butyricum CGMCC0313-1 (C. butyricum) can reduce ovalbumin (OVA)-induced allergic airway inflammation in a mouse model. *METHODS*: Mouse model of allergic airway inflammation induced via OVA was used in this study. C. butyricum was administered daily by the oral route during or after the sensitization. Airway function, pulmonary airway inflammation, mast cell degranulation, T helper (Th)-specific and anti-inflammatory cytokines, OVA-specific Ig, matrix metalloproteinase 9 (MMP-9) and histopathological alterations were examined. *RESULTS*: C. butyricum significantly reduced lung resistance in the asthmatic mice. Pulmonary airway inflammation, mast cell degranulation, airway remodelling and the expression of OVA-specific IgE/G1 were suppressed by oral C. butyricum. It also reversed the imbalance of Th1/Th2 and increased the anti-inflammatory cytokine IL-10. *CONCLUSION*: C. butyricum reduces OVA-induced allergic airway inflammation in mice and might be an additional or supplementary therapy for allergic asthma.

Jugan, M. C., Rudinsky, A. J., Parker, V. J., and Gilor, C. Use of probiotics in small animal veterinary medicine. J.Am.Vet.Med.Assoc. 3-1-2017; 250(5):519-528; PM: 28207322

No Abstract Available.

Jung, M. Y., Lee, J., Park, B., Hwang, H., Sohn, S. O., Lee, S. H., Lim, H. I., Park, H. W., and Lee, J. H. Applicability of a colorimetric method for evaluation of lactic acid bacteria with probiotic properties. Food Microbiol. 2017; 64:33-38; PM: 28213032

ABSTRACT: Rapid colorimetric methods using various indicator reagents have been developed to monitor bacterial viability. Here, we examined the applicability of a method based on the reduction of resazurin or water-soluble tetrazolium salt-8 (WST-8) to screen lactic acid bacteria (LAB) for growth, tolerance against bile acid and low pH. The resazurin reduction test proved unsuitable for screening LAB such as Lactobacillus plantarum and Leuconostoc mesenteroides since it reacted with acid present in the cultures. LAB growth could be indirectly quantified by measuring WST-8 reduction. This method proved more sensitive and quickly results than counting bacterial colony forming units and turbidity at 600 nm in the presence of bile and acid. Our results suggested that the WST-8-based method could be useful for the characterization of growth and tolerance of the lactic acid producing bacteria.

Kabbani, T. A., Pallav, K., Dowd, S. E., Villafuerte-Galvez, J., Vanga, R. R., Castillo, N. E., Hansen, J., Dennis, M., Leffler, D. A., and Kelly, C. P. Prospective randomized controlled study on the effects of Saccharomyces boulardii CNCM I-745 and amoxicillin-clavulanate or the

combination on the gut microbiota of healthy volunteers. Gut Microbes. 1-2-2017; 8(1):17-32; PM: 27973989

ABSTRACT: Probiotics are believed to be beneficial in maintaining a healthy gut microbiota whereas antibiotics are known to induce dysbiosis. This study aimed to examine the effects of the probiotic Saccharomyces boulardii CNCM I-745 (SB), the antibiotic Amoxicillin-Clavulanate (AC) and the combination on the microbiota and symptoms of healthy humans. Healthy subjects were randomized to one of 4 study groups: SB for 14 days, AC for 7 days, SB plus AC, Control (no treatment). Participants gave stool samples and completed gastro-intestinal symptom questionnaires. Microbiota changes in stool specimens were analyzed using 16s rRNA gene pyrosequencing (bTEFAP). Only one subject withdrew prematurely due to adverse events. Subjects treated by S boulardii + AC had fewer adverse events and tolerated the study regimen better than those receiving the AC alone. Control subjects had a stable microbiota throughout the study period. Significant microbiota changes were noted in the AC alone group during antibiotic treatment. AC associated changes included reduced prevalence of the genus Roseburia and increases in Escherichia, Parabacteroides, and Enterobacter. Microbiota alterations reverted toward baseline, but were not yet completely restored 2 weeks after antibiotherapy. No significant shifts in bacterial genera were noted in the SB alone group. Adding SB to AC led to less pronounced microbiota shifts including less overgrowth of Escherichia and to a reduction in antibiotic-associated diarrhea scores. Antibiotic treatment is associated with marked microbiota changes with both reductions and increases in different genera. S. boulardii treatment can mitigate some antibiotic-induced microbiota changes (dysbiosis) and can also reduce antibiotic-associated diarrhea.

Kafshdooz, T., Akbarzadeh, A., Majdi, Seghinsara A., Pourhassan, M., Nasrabadi, H. T., and Milani, M. Role of Probiotics in Managing of Helicobacter Pylori Infection: A Review. Drug Res.(Stuttg). 2017; 67(2):88-93; PM: 27824431

ABSTRACT: Background:Helicobacter pylori is a prevalent pathogen which is considered as an etiological cause for gastroduodenal ulcers, and a substantial risk factor for gastric malignancies. The vital factor to take into account is that roughly half of the world's population is infected with this bacterium. However, most subjects colonized remain asymptomatic and do not require any treatment. Several antimicrobial agents such as amoxicillin, clarithromycin and metronidazole are used to eradicate the infection. However, these drug regiments do not eradicate H. pylori in all patients because of the anti-drug resistance. Aim: In this review we aim to discuss the role and mechanisms of probiotics, as supportive medicines, in management of H. pylori infection. Methods: We have reviewed the published articles in PubMed and Medline databases. Also, abstracts presented in international conferences on the management of H. pylori infections and treatment protocol, have been thoroughly reviewed. Results: The overall trend in the literature indicates the usefulness of probiotics in controlling H. pylori infection. This bacterium is among the most studied human pathogens regarding the efficacy of probiotics for treating its infection. Nevertheless, some studies suggest that probiotics do not efficiently eradicate H. pylori but retain the number of this bacterium at low levels inside the human stomach. Conclusion: The analyzed literature suggest that when probiotics are consumed in conjunction with antibiotics, the eradication rate may be improved through modulating the immune response and decreasing the adverse effects of routine drugs leading to gastroprotection.

Kahouli, I., Malhotra, M., Westfall, S., aoui-Jamali, M. A., and Prakash, S. Design and validation of an orally administrated active L. fermentum-L. acidophilus probiotic formulation using colorectal cancer Apc Min/+ mouse model. Appl.Microbiol.Biotechnol. 2017; 101(5):1999-2019; PM: 27837314

ABSTRACT: Probiotics have been shown to have beneficial properties in attenuating the risk of colorectal cancer (CRC) development. However, functional evidence to support such effects for some probiotic bacteria are relatively unknown. Here, we document a significant antioxidant, anti-proliferative and pro-apoptotic activities of Lactobacillus acidophilus ATCC 314 and Lactobacillus fermentum NCIMB 5221 on CRC cells, particularly when used in combination (La-Lf). Furthermore, a superior synergistic activity on the inhibition of tumor growth and modulation of cell proliferation and epithelial markers in the Apc Min/+ CRC mouse model was explored, based on the expression levels of Ki-67, E-cadherin, beta-catenin, and cleaved caspase-3 (CC3) proteins. The anti-cancer activity of La-Lf co-culture was significantly enhanced in vitro with significant reduced proliferation (38.8 +/- 6.9 %, P = 0.009) and increased apoptosis (413 RUL, P < 0.001) towards cancer cells, as well as significant protection of normal colon cell growth from toxic treatment (18.6 +/- 9.8 %, P = 0.001). La-Lf formulation (1010cfu/animal/day) altered aspects of intestinal tumorigenesis by significantly reducing intestinal tumor multiplicity (1.7-fold, P = 0.016) and downregulating cellular proliferation markers, including beta-catenin (P = 0.041) and Ki-67 (P = 0.008). In conclusion, La-Lf showed greater protection against intestinal tumorigenesis supporting a potential use as a biotherapeutic for the prevention of CRC.

Kalipatnapu, S., Kuppuswamy, S., Venugopal, G., Kaliaperumal, V., and Ramadass, B. Fecal total iron Concentration is inversely associated with Fecal Lactobacillus in preschool children. J.Gastroenterol.Hepatol. 1-11-2017; PM: 28076655

ABSTRACT: BACKGROUND: Iron deficiency is associated with stunting and poor performance in children. Oral iron supplementation is widely promoted to correct iron deficiency. However, excess iron may be toxic to beneficial luminal gut bacteria and could support growth of pathobionts. *OBJECTIVE*: To analyze the fecal total iron concentration and fecal Lactobacillus levels in a cohort of stunted and normal children. *DESIGN*: The study was undertaken in two different locations. One of them is a rural area and other is a semi-urban-slum area, both areas are located in the Vellore district of Tamilnadu state. 20 children (10 stunted and 10 normal growth) aged 2 to 5 years from each area were recruited. Both groups were nearly identical demographically. Fecal samples were collected. Fecal total iron was estimated, fecal DNA was extracted and subjected to 16S rDNA-targeted real-time polymerase chain reaction to determine the relative predominance of Lactobacillus and Escherichia coli. *RESULTS*: The fecal total iron concentration in rural children (3656 microg/ g wet wt. of feces) was significantly higher when compared to semi-urban-slum children (114.9 microg/ g wet wt. of feces, p < 0.005). Inversely, fecal Lactobacillus in rural children (Median 3.18 x 10-3 Relative difference compared with total bacteria) was significantly lower when compared to semi-urban-slum children (Median 59.33 x 10-3 , p < 0.005). There was no significant change observed between normal and stunted children. E.coli levels remained unaffected. *CONCLUSION*: The present study documents an inverse relationship between fecal iron concentration and Fecal Lactobacillus concentration in children belonging to two different localities independent of their nutritional status.

Kandasamy, S., Vlasova, A. N., Fischer, D. D., Chattha, K. S., Shao, L., Kumar, A., Langel, S. N., Rauf, A., Huang, H. C., Rajashekara, G., and Saif, L. J. Unraveling the Differences between Gram-Positive and Gram-Negative Probiotics in Modulating Protective Immunity to Enteric Infections. Front Immunol. 2017; 8:334; PM: 28396664

ABSTRACT: The role of intestinal microbiota and probiotics in prevention and treatment of infectious diseases, including diarrheal diseases in children and animal models, is increasingly recognized. Intestinal commensals play a major role in development of the immune system in neonates and in shaping host immune responses to pathogens. Lactobacilli spp. and Escherichia coli Nissle 1917 are two probiotics that are commonly used in children to treat various medical conditions including human rotavirus diarrhea and inflammatory bowel disease. Although the health benefits of probiotics have been confirmed, the specific effects of these established Gram-positive (G+) and Gram-negative (G-) probiotics in modulating immunity against pathogens and disease are largely undefined. In this review, we discuss the differences between G+ and G- probiotics/commensals in modulating the dynamics of selected infectious diseases and host immunity. These probiotics modulate the pathogenesis of infectious diseases and protective immunity against pathogens in a species- and strain-specific manner. Collectively, it appears that the selected G- probiotic is more effective than the various tested G+ probiotics in enhancing protective immunity against rotavirus in the gnotobiotic piglet model.

Kang, J., Chung, W. H., Lim, T. J., Whon, T. W., Lim, S., and Nam, Y. D. Complete Genome Sequence of Lactobacillus casei LC5, a Potential Probiotics for Atopic Dermatitis. Front Immunol. 2017; 8:413; PM: 28439274

No Abstract Available.

Kang, Y. B., Cai, Y., and Zhang, H. Gut microbiota and allergy/asthma: From pathogenesis to new therapeutic strategies. Allergol.Immunopathol.(Madr.). 2017; 45(3):305-309; PM: 28029408

ABSTRACT: Asthma and atopy, classically associated with hyper-activation of the T helper 2 (Th2) arm of adaptive immunity, are among the most common chronic illnesses worldwide. Emerging evidence relates atopy and asthma to the composition and function of gut microbiota composition. Moreover, certain gut microbial strains have been shown to inhibit or attenuate immune responses associated with chronic inflammation in experimental models. Although still a relatively nascent field of research, evidence to date suggests that the gut microbiome may represent fertile targets for prevention or management of allergic asthma and other diseases in which adaptive immune dysfunction is a prominent feature. The oral probiotics/prebiotic represents a possible therapeutic for improving asthma and allergic disease. Especially, recent technological developments that permit identification of microbes and their products using culture-independent molecular detection techniques. In this review, we literaturely summarise the aggravation or improvement of metabolic diseases by role of gut microbiota, probiotics/prebiotic treatment.

Kantor, R. and Silverberg, J. I. Environmental risk factors and their role in the management of atopic dermatitis. Expert.Rev.Clin.Immunol. 2017; 13(1):15-26; PM: 27417220

ABSTRACT: INTRODUCTION: The etiology of atopic dermatitis (AD) is multifactorial with interaction between genetics, immune and environmental factors. Areas covered: We review the role of prenatal exposures, irritants and pruritogens, pathogens, climate factors, including temperature, humidity, ultraviolet radiation, outdoor and indoor air pollutants, tobacco smoke exposure, water hardness, urban vs. rural living, diet, breastfeeding, probiotics and prebiotics on AD. *Expert commentary*: The increased global prevalence of AD cannot be attributed to genetics alone, suggesting that evolving environmental exposures may trigger and/or flare disease in predisposed individuals. There is a complex interplay between different environmental factors, including individual use of personal care products and exposure to climate, pollution, food and other exogenous factors. Understanding these complex risk factors is crucial to developing targeted interventions to prevent the disease in millions. Moreover, patients require counseling on optimal regimens for minimization of exposure to irritants and pruritogens and other harmful exposures.

Karthikeyan, G. and Bhat, B. V. The PiPS (Probiotics in Preterm Infants Study) Trial - Controlling the Confounding Factor of Cross-contamination Unveils Significant Benefits. Indian Pediatr. 2-15-2017; 54(2):162; PM: 28285299

No Abstract Available.

Kasatpibal, N., Whitney, J. D., Saokaew, S., Kengkla, K., Heitkemper, M. M., and Apisarnthanarak, A. Effectiveness of Probiotic, Prebiotic, and Synbiotic Therapies in Reducing Postoperative Complications: A Systematic Review and Network Meta-analysis. Clin.Infect.Dis. 5-15-2017; 64(suppl_2):S153-S160; PM: 28475793

ABSTRACT: Background: Microbiome-directed therapies are increasingly used preoperatively and postoperatively to improve postoperative outcomes. Recently, the effectiveness of probiotics, prebiotics, and synbiotics in reducing postoperative complications (POCs) has been questioned. This systematic review aimed to examine and rank the effectiveness of these therapies on POCs in adult surgical patients. *Methods*: We searched for articles from PubMed, Embase, Cochrane, Web of Science, Scopus, and CINAHL plus. From 2002 to 2015, 31 articles meeting the inclusion criteria were identified in the literature. Risk of bias and heterogeneity were assessed. Network meta-analyses (NMA) were performed using random-effects modeling to obtain estimates for study outcomes. Risk ratios (RRs) and 95% confidence intervals (CIs) were estimated. We then ranked the comparative effects of all regimens with the surface under the cumulative ranking (SUCRA) probabilities. *Results*: A total of 2,952 patients were included. We found that synbiotic therapy was the best regimen in reducing surgical site infection (SSI) (RR = 0.28; 95% CI, 0.12-0.64) in adult surgical patients. Synbiotic therapy was also the best intervention to reduce pneumonia (RR = 0.28; 95% CI, 0.09-0.90), sepsis (RR = 0.09; 95% CI, 0.01-0.94), hospital stay (mean = 9.66 days, 95% CI, 7.60-11.72), and duration of antibiotic administration (mean = 5.61 days, 95% CI, 3.19-8.02). No regimen significantly reduced mortality. *Conclusions*: This network meta-analysis suggests that synbiotic therapy is the first rank to reduce SSI, pneumonia, sepsis, hospital stay, and antibiotic use. Surgeons should consider the use of synbiotics as an adjunctive therapy to prevent POCs among adult surgical patients. Increasing use of synbiotics may help to reduce the use of antibiotics and multidrug resistance.

Katz-Agranov, N. and Zandman-Goddard, G. The microbiome and systemic lupus erythematosus. Immunol.Res. 2017; 65(2):432-437; PM: 28233089

ABSTRACT: The microbiota, which is comprised of the collective of all microbes inhabiting the gut and its effect on the human host in which it resides, has become a growing field of interest. Various parameters of health and disease have been found to be associated with the variation in the human gut microbiome. In recent years, many studies have demonstrated an important role of gut microbes in the development of various illnesses including autoimmune diseases, such as type 1 diabetes, rheumatoid arthritis, and multiple sclerosis. Although the mechanism of the disease involves both genetic and environmental factors, lupus has been found to be affected by the composition of the microbes lining the intestines. Several recent studies have suggested that alterations of the gut microbial composition may be correlated with SLE disease manifestations, while the exact roles of either symbiotic or pathogenic microbes in this disease have yet to be explored. Elucidation of the roles of gut microbes in SLE will shed light on how this autoimmune disorder develops and provide opportunities for improved biomarkers of the disease and the potential to probe new therapies. This new knowledge, along with that enabling alteration in composition of the gut microbiome, via diet modification, antibiotic, and probiotics, may bring forward a new era in the future of lupus treatment.

Kaur, R., Gulati, M., and Singh, S. K. Role of synbiotics in polysaccharide assisted colon targeted microspheres of mesalamine for the treatment of ulcerative colitis. Int.J.Biol.Macromol. 2017; 95:438-450; PM: 27876597

ABSTRACT: The present study explains the effect of concomitant administration of synbiotics with the polysaccharide based colon targeted delivery system. As the gut microflora get deranged on administration of mesalamine, drug release from such delivery systems is expected to be jeopardised because the release trigger is dependent solely on the colonic microbiota. To overcome this limitation, mesalamine was formulated as microspheres with guar gum and xanthan gum (prebiotics). These were combined with probiotics containing Lactobacillus acidophilus, L. rhamnosus, Bifidobacterium longumand Saccharomyces boulardi. Dissolution studies of the prepared formulation conducted in simulated colonic fluid clearly demonstrated its superiority over the marketed, delayed release dosage forms of mesalamine. The therapeutic benefit of the concomitant administration of synbiotic with mesalamine was evidenced by the comparative evaluation of faecal contents, weight gain trend and histopathological studies conducted in rats. The results suggest that co-administration of synbiotics with mesalamine can be used as a convenient methodology to achieve efficient and cost-effective targeting of the drug to colon.

Kawahara, T., Makizaki, Y., Oikawa, Y., Tanaka, Y., Maeda, A., Shimakawa, M., Komoto, S., Moriguchi, K., Ohno, H., and Taniguchi, K. Oral administration of Bifidobacterium bifidum G9-1 alleviates rotavirus gastroenteritis through regulation of intestinal homeostasis by inducing mucosal protective factors. PLoS.One. 2017; 12(3):e0173979; PM: 28346473

ABSTRACT: Human rotavirus (RV) infection is a leading cause of dehydrating diarrhea in infants and young children worldwide. Since therapeutic approaches to RV gastroenteritis are limited to alleviation of dehydration with oral rehydration solutions, more direct approaches to palliate symptoms of RV gastroenteritis are required.

Treatments with probiotics have been increasingly recognized as alternative safe and low cost treatments for moderate infectious diarrhea. In this study, Bifidobacterium bifidum G9-1 (BBG9-1), which has been used as an intestinal drug for several decades, was shown to have a remarkable protective effect against RV gastroenteritis in a suckling mice model. As well as prophylactic oral administration of BBG9-1 from 2 days before RV infection, therapeutic oral administration of BBG9-1 from 1 day after RV infection significantly alleviated RV-induced diarrhea. Therapeutic administration of BBG9-1 reduced various types of damage in the small intestine, such as epithelial vacuolization and villous shortening, and significantly diminished the infectious RV titer in mixtures of cecal contents and feces. It was also shown that therapeutic administration of BBG9-1 significantly increased the number of acidic mucin-positive goblet cells and the gene expression of mucosal protective factors including MUC2, MUC3, MUC4, TGFbeta1 and TFF3 in the small intestine. This led to alleviation of low gut permeability shown as decreased gene expression levels of occludin, claudin-1 and villin-1 after RV infection. Furthermore, in the small intestine, therapeutic administration of BBG9-1 significantly palliated the decreased gene expression of SGLT-1, which plays an important role in water absorption. In the large intestine, administered BBG9-1 was shown to replicate to assimilate undigested nutrients, resulting in normalization of the abnormally high osmotic pressure. These results suggested that water malabsorption caused by RV infection was alleviated in mice administered BBG9-1. Thus, the present study showed that oral administration of BBG9-1 palliated diarrhea partly through protection against RV-induced lesions by inducing mucosal protective factors. Oral administration of BBG9-1 is thought to be an efficient method for management of an RV epidemic for both prophylactic and therapeutic purposes.

Kelly, J. R., Allen, A. P., Temko, A., Hutch, W., Kennedy, P. J., Farid, N., Murphy, E., Boylan, G., Bienenstock, J., Cryan, J. F., Clarke, G., and Dinan, T. G. Lost in translation? The potential psychobiotic Lactobacillus rhamnosus (JB-1) fails to modulate stress or cognitive performance in healthy male subjects. Brain Behav.Immun. 2017; 61:50-59; PM: 27865949

ABSTRACT: BACKGROUND: Preclinical studies have identified certain probiotics as psychobiotics - live microorganisms with a potential mental health benefit. Lactobacillus rhamnosus (JB-1) has been shown to reduce stress-related behaviour, corticosterone release and alter central expression of GABA receptors in an anxious mouse strain. However, it is unclear if this single putative psychobiotic strain has psychotropic activity in humans. Consequently, we aimed to examine if these promising preclinical findings could be translated to healthy human volunteers. *OBJECTIVES*: To determine the impact of L. rhamnosus on stress-related behaviours, physiology, inflammatory response, cognitive performance and brain activity patterns in healthy male participants. *METHODS*: An 8 week, randomized, placebo-controlled, cross-over design was employed. Twenty-nine healthy male volunteers participated. Participants completed self-report stress measures, cognitive assessments and resting electroencephalography (EEG). Plasma IL10, IL1beta, IL6, IL8 and TNFalpha levels and whole blood Toll-like 4 (TLR-4) agonist-induced cytokine release were determined by multiplex ELISA. Salivary cortisol was determined by ELISA and subjective stress measures were assessed before, during and after a socially evaluated cold pressor test (SECPT). *RESULTS*: There was no overall effect of probiotic treatment on measures of mood, anxiety, stress or sleep quality and no significant effect of probiotic over placebo on subjective stress measures, or the HPA response to the SECPT. Visuospatial memory performance, attention switching, rapid visual information processing, emotion recognition and associated EEG measures did not show improvement over placebo. No significant anti-inflammatory effects were seen as

assessed by basal and stimulated cytokine levels. *CONCLUSIONS*: L. rhamnosus was not superior to placebo in modifying stress-related measures, HPA response, inflammation or cognitive performance in healthy male participants. These findings highlight the challenges associated with moving promising preclinical studies, conducted in an anxious mouse strain, to healthy human participants. Future interventional studies investigating the effect of this psychobiotic in populations with stress-related disorders are required.

Kepert, I., Fonseca, J., Muller, C., Milger, K., Hochwind, K., Kostric, M., Fedoseeva, M., Ohnmacht, C., Dehmel, S., Nathan, P., Bartel, S., Eickelberg, O., Schloter, M., Hartmann, A., Schmitt-Kopplin, P., and Krauss-Etschmann, S. D-tryptophan from probiotic bacteria influences the gut microbiome and allergic airway disease. J.Allergy Clin.Immunol. 2017; 139(5):1525-1535; PM: 27670239

ABSTRACT: BACKGROUND: Chronic immune diseases, such as asthma, are highly prevalent. Currently available pharmaceuticals improve symptoms but cannot cure the disease. This prompted demands for alternatives to pharmaceuticals, such as probiotics, for the prevention of allergic disease. However, clinical trials have produced inconsistent results. This is at least partly explained by the highly complex crosstalk among probiotic bacteria, the host's microbiota, and immune cells. The identification of a bioactive substance from probiotic bacteria could circumvent this difficulty. *OBJECTIVE*: We sought to identify and characterize a bioactive probiotic metabolite for potential prevention of allergic airway disease. *METHODS*: Probiotic supernatants were screened for their ability to concordantly decrease the constitutive CCL17 secretion of a human Hodgkin lymphoma cell line and prevent upregulation of costimulatory molecules of LPS-stimulated human dendritic cells. *RESULTS*: Supernatants from 13 of 37 tested probiotic strains showed immunoactivity. Bioassay-guided chromatographic fractionation of 2 supernatants according to polarity, followed by total ion chromatography and mass spectrometry, yielded C11H12N2O2 as the molecular formula of a bioactive substance. Proton nuclear magnetic resonance and enantiomeric separation identified D-tryptophan. In contrast, L-tryptophan and 11 other D-amino acids were inactive. Feeding D-tryptophan to mice before experimental asthma induction increased numbers of lung and gut regulatory T cells, decreased lung TH2 responses, and ameliorated allergic airway inflammation and hyperresponsiveness. Allergic airway inflammation reduced gut microbial diversity, which was increased by D-tryptophan. *CONCLUSIONS*: D-tryptophan is a newly identified product from probiotic bacteria. Our findings support the concept that defined bacterial products can be exploited in novel preventative strategies for chronic immune diseases.

Keung, H. Y., Li, T. K., Sham, L. T., Cheung, M. K., Cheung, P. C., and Kwan, H. S. Mechanistic Study of Utilization of Water-Insoluble Saccharomyces cerevisiae Glucans by Bifidobacterium breve Strain JCM1192. Appl.Environ.Microbiol. 4-1-2017; 83(7); PM: 28115383

ABSTRACT: Bifidobacteria exert beneficial effects on hosts and are extensively used as probiotics. However, due to the genetic inaccessibility of these bacteria, little is known about their mechanisms of carbohydrate utilization and regulation. Bifidobacterium breve strain JCM1192 can grow on water-insoluble yeast (Saccharomyces cerevisiae) cell wall glucans (YCWG), which were recently considered as potential prebiotics. According to the results of 1H nuclear magnetic resonance (NMR) spectrometry, the YCWG were composed of highly branched (1-->3,1-->6)-beta-glucans and (1-->4,1-->6)-

alpha-glucans. Although the YCWG were composed of 78.3% beta-glucans and 21.7% alpha-glucans, only alpha-glucans were consumed by the B. breve strain. The ABC transporter (malEFG1) and pullulanase (aapA) genes were transcriptionally upregulated in the metabolism of insoluble yeast glucans, suggesting their potential involvement in the process. A nonsense mutation identified in the gene encoding an ABC transporter ATP-binding protein (MalK) led to growth failure of an ethyl methanesulfonate-generated mutant with yeast glucans. Coculture of the wild-type strain and the mutant showed that this protein was responsible for the import of yeast glucans or their breakdown products, rather than the export of alpha-glucan-catabolizing enzymes. Further characterization of the carbohydrate utilization of the mutant and three of its revertants indicated that this mutation was pleiotropic: the mutant could not grow with maltose, glycogen, dextrin, raffinose, cellobiose, melibiose, or turanose. We propose that insoluble yeast alpha-glucans are hydrolyzed by extracellular pullulanase into maltose and/or maltooligosaccharides, which are then transported into the cell by the ABC transport system composed of MalEFG1 and MalK. The mechanism elucidated here will facilitate the development of B. breve and water-insoluble yeast glucans as novel synbiotics.IMPORTANCE In general, Bifidobacterium strains are genetically intractable. Coupling classic forward genetics with next-generation sequencing, here we identified an ABC transporter ATP-binding protein (MalK) responsible for the import of insoluble yeast glucan breakdown products by B. breve JCM1192. We demonstrated the pleiotropic effects of the ABC transporter ATP-binding protein in maltose/maltooligosaccharide, raffinose, cellobiose, melibiose, and turanose transport. With the addition of transcriptional analysis, we propose that insoluble yeast glucans are broken down by extracellular pullulanase into maltose and/or maltooligosaccharides, which are then transported into the cell by the ABC transport system composed of MalEFG1 and MalK. The mechanism elucidated here will facilitate the development of B. breve and water-insoluble yeast glucans as novel synbiotics.

Khalsa, J., Duffy, L. C., Riscuta, G., Starke-Reed, P., and Hubbard, V. S. Omics for Understanding the Gut-Liver-Microbiome Axis and Precision Medicine. Clin.Pharmacol.Drug Dev. 2017; 6(2):176-185; PM: 28263462

ABSTRACT: Human metabolic disease opens a new view to understanding the contribution of the intestinal microbiome to drug metabolism and drug-induced toxicity in gut-liver function. The gut microbiome, a key determinant of intestinal inflammation, also plays a direct role in chronic inflammation and liver disease. Gut bacterial communities directly metabolize certain drugs, reducing their bioavailability and influencing individual variation in drug response. In addition, some microbiome-produced compounds may affect drug pharmacokinetics and pharmacodynamics via altered expression of metabolizing enzymes and drug transporters or genes coding for drug target proteins, drug response phenotypes, and disease states. Molecular-based high-throughput technologies are providing novel insight about host-gut microbiome interactions, homeostasis, and xenobiotic effects associated with wide variation in efficacy or toxicity in humans. It is envisioned that future approaches to treating and preventing liver disease will benefit from in-depth studies of the liver-microbiome axis. Thus, the microbiome shares a fundamental role in human physiology with various organ systems, and its importance must be considered in the rapid evolution of precision medicine. A new emerging perspective of understanding the effect of the gut microbiome on human response to drugs would be indispensable for developing efficacious, safe, and cost-effective precision therapies.

Khatri, I., Tomar, R., Ganesan, K., Prasad, G. S., and Subramanian, S. Complete genome sequence and comparative genomics of the probiotic yeast Saccharomyces boulardii. Sci.Rep. 3-23-2017; 7(1):371; PM: 28336969

ABSTRACT: The probiotic yeast, Saccharomyces boulardii (Sb) is known to be effective against many gastrointestinal disorders and antibiotic-associated diarrhea. To understand molecular basis of probiotic-properties ascribed to Sb we determined the complete genomes of two strains of Sb i.e. Biocodex and unique28 and the draft genomes for three other Sb strains that are marketed as probiotics in India. We compared these genomes with 145 strains of S. cerevisiae (Sc) to understand genome-level similarities and differences between these yeasts. A distinctive feature of Sb from other Sc is absence of Ty elements Ty1, Ty3, Ty4 and associated LTR. However, we could identify complete Ty2 and Ty5 elements in Sb. The genes for hexose transporters HXT11 and HXT9, and asparagine-utilization are absent in all Sb strains. We find differences in repeat periods and copy numbers of repeats in flocculin genes that are likely related to the differential adhesion of Sb as compared to Sc. Core-proteome based taxonomy places Sb strains along with wine strains of Sc. We find the introgression of five genes from Z. bailii into the chromosome IV of Sb and wine strains of Sc. Intriguingly, genes involved in conferring known probiotic properties to Sb are conserved in most Sc strains.

Khavari-Daneshvar, H., Mosavi, M., Khodayari, H., Rahimi, E., Ranji, P., Mohseni, A. H., Mahmudian, R., Shidfar, F., Agah, S., and Alizadeh, A. M. Modifications of mice gut microflora following oral consumption ofLactobacillus acidophilus and Bifidobacterium bifidum probiotics. Turk.J.Med.Sci. 4-18-2017; 47(2):689-694; PM: 28425267

ABSTRACT: BACKGROUND/AIM: Thirty male BALB/c mice were equally divided into three groups: control, L. acidophilus, and B. bifidum for the assessment of the probiotics' stability in the gut microflora. *MATERIALS AND METHODS*: First, the gut microflora of the mice was checked every 3 days (days 3, 6, 9, and 12) without probiotic consumption, and then the mice were daily given orally 1.5 g of probiotics in 30 cc of drinking water. The consumption of probiotics was then stopped for recovery and then the consumption continued for 5 months. *RESULTS*: On day 9 after the consumption of the probiotics, L. acidophilus and B. bifidum were significantly increased from 4% to 83% and from 1% to 61%, respectively. L. acidophilus count showed no significant decrease at the end of 5 months compared to day 9 of probiotic consumption (74%), but B. bifidum count was dramatically decreased to 45% and 36% at the end of 1 and 5 months, respectively. *CONCLUSION*: Our results revealed that, unlike B. bifidum, the amount of L. acidophilus remained almost unchanged in the long term, indicating more stability of L. acidophilus than B. bifidum in the gut microflora.

Khorasani, A. C. and Shojaosadati, S. A. Pectin-non-starch nanofibers biocomposites as novel gastrointestinal-resistant prebiotics. Int.J.Biol.Macromol. 2017; 94(Pt A):131-144; PM: 27720960

ABSTRACT: Incorporation of nanofibers of chitin (NC), lignocellulose (NLC) and bacterial cellulose (BNC) in pectin was studied to improve prebiotic activity and gastrointestinal resistance of the pectin-nanofibers biocomposites for protection of probiotics under simulated gastrointestinal conditions. The biocomposites were prepared using various compositions of pectin and nanofibers, which were designed using D-optimal mixture

method. The incorporation of the nanofibers in pectin led to a slow degradation of the pectin-nanofibers biocomposites in contrast to their rapid swelling. AFM analysis indicated the homogenous distribution of interconnected nanofibers network structure in the pectin-nanofibers biocomposite. FTIR spectra demonstrated fabrication of the biocomposites based on the inter- and intra-molecular hydrogen bonding and ionic interaction of pectin-Ca2+. XRD patterns revealed the amorphous structures of the biocomposites as compared to the crystalline structures of the nanofibers. Among the compositions, the optimal compositions were as follows: 60% pectin+40% NC, 50% pectin+50% NLC and 60% pectin+40% BNC, where the prebiotic score, probiotic survival under simulated gastric and intestinal conditions were optimum. The optimal biocomposite pectin-NC exhibited the highest survival of the entrapped probiotic bacteria under simulated gastric (97.7%) and intestinal (95.8%) conditions when compared with the corresponding to free cells (76.2 and 73.4%).

Kim, J. S., Hosseindoust, A., Lee, S. H., Choi, Y. H., Kim, M. J., Lee, J. H., Kwon, I. K., and Chae, B. J. Bacteriophage cocktail and multi-strain probiotics in the feed for weanling pigs: effects on intestine morphology and targeted intestinal coliforms and Clostridium. Animal. 2017; 11(1):45-53; PM: 27353334

ABSTRACT: Two experiments were conducted to investigate the effects of dietary supplementation of bacteriophage cocktail, probiotics and a combination of these two supplements on performance and gut health of weanling pigs. In Experiment 1, 150 weaned piglets were randomly allotted to three treatments on the basis of BW. The dietary treatments included a basal diet supplemented with 0 (control), 1.0 and 1.5 g/kg bacteriophage cocktail. Pigs fed 1.0 and 1.5 g/kg bacteriophage product had greater ($P<0.05$) average daily gain (ADG), apparent total tract digestibility of dry matter from day 22 to 35, ileal Lactobacillus spp., villus height (duodenum and jejunum), and fewer coliforms (ileum) and Clostridium spp. (ileum). In Experiment 2, 200 weaned piglets were randomly allotted to four treatments. Dietary treatments included basal diet, basal diet supplemented with 3.0 g/kg fermented probiotic product (P), 1.0 g/kg bacteriophage cocktail (B) and combination of 1.0 g/kg bacteriophage cocktail and 3.0 g/kg fermented probiotic product. Pigs fed bacteriophage cocktail diets had greater ($P<0.05$) overall ADG, gain to feed ratio (G : F), fecal score from day 8 to day 21, and pigs fed bacteriophage cocktail diets had fewer coliforms (ileum) Clostridium spp. (ileum and cecum). Probiotics significantly increased G : F, colonization of Lactobacillus spp. in ileum. At day 35, bacteriophage treatment group showed greater ($P<0.05$) villus height of the duodenum, but a deeper crypt in duodenum. The present results indicate that the bacteriophage cocktail had a potential to enhance the performance and gut health of weanling pigs, however their combination with probiotics did not show an interaction.

Kim, J. Y., Awji, E. G., Park, N. H., Park, J. Y., Kim, J. C., Lee, S. P., Suh, J. W., and Park, S. C. Probiotic properties and adsorption of Enterococcus faecalis PSCT3-7 to vermiculite. J.Vet.Sci. 3-30-2017; 18(1):95-99; PM: 27456777

ABSTRACT: The probiotic properties of Enterococcus (E.) faecalis PSCT3-7, a new strain isolated from the intestines of pigs fed dietary fiber containing 50% sawdust, were investigated. E. faecalis PSCT3-7 tolerated a pH range of 3 to 8 and 0.3% bile salts, and it inhibited the growth of Salmonella Typhimurium in a concentration-dependent manner. In addition, E. faecalis showed resistance to several antibacterial agents. Vermiculite, a nutrient and microbial carrier, increased the bile tolerance of the strain. Scanning

electron microscope images revealed good adsorption of E. faecalis PSCT3-7 onto vermiculite. E. faecalis PSCT3-7 represents a potential probiotic candidate to administer with vermiculite to swine.

Kim, M., Kim, M., Kang, M., Yoo, H. J., Kim, M. S., Ahn, Y. T., Sim, J. H., Jee, S. H., and Lee, J. H. Effects of weight loss using supplementation with Lactobacillus strains on body fat and medium-chain acylcarnitines in overweight individuals. Food Funct. 1-25-2017; 8(1):250-261; PM: 28001147

ABSTRACT: Our previous study showed that supplementation with a combination of Lactobacillus curvatus (L. curvatus) HY7601 and Lactobacillus plantarum (L. plantarum) KY1032 reduced the body weight, body fat percentage, body fat mass and L1 subcutaneous fat area in overweight subjects. We aimed to evaluate whether the changes in adiposity after supplementation with Lactobacillus strains were associated with metabolic intermediates. A randomized, double-blind, placebo-controlled study was conducted on 66 non-diabetic and overweight individuals. Over a 12-week period, the probiotic group consumed 2 g of probiotic powder, whereas the placebo group consumed the same product without the probiotics. To investigate metabolic alterations, we performed plasma metabolomics using ultra-performance liquid chromatography and mass spectrometry (UPLC-LTQ/Orbitrap MS). Probiotic supplementation significantly increased the levels of octenoylcarnitine (C8:1), tetradecenoylcarnitine (C14:1), decanoylcarnitine (C10) and dodecenoylcarnitine (C12:1) compared with the levels from placebo supplementation. In the probiotic group, the changes in the body weight, body fat percentage, body fat mass and L1 subcutaneous fat area were negatively associated with changes in the levels of C8:1, C14:1, C10 and C12:1 acylcarnitines. In overweight individuals, probiotic-induced weight loss and adiposity reduction from the probiotic supplementation were associated with an increase in medium-chain acylcarnitines.

Kim, M. S., Byun, J. S., Yoon, Y. S., Yum, D. Y., Chung, M. J., and Lee, J. C. A probiotic combination attenuates experimental colitis through inhibition of innate cytokine production. Benef.Microbes. 4-26-2017; 8(2):231-241; PM: 28008786

ABSTRACT: Inflammatory bowel disease (IBD) is a severe immune cell-mediated syndrome characterised by extensive inflammatory and effector mucosal responses leading to tissue destruction in the colon and small intestine. The leading hypothesis is that dysbiosis of the gut flora causes an excessive immune response and inflammation in the gastrointestinal track. Lactic acid bacteria (LAB) can correct dysbiosis of the normal microbiota. In the current study, the therapeutic potential of seven LAB strains in combination to treat IBD was evaluated using experimental colitis model. This LAB cocktail, designated GI7, includes four strains of Lactobacillus acidophilus, Lactobacillus plantarum, Lactobacillus rhamnosus, Lactococcus lactis, two strains of Bifidobacterium bifidum, Bifidobacterium breve, and one strain of Streptococcus thermophilus. We confirmed that GI7 suppressed pro-inflammatory cytokines in Raw264.7 macrophages. When dextran sulphate sodium-induced colitic mice were treated with GI7, their symptoms of colitis, as assessed by body weight, colon length, myeloperoxidase activity, intestinal bleeding, and histological damage, were reduced compared to untreated mice. In addition, GI7 treatment significantly inhibited the production of innate pro-inflammatory cytokines during colitic progression. Therefore, we suggest that GI7, a combination of seven LAB, has a potential role in the treatment of IBD.

Kim, S. J., Park, S. H., Sin, H. S., Jang, S. H., Lee, S. W., Kim, S. Y., Kwon, B., Yu, K. Y., Kim, S. Y., and Yang, D. K. Hypocholesterolemic Effects of Probiotic Mixture on Diet-Induced Hypercholesterolemic Rats. Nutrients. 3-16-2017; 9(3); PM: 28300786

ABSTRACT: Growing evidence has indicated that supplementation with probiotics improves lipid metabolism. We aimed to investigate the beneficial effects of a probiotics mixture (PM) of three strains belonging to the species Bifidobacterium (B. longum, B. lactis, and B. breve) and two strains belonging to the species Lactobacillus (L. reuteri and L. plantarum) on cholesterol-lowering efficacy in hypercholesterolemic rats. A hypercholesterolemic rat model was established by feeding a high-cholesterol diet for eight weeks. To test the effects of PM on hypercholesterolemia, hypercholesterolemic rats were assigned to four groups, which were treated daily with low (1.65 x 10(8) cfu/kg), medium (5.5 x 10(8) cfu/kg), or high (1.65 x 1010 cfu/kg) doses of probiotic mixture or simvastatin for eight weeks. Significant reductions of serum total cholesterol (TC), triacylglycerol (TG), and low-density lipoprotein (LDL)-cholesterol levels, but increases of high-density lipoprotein (HDL)-cholesterol were observed after supplementation of PM in hypercholesterolemic rats. In PM-supplemented hypercholesterolemic rats, hepatic tissue contents of TC and TG also significantly decreased. Notably, the histological evaluation of liver tissues demonstrated that PM dramatically decreased lipid accumulation. For their underlying mechanisms, we demonstrated that PM reduced expressions of cholesterol synthesis-related proteins such as sterol regulatory element-binding protein 1 (SREBP1), fatty acid synthase (FAS), and acetyl-CoA carboxylase (ACC) in the liver. Taken together, these findings suggest that PM has beneficial effects against hypercholesterolemia. Accordingly, our PM might be utilized as a novel therapeutic agent for the management of hypercholesterolemia.

Kobayashi, R., Kobayashi, T., Sakai, F., Hosoya, T., Yamamoto, M., and Kurita-Ochiai, T. Oral administration of Lactobacillus gasseri SBT2055 is effective in preventing Porphyromonas gingivalis-accelerated periodontal disease. Sci.Rep. 4-3-2017; 7(1):545; PM: 28373699

ABSTRACT: Probiotics have been used to treat gastrointestinal disorders. However, the effect of orally intubated probiotics on oral disease remains unclear. We assessed the potential of oral administration of Lactobacillus gasseri SBT2055 (LG2055) for Porphyromonas gingivalis infection. LG2055 treatment significantly reduced alveolar bone loss, detachment and disorganization of the periodontal ligament, and bacterial colonization by subsequent P. gingivalis challenge. Furthermore, the expression and secretion of TNF-alpha and IL-6 in gingival tissue was significantly decreased in LG2055-administered mice after bacterial infection. Conversely, mouse beta-defensin-14 (mBD-14) mRNA and its peptide products were significantly increased in distant mucosal components as well as the intestinal tract to which LG2055 was introduced. Moreover, IL-1beta and TNF-alpha production from THP-1 monocytes stimulated with P. gingivalis antigen was significantly reduced by the addition of human beta-defensin-3. These results suggest that gastrically administered LG2055 can enhance immunoregulation followed by periodontitis prevention in oral mucosa via the gut immune system; i.e., the possibility of homing in innate immunity.

Kobyliak, N., Falalyeyeva, T., Bodnar, P., and Beregova, T. Probiotics Supplemented with Omega-3 Fatty Acids are More Effective for Hepatic Steatosis Reduction in an Animal Model of Obesity. Probiotics.Antimicrob.Proteins. 2017; 9(2):123-130; PM: 27660157

ABSTRACT: Today probiotics have been suggested as a treatment for the prevention of NAFLD. Omega-3 fatty acid supplementation may have beneficial effects in regulating hepatic lipid metabolism, adipose tissue function and inflammation. The present study was designed to determine whether probiotics plus omega-3 are superior to probiotics alone on the monosodium glutamate (MSG)-induced NAFLD model in rats. We included 60 rats divided into four groups, 15 animals in each. Rats of group I were intact. Newborn rats of groups II-IV were injected with MSG. The III (Symbiter) group received 2.5 ml/kg of multiprobiotic "Symbiter" containing concentrated biomass of 14 probiotic bacteria genera. The IV (Symbiter-Omega) groups received "Symbiter-Omega" combination of probiotic biomass supplemented with flax and wheat germ oil (250 mg of each, concentration of omega-3 fatty acids 1-5 %). In both interventional groups reduction in total NAS score was observed. Supplementation of alive probiotic mixture with omega-3 fatty acids lead to 20 % higher decrease in steatosis score (0.73 +/- 0.11 vs 0.93 +/- 0.22, p = 0.848) and reduction by 16.6 % of triglycerides content in liver as compared to probiotic alone. Our study demonstrated more pronounced reduction in hepatic steatosis and hepatic lipid accumulation after treatment with combination of alive probiotics and omega-3 as compared to probiotics alone.

Koekkoek, K. W. and van Zanten, A. R. Nutrition in the critically ill patient. Curr.Opin.Anaesthesiol. 2017; 30(2):178-185; PM: 28151828

ABSTRACT: PURPOSE OF REVIEW: To summarize recent relevant studies regarding nutrition during critical illness and provide recommendations for clinical practice. *RECENT FINDINGS*: Recently acquired knowledge regarding nutritional status and risk assessment, body composition, gastric residual volume, prokinetics, tube positioning, enteral vs parenteral nutrition, nutritional dose and timing of initiation, pharmaconutrition, dysbiosis and probiotics are discussed. *SUMMARY*: Body composition especially lean body mass is associated with clinical outcomes. The modified NUTrition Risk in the Critically ill score was validated for nutritional risk assessment and identifies patients that benefit from higher nutritional intake; however, caloric restriction decreases mortality in refeeding syndrome. Gastric residual volume monitoring is debated, as abandoning its application doesn't worsen outcome. There is no consensus regarding benefits of gastric vs postpyloric tube placement. Current prokinetics temporarily reduce feeding intolerance, new prokinetics are developed. Enteral remains preferable over parenteral nutrition, although no inferiority of parenteral nutrition is reported in recent studies. Studies imply no harm of hypocaloric feeding when protein requirements are met. Optimal protein provision may be more important than caloric adequacy. Pharmaconutrition confers no superior outcomes and may even confer harm. Dysbiosis is frequently encountered and associated with worse outcomes. Probiotics reduce infectious complications, but not mortality, and may contribute to earlier recovery of gut function.

Kolacek, S., Hojsak, I., Canani, R. B., Guarino, A., Indrio, F., Orel, R., Pot, B., Shamir, R., Szajewska, H., Vandenplas, Y., van, Goudoever J., and Weizman, Z. Commercial probiotic products: A call for improved quality control. A Position Paper by the ESPGHAN Working Group for Probiotics and Prebiotics. J.Pediatr.Gastroenterol.Nutr. 4-11-2017; PM: 28403036

ABSTRACT: Probiotics have been proposed for a number of indications ranging from the hypothetical long term immunomodulatory effects to proven benefits in the management of different clinical conditions.An increasing number of commercial

products containing probiotics are available. In those products, irrespective if it is food, food supplement, medical food or drug, the probiotic microorganisms have to be present in a sufficient number by the end of the shelf-life, to pass through the gastrointestinal tract resisting acid and bile, to colonize the gut, and to retain functional properties required to obtain the suggested beneficial effect. Finally it should be contamination free.Studies organized worldwide and summarized in this paper have shown that inconsistencies and deviations from the information provided on the product label are surprisingly common. Frequently strains are misidentified and misclassified, products are occasionally contaminated, sometimes with even facultative or obligatory pathogens, strains are not viable, the labelled number of colonies cannot be verified or the functional properties are diminished to the extent that preclude the proposed health benefit. As the probiotic preparations are commonly used for a wide range of conditions, the aim of the Working Group was to summarize results of the studies looking into the quality of the probiotic products and to raise the awareness of the important issue of their quality control.Based on the results obtained, we strongly suggest a more stringent quality control process. This process should ensure that the probiotic content as mentioned on the label meets the actual content throughout the shelf life of the product, while no contamination is present.

Kolodziej, M. and Szajewska, H. Lactobacillus reuteri DSM 17938 in the prevention of antibiotic-associated diarrhoea in children: protocol of a randomised controlled trial. BMJ Open. 1-5-2017; 7(1):e013928; PM: 28057659

ABSTRACT: INTRODUCTION: Administration of some probiotics appears to reduce the risk of antibiotic-associated diarrhoea (AAD). The effects of probiotics are strain-specific, thus, the efficacy and safety of each probiotic strain should be established separately. We aim to assess the effects of Lactobacillus reuteri DSM 17938 administration for the prevention of diarrhoea and AAD in children. *METHODS AND ANALYSIS*: A total of 250 children younger than 18 years treated with antibiotics will be enrolled in a double-blind, randomised, placebo-controlled trial in which they will additionally receive L. reuteri DSM 17938 at a dose 108 colony-forming units or an identically appearing placebo, orally, twice daily, for the entire duration of antibiotic treatment. The primary outcome measures will be the frequencies of diarrhoea and AAD. Diarrhoea will be defined according to 1 of 3 definitions: (1) >/=3 loose or watery stools per day for a minimum of 48 hours during antibiotic treatment; (2) >/=3 loose or watery stools per day for a minimum of 24 hours during antibiotic treatment; or (3) >/=2 loose or watery stools per day for a minimum of 24 hours during antibiotic treatment. AAD will be diagnosed in cases of diarrhoea, defined clinically as above, caused by Clostridium difficile or for otherwise unexplained diarrhoea (ie, negative laboratory stool tests for infectious agents). *ETHICS AND DISSEMINATION*: The Bioethics Committee approved the study protocol. The findings of this trial will be submitted to a peer-reviewed paediatric journal. Abstracts will be submitted to relevant national and international conferences. *TRIAL REGISTRATION NUMBER*: NCT02871908.

Komatsu, S., Yokoyama, Y., and Nagino, M. Gut microbiota and bacterial translocation in digestive surgery: the impact of probiotics. Langenbecks Arch.Surg. 2017; 402(3):401-416; PM: 28321508

ABSTRACT: PURPOSE: It is conceivable that manipulation of the gut microbiota could reduce the incidence or magnitude of surgical complications in digestive surgery.

However, the evidence remains inconclusive, although much effort has been devoted to randomized controlled trials (RCTs) and meta-analyses on probiotics. Furthermore, the mechanism behind the protective effects of probiotics appears elusive, our understanding of probiotic actions being fragmentary. The objective of this review is to assess the clinical relevance of the perioperative use of probiotics in major digestive surgery, based on a comprehensive view of the gut microbiota, bacterial translocation (BT), and host defense system. *METHODS*: The first part of this article describes the pathophysiological events associated with the gut microbiota. Results of RCTs for the perioperative use of probiotics in major digestive surgery are reviewed in the latter part. *RESULTS*: The development of the structural and functional barrier to protect against BT primarily results from the generally cooperative interactions between the host and resident microbiota. There is a large body of evidence indicating that probiotics, by enhancing beneficial interactions, reinforce the host defense system to limit BT. The perioperative use of probiotics in patients undergoing hepatobiliary and pancreatic surgery is a promising approach for the prevention of postoperative infectious complications, while the effectiveness in colorectal surgery remains controversial due to substantial heterogeneity among the RCTs with small sample populations. *CONCLUSIONS*: Further studies, such as multi-center RCTs with a larger sample size, are necessary to confirm the clinical relevance of probiotic agents in major digestive surgery.

Konturek, P. C., Haziri, D., Helfritzsch, H., Hess, T., and Harsch, I. A. Successful Therapy of Severe Pseudomembranous Clostridium difficile Colitis Using a Combination of Fecal Microbiota Therapy and Fidaxomicin. Med.Princ.Pract. 2017; 26(2):182-184; PM: 27978522

ABSTRACT: OBJECTIVE: The aim of this work was to describe the use of a combination of fidaxomicin and fecal microbiota therapy (FMT) in Clostridium difficile infection (CDI). *CLINICAL PRESENTATION AND INTERVENTION*: A 78-year-old female, who was admitted for surgery due to acute diverticulitis caused by postoperative complications and broad antibiotic therapy, developed CDI-induced colitis. Despite the introduction of metronidazole and vancomycin therapy, her clinical condition continued to deteriorate. She was transferred to the intensive care unit where FMT followed by fidaxomicin were performed because her C-reactive protein and leucocyte levels remained elevated. Further clinical improvement and the resolution of colitis was observed. *CONCLUSION*: In this case, severe CDI colitis was successfully treated with the combination of FMT and fidaxomicin.

Krezalek, M. A., Yeh, A., Alverdy, J. C., and Morowitz, M. Influence of nutrition therapy on the intestinal microbiome. Curr.Opin.Clin.Nutr.Metab Care. 2017; 20(2):131-137; PM: 27997410

ABSTRACT: PURPOSE OF REVIEW: This review describes the relationship between nutritional therapies and the intestinal microbiome of critically ill patients. *RECENT FINDINGS*: The intestinal microbiome of the critically ill displays a near complete loss of health-promoting microbiota with overgrowth of virulent healthcare-associated pathogens. Early enteral nutrition within 24 h of admission to the ICU has been advocated in medical and surgical patients to avoid derangements of the intestinal epithelium and the microbiome associated with starvation. Contrary to previous dogma, permissive enteral underfeeding has recently been shown to have similar outcomes to full feeding in the critically ill, whereas overfeeding has been shown to be deleterious in those patients who are not malnourished at baseline. Randomized clinical trials suggest that peripheral nutrition can be used safely either as the sole or supplemental source of nutrition even during the early

phases of critical care. The use of probiotics has been associated with a significant reduction in infectious complications in the critically ill without a notable mortality benefit. *SUMMARY*: Focus of research is shifting toward strategies that augment the intestinal environment to facilitate growth of beneficial microorganisms, strengthen colonization resistance, and maintain immune homeostasis.

Ku, H. J., Kim, Y. T., and Lee, J. H. Genomic Insights of Weissella jogaejeotgali FOL01T, Reveals Its Food Fermentation Ability and Human Gut Adaptive Potential for Probiotic Applications in Food Industries. J.Microbiol.Biotechnol. 3-9-2017; PM: 28274098

ABSTRACT: While the genus Leuconostoc has often been suggested to be a novel probiotic for food fermentation and health promotion, the strains in this genus showed low acid tolerance and low osmotic stress resistance activities. Recently, a novel species of Weissella, W. jogaejeotgali FOL01T (= KCCM 43128 = JCM 30580), was isolated from Korean fermented clams. Its genome was completely sequenced and analyzed, consisting of a 2.1-Mb circular chromosome and a 35.4-kb plasmid pFOL01. The genome analysis showed potential for use in food fermentation and osmotic stress resistance abilities for processing in food industries. In addition, this strain was predicted to have acid tolerance and adhesion to the mucosal layer for survival and colonization in the gut. Subsequent experiments substantiated these abilities, suggesting that W. jogaejeotgali may have probiotic potential and a high survival rate during food fermentation. Therefore, it may be suitable as a novel probiotic strain for various applications in food industries.

Kubasova, I., Strompfova, V., and Laukova, A. Safety assessment of commensal enterococci from dogs. Folia Microbiol.(Praha). 3-18-2017; PM: 28316009

ABSTRACT: Enterococci form a complex, diverse, and very important group of bacteria from the technological and food safety aspect, or from the health-improving aspect as probiotics. Generally, enterococci are considered to be of low pathogenic potential, which is associated mostly with clinical strains. In these strains, production of virulence factors as well as resistance to many antimicrobial drugs could complicate treatment of nosocomial infections. Because there is a lack of information on incidence of these attributes in animal commensal enterococci, we screened 160 strains originating from feces of clinically healthy dogs in Eastern Slovakia (n = 105). The predominant species were Enterococcus faecium (57.5%) followed by Enterococcus faecalis (21.9%), and Enterococcus hirae (17.5%), while Enterococcus casseliflavus (1.9%) and Enterococcus mundtii (1.2%) rarely occurred. Among the tested antibiotics, gentamicin (high level) was the most effective drug against canine enterococci (95% of isolates were sensitive). In contrast, the highest resistance recorded (71.9%) was to teicoplanin. PCR screening showed the highest incidence of virulence genes in E. faecalis species. The most frequently detected were genes encoding adhesins efa Afm and efa Afs and sex pheromone cpd. IS16 gene, a marker specific for hospital strains, appeared in nine E. faecium strains. No strain was positive for DNase activity, 8.8% of the isolated strains showed gelatinase activity, and almost 100% strains produced tyramine. It seems commensal-derived enterococci from dogs could also to some extent be potential reservoir of risk factors for other microbiota or organisms.

Kumar, J., Kumar, M., Pandey, R., and Chauhan, N. S. Physiopathology and Management of Gluten-Induced Celiac Disease. J.Food Sci. 2017; 82(2):270-277; PM: 28140462

ABSTRACT: Proline- and glutamine-rich gluten proteins are one of the major constituents of cereal dietary proteins, which are largely resistant to complete cleavage by the human gastrointestinal (GI) digestive enzymes. Partial digestion of gluten generates approximately 35 amino acids (aa) immunomodulatory peptides which activate T-cell-mediated immune system, followed by immunological inflammation of mucosa leading to the onset of celiac disease (CD). CD is an autoimmune disease associated with HLA-DQ2/DQ8 polymorphism and dysbiosis of gut microbiota. CD is either diagnosed using duodenal mucosal biopsis or serological testing for transglutaminase 2 (TG2) specific antibodies (IgA and IgG). Current therapy for CD management is gluten-free diet, while other therapies like glutenase, probiotics, immunomodulation, jamming of HLA-DQ2, inhibition of TG2, and gluten tolerance aided by gluten tolerizing vaccines are being developed.

Kumar, M., Kissoon-Singh, V., Coria, A. L., Moreau, F., and Chadee, K. Probiotic mixture VSL#3 reduces colonic inflammation and improves intestinal barrier function in Muc2 mucin-deficient mice. Am.J.Physiol Gastrointest.Liver Physiol. 1-1-2017; 312(1):G34-G45; PM: 27856417

ABSTRACT: MUC2 mucin is the major glycoprotein in colonic mucus that separates intestinal microbiota from underlying host cells and serves as a food source for some eubacteria. MUC2 deficiency results in impaired epithelial barrier function, imbalance in gut microbiota, and spontaneous colitis. Probiotics have been shown to have a protective effect against colitis. In this study we used Muc2 mucin-deficient (Muc2-/-) and Muc2+/+ littermates to test whether the probiotic mixture VSL#3 requires an intact mucin barrier to exert its beneficial effect. VSL#3 alone reduced basal colonic proinflammatory cytokine levels and improved epithelial barrier function in Muc2-/- animals. Similarly, in dextran sulfate sodium-induced colitis, VSL#3 dampened the proinflammatory chemokines KC, monocyte chemoattractant protein-1, and macrophage inflammatory protein-2 and upregulated the tissue regeneration growth factors transforming growth factor-beta, fibroblast growth factor-1, and vascular endothelial growth factor-A, which accelerated resolution of colitis symptoms in Muc2-/- animals. Importantly, improved colonic health in VSL#3-treated animals was associated with attenuated reactive oxygen species production by peritoneal macrophages, restoration of antimicrobial peptide gene expression in the small intestine, and increased abundance of bacterial commensals in the gut. The beneficial effects of VSL#3 in Muc2-/- animals were mediated by acetate, an important short-chain fatty acid produced by gut bacteria. These studies provide evidence for the first time that VSL#3 can enhance epithelial barrier function by dampening the proinflammatory cytokine and chemokine response, accelerating restitution, and altering commensal microbiota in the absence of a functional mucus barrier. NEW & NOTEWORTHY: It is unclear whether probiotics require an intact mucin barrier to first colonize and/or exert their protective functions. In this study we used mucin-deficient (Muc2-/-) mice to interrogate if the multispecies probiotic mixture VSL#3 could enhance epithelial barrier function. In the absence of a mucus bilayer, VSL#3 dampened proinflammatory and chemokine production, accelerated restitution, and markedly improved gut permeability mediated by the short-chain fatty acid acetate in the colon.

Kumar, N., Kumar, V., Panwar, R., and Ram, C. Efficacy of indigenous probiotic Lactobacillus strains to reduce cadmium bioaccessibility - An in vitro digestion model. Environ.Sci.Pollut.Res.Int. 2017; 24(2):1241-1250; PM: 27770327

ABSTRACT: The toxic heavy metal cadmium (Cd) appears as one of the major global threats to human and animal health. Human being and aquatic life are exposed to Cd by breathing, eating, or drinking when industrial effluents released into environment. The study was aimed to identify cadmium-binding Lactobacillus strain to reduce its bioaccessibility in in vitro digestion model. In this context, forty-eight lactobacilli strains isolated and characterized from fermented dairy products and human origin were screened for their Cd biosorption potential using Flame Atomic Absorption Spectroscopy (FAAS). The present study revealed that Cd biosorption potential of 48 lactobacilli strains ranged from 1.0832 +/- 0.012 to 3.562 +/- 0.03 mg Cd g-1 of cells from initial 10 mg L-1 cadmium chloride (CdCl2) aqueous solution. Lactobacillus plantarum strain HD 48 demonstrated highest biosorption of 3.562 +/- 0.03 mg Cd g-1 of cells. Lactobacilli-Cd complex stability indicated its strong stability as even after three washes with Milli-Q water metal desorption was nonsignificant ($p < 0.05$) and further studies to delineate the influence of Cd (100 mg L-1 CdCl2) on their growth. Moreover, these strains were able to reduce Cd bioaccessibility in the in vitro digestion model in the range of 24.71 to 41.62 %. Transmission electron microscopy (TEM) investigations on Cd bioadsorption also revealed its surface associated bioadsorption phenomenon. These findings depicted that probiotic strain L. plantarum HD 48 was found to be endowed with remarkable Cd biosorption ability as well as reduction in its bioaccessibility. These results suggest that probiotic strain L. plantarum HD 48 has immense potential to sequester Cd from aqueous solution which could be further explored as a potent source to diminish body Cd burden.

Kumar, P., Chatli, M. K., Verma, A. K., Mehta, N., Malav, O. P., Kumar, D., and Sharma, N. Quality, functionality, and shelf life of fermented meat and meat products: A review. Crit Rev.Food Sci.Nutr. 9-2-2017; 57(13):2844-2856; PM: 26463373

ABSTRACT: Fermentation of meat is a traditional preservation method used widely for improving quality and shelf life of fermented meat products. Fermentation of meat causes a number of physical, biochemical, and microbial changes, which eventually impart functional properties, sensory characteristics, and nutritional aspects to these products and inhibit the growth of various pathogenic and spoilage microorganisms. These changes include acidification (carbohydrate catabolism), solubilization and gelation of myofibrillar and sarcoplasmic proteins of muscle, degradation of proteins and lipids, reduction of nitrate into nitrite, formation of nitrosomyoglobin, and dehydration. Dry-fermented sausages are increasingly being used as carrier of probiotics. The production of biogenic amines during fermentation can be controlled by selecting proper starter cultures and other preventive measures such as quality of raw materials, hygienic measures, temperature, etc.

Kumar, R. and Dhanda, S. Mechanistic Insight of Probiotics Derived Anticancer Pharmaceuticals: A Road Forward for Cancer Therapeutics. Nutr.Cancer. 2017; 69(3):375-380; PM: 28107082

ABSTRACT: Probiotics are living organisms that confer health benefits when administered

in adequate amounts. Probiotics are continuously being explored for their different health beneficiary activities. Anticancer activity is one of the most important benefits both from a preventive and therapeutic point of view. Though not many studies have been conducted to date in this area, a number suggest using laboratory animal models and different cell lines that there may be a mechanistic basis for the anticancer effects of probiotics and require more scientific justification and clinical trials. Most studies of probiotics are conducted for colon cancer associated with inflammatory bowel disease. Studies are also being extended to other types of cancer in different cell lines. This review summarizes studied probiotics considered for treatment of colon cancer and some other cancers (in cancer cell lines) and also proposed mechanism how probiotics are inhibiting cancer growth along with some challenges and future perspectives.

Kumar, S., Pattanaik, A. K., Sharma, S., Jadhav, S. E., Dutta, N., and Kumar, A. Probiotic Potential of a Lactobacillus Bacterium of Canine Faecal-Origin and Its Impact on Select Gut Health Indices and Immune Response of Dogs. Probiotics.Antimicrob.Proteins. 2-10-2017; PM: 28188477

ABSTRACT: The objective of the present study was to develop a probiotic of canine-origin for its potential application in pet nutrition. Accordingly, 32 lactic acid bacteria (LAB) strains were isolated from faeces of dogs, out of which 9 strains were short-listed for further in vitro testing based on the aggregation time and cell surface hydrophobicity. The results of acid-, bile- and phenol-tolerance tests indicated that out of the nine, isolate cPRO23 was having better resistance to these adverse conditions likely to be encountered in the gastrointestinal tract. The isolate also showed optimal enzymatic activities for amylase, lipase and protease. Further assessments also indicated its superiority in terms of co-aggregation and antagonistic activity against pathogenic strains of Salmonella typhimurium and Salmonella enteritidis. Subsequently, the isolate was identified through 16S rRNA sequencing and sequence homology, and designated as Lactobacillus johnsonii CPN23. The candidate probiotic was then evaluated in vivo using 15 adult Labrador dogs, divided into 3 groups, viz. CON (with no probiotics), dPRO (with Lactobacillus acidophilus NCDC 15 as a conventional dairy-origin probiotic) and cPRO (with L. johnsonii CPN23 as a canine-origin probiotic). Results of the 9-week study indicated that supplementation of cPRO improved ($P < 0.05$) the faecal concentration of acetate and butyrate with a concomitant reduction ($P < 0.05$) in faecal ammonia. The cell-mediated immune response, assessed as delayed-type hypersensitivity reaction to phytohaemagglutinin-P, was better ($P < 0.05$) in dogs fed cPRO as compared to the CON dogs. There were, however, no variations evident in the antibody response to sheep-erythrocytes among the three groups. It is concluded that the canine-origin L. johnsonii CPN23, in addition to possessing all the in vitro functional attributes of a candidate probiotic, also has the potential to be used as a probiotic in pet nutrition programs.

Kumar, V., Yadav, A. N., Verma, P., Sangwan, P., Saxena, A., Kumar, K., and Singh, B. beta-Propeller phytases: Diversity, catalytic attributes, current developments and potential biotechnological applications. Int.J.Biol.Macromol. 2017; 98:595-609; PM: 28174082

ABSTRACT: Phytases are phosphatases which stepwise remove phosphates from phytic acid or its salts. beta-Propeller phytase (BPPhy) belongs to a special class of microbial phytases that is regarded as most diverse, isolated and characterized from different microbes, mainly from Bacillus spp. BPPhy class is unique for its Ca2+-dependent catalytic

activity, strict substrate specificity, active at neutral to alkaline pH and high thermostability. Numerous sequence and structure based studies have revealed unique attributes and catalytic properties of this class, as compared to other classes of phytases. Recent studies including cloning and expression and genetic engineering approaches have led to improvements in BPPhy which provide an opportunity for extended utilization of this class of phytases in improving animal nutrition, human health, plant growth promotion, and environmental protection, etc. This review describes the sources and diversity of BPPhy genes, biochemical properties, Ca2+ dependence, current developments in structural elucidation, heterogeneous expression and catalytic improvements, and multifarious applications of BPPhy.

Kvasnovsky, C. L., Bjarnason, I., Donaldson, A. N., Sherwood, R. A., and Papagrigoriadis, S. A randomized double-blind placebo-controlled trial of a multi-strain probiotic in treatment of symptomatic uncomplicated diverticular disease. Inflammopharmacology. 5-20-2017; PM: 28528364

ABSTRACT: BACKGROUND: Diverticular disease is a significant burden on healthcare systems that is managed, surgically or medically, mainly as an emergency or acute condition. There are no standardized treatment recommendations for symptomatic uncomplicated disease. We hypothesized that a probiotic would reduce abdominal pain in such patients. *METHODS*: We conducted a single-center, double-blind, placebo-controlled trial of probiotic treatment (Symprove) in adult patients with moderate-to-severe chronic, non-acute symptomatic diverticular disease. 143 patients were randomized to receive 1 mL/kg/day of probiotic liquid (N = 72) or placebo (N = 71) daily for 3 months. The primary endpoint was abdominal pain severity. Secondary endpoints consisted of the change in the frequency of eight abdominal symptoms and the level of intestinal inflammation (fecal calprotectin). *RESULTS*: 120 patients completed the trial. Abdominal pain score, the primary end point, decreased in both groups, but no significant difference between the groups was found (P = 0.11). In relation to placebo, the probiotic significantly decreased the frequency of four of the eight secondary endpoints: constipation, diarrhea, mucorrhea, and back pain (P < 0.04). No significant differences were found in frequency of abdominal pain, PR bleeding, dysuria, and bloating. *CONCLUSIONS*: Multi-strain liquid probiotic did not improve abdominal pain scores significantly, but significantly improved the frequency of four other symptoms associated with chronic, non-acute symptomatic diverticular disease.

Lan, R., Koo, J., and Kim, I. Effects of Lactobacillus acidophilus supplementation on growth performance, nutrient digestibility, fecal microbial and noxious gas emission in weaning pigs. J.Sci.Food Agric. 2017; 97(4):1310-1315; PM: 27342084

ABSTRACT: BACKGROUND: Antibiotics used as growth promoters in livestock have been banned in the European Union since 2006. Antibiotics alternatives have focused on probiotics, such as Lactobacillus acidophilus. The concentration of L. acidophilus is considered crucial for obtaining the desired effects. However, limited studies have been conducted to test the dose-dependent effects of L. acidophilus. Therefore, the present study aimed to test the dose-dependent effects of L. acidophilus on growth performance, nutrient digestibility, fecal microbial flora and fecal noxious gas emission in weaning pigs. *RESULTS*: Lactobacillus acidophilus supplementation increased (P < 0.05) average daily gain, average daily feed intake, apparent nutrient digestibility of dry matter, nitrogen and gross energy, and Lactobacillus counts compared to the basal diet treatment, and a linear effect (P < 0.05) was observed on those criteria. Escherichia coli

counts and NH3 emission were decreased (P < 0.05) by L. acidophilus supplementation, and a linear effect (P < 0.05) was observed on E. coli counts. *CONCLUSION*: These results suggest that L. acidophilus could be used as an antibiotic alternative by improving growth performance, nutrient digestibility and gut balance (i.e. increased Lactobacillus counts and decreased E. coli counts), and decreasing NH3 emission, of weaning pigs. (c) 2016 Society of Chemical Industry.

Lan, R., Tran, H., and Kim, I. Effects of probiotic supplementation in different nutrient density diets on growth performance, nutrient digestibility, blood profiles, fecal microflora and noxious gas emission in weaning pig. J.Sci.Food Agric. 2017; 97(4):1335-1341; PM: 27342952

ABSTRACT: BACKGROUND: Probiotics can serve as alternatives to antibiotics to increase the performance of weaning pigs, and the intake of probiotics is affected by dietary nutrient density. The objective of this study was to evaluate the effects of a probiotic complex in different nutrient density diets on growth performance, digestibility, blood profiles, fecal microflora and noxious gas emission in weaning pigs. *RESULTS*: From day 22 to day 42, both high-nutrient-density and probiotic complex supplementation diets increased (P < 0.05) the average daily gain. On day 42, the apparent total tract digestibility (ATTD) of dry matter, nitrogen and gross energy (GE), blood urea nitrogen concentration and NH3 and H2 S emissions were increased (P < 0.05) in pigs fed high-nutrient-density diets. Pigs fed probiotic complex supplementation diets had higher (P < 0.05) ATTD of GE than pigs fed non-supplemented diets. Fecal Lactobacillus counts were increased whereas Escherichia coli counts and NH3 and H2 S emissions were decreased (P < 0.05) in pigs fed probiotic complex supplementation diets. Interactive effects on average daily feed intake (ADFI) were observed from day 22 to day 42 and overall, where probiotic complex improved ADFI more dramatically in low-nutrient-density diets. *CONCLUSION*: The beneficial effects of probiotic complex (Bacillus coagulans, Bacillus licheniformis, Bacillus subtilis and Clostridium butyricum) supplementation on ADFI is more dramatic with low-nutrient-density diets. (c) 2016 Society of Chemical Industry.

Lan, R. X. and Kim, I. H. Effects of dietary supplementation with a probiotic (Enterococcus faecium DSM 7134) on growth performance, nutrient digestibility, and gut health status in weaning pigs. J.Sci.Food Agric. 4-12-2017; PM: 28403547

ABSTRACT: BACKGROUND: Probiotics have been suggested as desirable antibiotic alternatives to pigs by improving gut health and growth performance. However, limited studies of the effectiveness of E. faecium in weaning pigs, the objective of this study was to investigate the effects of E. faecium DSM 7134 supplementation on growth performance, nutrient digestibility, antioxidant parameters, volatile fatty acids concentration, intestinal histomorphology, and diarrhea score in weaning pig. *RESULTS*: E. faecium supplementation linear increased (P<0.05) average daily gain, gain:feed, apparent total tract digestibility of nitrogen and energy, superoxide dismutase, glutathione peroxidase, glutathione, acetic acid, propionic acid, and butyrate acid concentration, villus height, and fecal Lactobacillus counts. Malonadialdehyde concentration, crypt depth, fecal E.coli counts, and diarrhea score were linear decreased (P<0.05) by E. faecium supplementation. *CONCLUSION*: Dietary supplementation of E. faecium DSM 7134 improved growth performance, VFAs concentration, the maturation of intestinal structure by increasing villus height and decreasing crypt depth, alleviated antioxidant status by increasing superoxide dismutase, glutathione peroxidase, and glutathione, as well as decreasing

malonadialdehyde concentration, shifted microbiota by increasing fecal Lactobacillus and decreasing E.coli counts, as well as decreased diarrhea score in weaning pigs.

Landete, J. M. A review of food-grade vectors in lactic acid bacteria: from the laboratory to their application. Crit Rev.Biotechnol. 2017; 37(3):296-308; PM: 26918754

ABSTRACT: Lactic acid bacteria (LAB) have a long history of use in fermented foods and as probiotics. Genetic manipulation of these microorganisms has great potential for new applications in food safety, as well as in the development of improved food products and in health. While genetic engineering of LAB could have a major positive impact on the food and pharmaceutical industries, progress could be prevented by legal issues related to the controversy surrounding this technology. The safe use of genetically modified LAB requires the development of food-grade cloning systems containing only the DNA from homologous hosts or generally considered as safe organisms, and not dependent antibiotic markers. The rationale for the development of cloning vectors derived from cryptic LAB plasmids is the need for new genetic engineering tools, therefore a vision from cryptic plasmids to applications in food-grade vectors for LAB plasmids is shown in this review. Replicative and integrative vectors for the construction of food-grade vectors, and the relationship between resistance mechanism and expression systems, will be treated in depth in this paper. Finally, we will discuss the limited use of these vectors, and the problems arising from their use.

Larussa, T., Imeneo, M., and Luzza, F. Potential role of nutraceutical compounds in inflammatory bowel disease. World J.Gastroenterol. 4-14-2017; 23(14):2483-2492; PM: 28465632

ABSTRACT: Conventional therapies for inflammatory bowel diseases (IBD) involve combinations of pharmacologic agents such as aminosalicylates, azathioprine, and corticosteroids. Recently, the therapeutic scenario has been heavily increased by the introduction of agents including monoclonal antibodies targeted to specific proinflammatory cytokines, to adhesion molecules, and the induction of anti-inflammatory cytokines and T-cell activation. However, the use of these drugs is accompanied by a certain number of side effects, with some of them being quite severe, rising concerns about the safety profile. Furthermore, the cost of these emerging therapeutic strategies is significant , considering the increasing incidence and the chronic trend of IBD. Nutraceuticals is a broad term used to describe any product derived from food sources claiming extra health benefits beyond the intrinsic nutritional value found in foods. The beneficial effects of nutraceutical compounds in human health have been emerging in the last decades. Although few clinical trials have been performed in IBD patients, nutraceuticals, such as herbal products or vitamins, are generally accepted as safer alternative/supplementation to conventional therapy. In vitro and IBD-animal models studies have shown their involvement in several biological processes, including antioxidant defenses, cell proliferation, gene expression, which could account for a role in the maintenance of the mucosal barrier integrity, the control of the inflammatory pathways and the modulation of the immune response. These data suggest a wide spectrum of positive effects exerted by nutraceuticals, with a high potential for a therapeutic use in humans. In the present review, the beneficial effects of the most investigated nutraceutical compounds in the setting of human IBD are discussed.

Latalova, K., Hajda, M., and Prasko, J. Can gut microbes play a role in mental disorders and their treatment? Psychiatr.Danub. 2017; 29(1):28-30; PM: 28291971

ABSTRACT: The gut microbes, collectively called microbiota, are linked to the brain through a bidirectional system that involves the vagus nerve, the immune system, and various neurotransmitters. Stress response, memory functions, social behavior, and mood are modulated by microbiota. Furthermore, microbiota play a role in the development of the central nervous system. These features, established largely in rodent studies, have informed hypotheses about the role of microbiota in human psychiatric disorders. Microbiota affect phenomena that are known to be parts of the depression phenotype, such as exaggerated response to stress and inflammatory features. Furthermore, the role of microbiota in neurodevelopment and in the modulation of social behavior suggests the possibility of its role in autism spectrum disorder and in schizophrenia. If altered, microbiota play a role in psychiatric disorders, then efforts to normalize the gut microbial population by the ingestion of probiotics (live bacteria) could have antidepresssant or antipsychotic effects. Testing such hypotheses in translational human studies is a matter of future research.

Latha, S., Sivaranjani, G., and Dhanasekaran, D. Response surface methodology: A non-conventional statistical tool to maximize the throughput of Streptomyces species biomass and their bioactive metabolites. Crit Rev.Microbiol. 1-27-2017; 1-16; PM: 28129718

ABSTRACT: Among diverse actinobacteria, Streptomyces is a renowned ongoing source for the production of a large number of secondary metabolites, furnishing immeasurable pharmacological and biological activities. Hence, to meet the demand of new lead compounds for human and animal use, research is constantly targeting the bioprospecting of Streptomyces. Optimization of media components and physicochemical parameters is a plausible approach for the exploration of intensified production of novel as well as existing bioactive metabolites from various microbes, which is usually achieved by a range of classical techniques including one factor at a time (OFAT). However, the major drawbacks of conventional optimization methods have directed the use of statistical optimization approaches in fermentation process development. Response surface methodology (RSM) is one of the empirical techniques extensively used for modeling, optimization and analysis of fermentation processes. To date, several researchers have implemented RSM in different bioprocess optimization accountable for the production of assorted natural substances from Streptomyces in which the results are very promising. This review summarizes some of the recent RSM adopted studies for the enhanced production of antibiotics, enzymes and probiotics using Streptomyces with the intention to highlight the significance of Streptomyces as well as RSM to the research community and industries.

Le, D. H. 4th Microbiome R&D and Business Collaboration Forum, and Probiotics Congress, April 3-4, 2017, Amsterdam, The Netherlands. EBioMedicine. 4-13-2017; PM: 28427947

No Results Available.

Leclercq, S., de, Timary P., Delzenne, N. M., and Starkel, P. The link between inflammation, bugs, the intestine and the brain in alcohol dependence. Transl.Psychiatry. 2-28-2017; 7(2):e1048; PM: 28244981

ABSTRACT: In recent years, some new processes have been proposed to explain how alcohol may influence behavior, psychological symptoms and alcohol seeking in alcohol-dependent subjects. In addition to its important effect on brain and neurotransmitters equilibrium, alcohol abuse also affects peripheral organs including the gut. By yet incompletely understood mechanisms, chronic alcohol abuse increases intestinal permeability and alters the composition of the gut microbiota, allowing bacterial components from the gut lumen to reach the systemic circulation. These gut-derived bacterial products are recognized by immune cells circulating in the blood or residing in target organs, which consequently synthesize and release pro-inflammatory cytokines. Circulating cytokines are considered important mediators of the gut-brain communication, as they can reach the central nervous system and induce neuroinflammation that is associated with change in mood, cognition and drinking behavior. These observations support the possibility that targeting the gut microbiota, by the use of probiotics or prebiotics, could restore the gut barrier function, reduce systemic inflammation and may have beneficial effect in treating alcohol dependence and in reducing alcohol relapse.

Lee, C. Y., Shih, H. C., Yu, M. C., Lee, M. Y., Chang, Y. L., Lai, Y. Y., Lee, Y. C., Kuan, Y. H., and Lin, C. C. Evaluation of the potential inhibitory activity of a combination of L. acidophilus, L. rhamnosus and L. sporogenes on Helicobacter pylori: A randomized double-blind placebo-controlled clinical trial. Chin J.Integr.Med. 2017; 23(3):176-182; PM: 27761791

ABSTRACT: *OBJECTIVES*: To investigate whether three strains of probiotics, L. acidophilus, L. rhamnosus, and L. sporogenes, had signifificant inhibitive effects on Helicobacter pylori (H. pylori). *METHODS*: This is a 4-week, randomly assigned, parallel-group, doubled-blind, and placebo-controlled study. Fifty patients with a positive H. pylori infection urea breath test (big up tri, openUBT) result > 10% and without ulcer symptoms were randomized into a treatment group and a placebo group by a computer generated allocation sheet with 1:1. These subjects took one capsule of probiotics or placebo twice daily. The primary measurement was the change in big up tri, openUBT values. *RESULTS*: The big up tri, openUBT values during the 4-week treatment period and the 2-week follow-up period were not signifificantly different between the treatment group and the placebo group, indicating that the inhibitive effects on H. pylori were comparable between both groups. The monocyte count (%) was 5.77+/-1.11 in the treatment group versus 5.09+/-1.12 in the placebo group (P=0.044), and the basophile count was 0.55+/-0.32 in the treatment group versus 0.36+/-0.23 in the placebo group (P=0.024) at week 2 of the treatment period, both of which reached statistical signifificance. The monocyte count was 5.75+/-1.26 in the treatment group and 4.72+/-0.99 in the placebo group at the end of the follow-up period (P=0.003). *CONCLUSION*: There was no signifificant inhibitive effects of the three probiotic strains (L. acidophilus, L. rhamnosus, and L. sporogenes) on H. pylori. Probiotics can not play the same role as antibiotics in the eradication of H. pylori, the role of probiotics is likely to be important as adjuvant to the triple or quadruple therapy for H. pylori, especially in resistance cases.

Lee, H. J., Choi, J. K., Ryu, H. S., Choi, C. H., Kang, E. H., Park, K. S., Min, Y. W., and Hong, K. S. Therapeutic Modulation of Gut Microbiota in Functional Bowel Disorders. J.Neurogastroenterol.Motil. 1-30-2017; 23(1):9-19; PM: 28049862

ABSTRACT: Functional bowel disorders (FBDs) are functional gastrointestinal disorders with

symptoms attributable to the middle or lower gastrointestinal tract. These include irritable bowel syndrome, functional bloating, functional constipation, functional diarrhea, and unspecified FBD. Increasing evidence has emerged of late that intestinal microbiota is involved in the pathogenesis of FBDs. In this review, the therapeutic benefits and future perspectives of the currently available strategies for modifying the gut microbiota in FBDs are described, focusing primarily on irritable bowel syndrome and functional constipation.

Lee, J. Y., Han, G. G., Choi, J., Jin, G. D., Kang, S. K., Chae, B. J., Kim, E. B., and Choi, Y. J. Pan-Genomic Approaches in Lactobacillus reuteri as a Porcine Probiotic: Investigation of Host Adaptation and Antipathogenic Activity. Microb.Ecol. 4-24-2017; PM: 28439658

ABSTRACT: After the introduction of a ban on the use of antibiotic growth promoters (AGPs) for livestock, reuterin-producing Lactobacillus reuteri is getting attention as an alternative to AGPs. In this study, we investigated genetic features of L. reuteri associated with host specificity and antipathogenic effect. We isolated 104 L. reuteri strains from porcine feces, and 16 strains, composed of eight strains exhibiting the higher antipathogenic effect (group HS) and eight strains exhibiting the lower effect (group LS), were selected for genomic comparison. We generated draft genomes of the 16 isolates and investigated their pan-genome together with the 26 National Center for Biotechnology Information-registered genomes. L. reuteri genomes organized six clades with multi-locus sequence analysis, and the clade IV includes the 16 isolates. First, we identified six L. reuteri clade IV-specific genes including three hypothetical protein-coding genes. The three annotated genes encode transposases and cell surface proteins, indicating that these genes are the result of adaptation to the host gastrointestinal epithelia and that these host-specific traits were acquired by horizontal gene transfer. We also identified differences between groups HS and LS in the pdu-cbi-cob-hem gene cluster, which is essential for reuterin and cobalamin synthesis, and six genes specific to group HS are revealed. While the strains of group HS possessed all genes of this cluster, LS strains have lost many genes of the cluster. This study provides a deeper understanding of the relationship between probiotic properties and genomic features of L. reuteri.

Lee, S., Katya, K., Park, Y., Won, S., Seong, M., Hamidoghli, A., and Bai, S. C. Comparative evaluation of dietary probiotics Bacillus subtilis WB60 and Lactobacillus plantarum KCTC3928 on the growth performance, immunological parameters, gut morphology and disease resistance in Japanese eel, Anguilla japonica. Fish.Shellfish.Immunol. 2017; 61:201-210; PM: 28034835

ABSTRACT: The current experiment was conducted to evaluate and compare the efficacy of two different probiotics Bacillus subtilis WB60 and Lactobacillus plantarum KCTC3928 in diet of Japanese eel, Anguilla japonica. Seven experimental diets were formulated to contain no probiotics (CON), three graded levels of B. subtilis at 106 (BS1), 107 (BS2), 108 (BS3) and L. plantarum at 106 (LP1), 107 (LP2), 108 (LP3) CFU/g diet. Twenty fish averaging 8.29 +/- 0.06 g were distributed in to 21 aquaria and were randomly assigned to one of the experimental diets in triplicate groups. Average weight gain (WG), feed efficiency (FE), and protein efficiency ratio (PER) of fish fed B. subtilis at 107 (BS2) and 108 (BS3) CFU/g diet were significantly higher than those of fish fed other experimental diets ($P < 0.05$). Nonspecific enzymatic activities including lysozyme, superoxide dismutase (SOD), myeloperoxidase (MPO) from fish fed B. subtilis at 107 (BS2)

and 108 (BS3) CFU/g diet were detected to be significantly higher than that from fish fed CON diet ($P < 0.05$). Whereas, level of intestine glyceraldehyde-3-phosphate dehydrogenase (GAPDH), heat shock protein 70, 90 (HSP70, 90) and immunoglobulin (IgM) from fish fed B. subtilis at 107 and 108 CFU/g diet were recorded to be significantly higher than those of fish fed other experimental diets ($P < 0.05$). Parameters for intestinal morphology and histology suggested a healthier gut for the fish fed108 (BS3) CFU/g diet as compared to other treatment groups. Whereas, results from the disease challenge test with bacteria Vibrio angulillarum showed significantly lower survival rate for fish fed CON diet than those of fish fed other experimental diets. Therefore, these results indicated that oral supplement of B. subtilis at 108 (BS3) CFU/g diet could be a more effective source of probiotic compared to L. plantarum in Japanese eel.

Lehri, B., Seddon, A. M., and Karlyshev, A. V. Potential probiotic-associated traits revealed from completed high quality genome sequence of Lactobacillus fermentum 3872. Stand.Genomic.Sci. 2017; 12:19; PM: 28163828

ABSTRACT: The article provides an overview of the genomic features of Lactobacillus fermentum strain 3872. The genomic sequence reported here is one of three L. fermentum genome sequences completed to date. Comparative genomic analysis allowed the identification of genes that may be contributing to enhanced probiotic properties of this strain. In particular, the genes encoding putative mucus binding proteins, collagen-binding proteins, class III bacteriocin, as well as exopolysaccharide and prophage-related genes were identified. Genes related to bacterial aggregation and survival under harsh conditions in the gastrointestinal tract, along with the genes required for vitamin production were also found.

Li, Bassi G., Senussi, T., and Aguilera, Xiol E. Prevention of ventilator-associated pneumonia. Curr.Opin.Infect.Dis. 2017; 30(2):214-220; PM: 28118221

ABSTRACT: PURPOSE OF REVIEW: Ventilator-associated pneumonia (VAP) is an iatrogenic disease. Here we appraise recent advancements in the development and testing of strategies to prevent VAP. We also provide recommendations on the most promising interventions that should be applied. *RECENT FINDINGS*: In the last year, preventive bundles have consistently let to a reduction of VAP. A few trials on endotracheal tubes (ETTs) with novel cuffs failed to translate positive bench findings into clinical settings. In addition, meta-analyses confirmed the primary role of subglottic secretion aspiration in VAP prevention. A relatively new ETT, with an innovative cuff design, has been tested in clinical trials confirming potential value. Meta-analyses confirmed reduction of VAP with the use of chlorhexidine for oropharyngeal decontamination. However, prophylactic inhaled or oral antibiotics are ineffective. Finally, there is growing interest in orally ingested probiotics to prevent VAP. The results of ongoing studies on probiotics are much-awaited. *SUMMARY*: In conclusion, in the past year, new evidence elucidated limitations of new ETT cuffs in the prevention of VAP; whereas, subglottic secretion aspiration proved consistent benefits. Modulation of oropharyngeal colonization with chlorhexidine decreases risks of VAP and should be widely implemented. Finally, preventive measures with proven preventive value should be grouped into bundles.

Li, N., Tian, H., Ma, C., Ding, C., Ge, X., Gu, L., Zhang, X., Yang, B., Hua, Y., Zhu, Y., and Zhou, Y. [Efficacy analysis of fecal microbiota transplantation in the treatment of 406 cases with

gastrointestinal disorders]. Zhonghua Wei Chang Wai Ke.Za Zhi. 1-25-2017; 20(1):40-46; PM: 28105618

ABSTRACT: OBJECTIVE: To evaluate the efficacy and safety of fecal microbiota transplantation (FMT) for gastrointestinal disorders. *METHODS*: Retrospective analysis of the clinical data of 406 patients who underwent FMT from May 2014 to April 2016 in the Intestinal Microenvironment Treatment Centre of Nanjing General Hospital was performed, including patients with constipation (276 cases), recurrent Clostridium Difficile infection (RCDI, 61 cases), ulcerative colitis(44 cases), irritable bowel syndrome (15 cases) and Crohn's disease(10 cases). Donors were completely unrelated, 18- to 50-year-old non-pregnant healthy adult, with healthy lifestyle and habits, without taking antibiotics, probiotics and other probiotics history within 3 months. There were three routes of FMT administration: patients received 6 days of frozen FMT by nasointestinal tube placed in the proximal jejunum under gastroscope (319 cases); patients received capsules FMT per day for 6 consecutive days (46 cases) or once 600 ml of treated fecal liquid infusion into colon and terminal ileum by colonoscopy(41 cases). *RESULTS*: Clinical cure rate and improvement rate of different diseases receiving FMT were respectively as follows: RCDI was 85.2% (52/61) and 95.1%(58/61); constipation was 40.2%(111/276) and 67.4%(186/276); ulcerative colitis was 34.1%(15/44) and 68.2% (30/44); irritable bowel syndrome was 46.7% (7/15) and 73.3% (11/15) and Crohn disease was 30.0%(3/10) and 60.0%(6/10). RCDI had the best efficacy among these diseases($P<0.01$). There was no significant difference between the three routes of FMT administration($P=0.829$). The clinical cure rate and improvement rate of different routes were 43.3%(138/319) and 58.6% (187/319) respectively in nasogastric transplantation group, 41.5%(17/41) and 61.0%(25/41) in colonoscopy group, 37.0%(17/46) and 63.0% (29/46) in the capsule transplantation group. There was no serious adverse event during the follow-up. The most common side effects were respiratory discomfort (27.3%, 87/319) and increased venting (51.7%, 165/319) in nasogastric transplantation group. Diarrhea was the most common complication in colonoscopy group (36.6%, 15/41). The main symptoms were increased venting (50.0%, 23/46) and nausea(34.8%, 16/46) in oral capsule group. Side effect symptoms disappeared after the withdraw of nasogastric tube, or at the end of treatment, or during hospitalization for 1-3 days. *CONCLUSIONS*: FMT is effective for many gastrointestinal disorders. No significant adverse event is found, while the associated mechanism should be further explored.

Li, P., Niu, Q., Wei, Q., Zhang, Y., Ma, X., Kim, S. W., Lin, M., and Huang, R. Microbial shifts in the porcine distal gut in response to diets supplemented with Enterococcus Faecalis as alternatives to antibiotics. Sci.Rep. 2-6-2017; 7:41395; PM: 28165001

ABSTRACT: Gut microbiota plays an important role in host health and nutrient digestion of animals. Probiotics have become one of effective alternatives to antibiotics enhancing animal health and performance through modulating gut microbiota. Previously, our research demonstrated that dietary Enterococcus Faecalis UC-100 substituting antibiotics enhanced growth and health of weaned pigs. To investigate the alterations of microbiota in the distal gut of pigs fed E. faecalis UC-100 substituting antibiotics, this study assessed fecal microbiota in pigs from different dietary treatments: the basal diet group, the E. faecalis group, and the antibiotic group on d 0, 14, and 28 of feeding through 16 S rRNA sequencing. Twenty-one phyla and 137 genera were shared by all pigs, whereas 12 genera were uniquely identified in the E. faecalis group on d 14 and 28. Bacterial abundance and diversity in the E. faecalis group, bacterial diversity in the antibiotic group, especially abundances of Fibrobacteres phylum and 12 genera in the E. faecalis

group and antibiotics group were lower than that in the basal diet group on d 28. These results showed that microbial shifts in the porcine gut in response to diets containing E. faecalis were similar to the response to which containing antibiotics.

Li, Q., Han, Y., Dy, A. B. C., and Hagerman, R. J. The Gut Microbiota and Autism Spectrum Disorders. Front Cell Neurosci. 2017; 11:120; PM: 28503135

ABSTRACT: Gastrointestinal (GI) symptoms are a common comorbidity in patients with autism spectrum disorder (ASD), but the underlying mechanisms are unknown. Many studies have shown alterations in the composition of the fecal flora and metabolic products of the gut microbiome in patients with ASD. The gut microbiota influences brain development and behaviors through the neuroendocrine, neuroimmune and autonomic nervous systems. In addition, an abnormal gut microbiota is associated with several diseases, such as inflammatory bowel disease (IBD), ASD and mood disorders. Here, we review the bidirectional interactions between the central nervous system and the gastrointestinal tract (brain-gut axis) and the role of the gut microbiota in the central nervous system (CNS) and ASD. Microbiome-mediated therapies might be a safe and effective treatment for ASD.

Li, Q., Lauber, C. L., Czarnecki-Maulden, G., Pan, Y., and Hannah, S. S. Effects of the Dietary Protein and Carbohydrate Ratio on Gut Microbiomes in Dogs of Different Body Conditions. MBio. 1-24-2017; 8(1); PM: 28119466

ABSTRACT: Obesity has become a health epidemic in both humans and pets. A dysbiotic gut microbiota has been associated with obesity and other metabolic disorders. High-protein, low-carbohydrate (HPLC) diets have been recommended for body weight loss, but little is known about their effects on the canine gut microbiome. Sixty-three obese and lean Labrador retrievers and Beagles (mean age, 5.72 years) were fed a common baseline diet for 4 weeks in phase 1, followed by 4 weeks of a treatment diet, specifically, the HPLC diet (49.4% protein, 10.9% carbohydrate) or a low-protein, high-carbohydrate (LPHC) diet (25.5% protein, 38.8% carbohydrate) in phase 2. 16S rRNA gene profiling revealed that dietary protein and carbohydrate ratios have significant impacts on gut microbial compositions. This effect appeared to be more evident in obese dogs than in lean dogs but was independent of breed. Consumption of either diet increased the bacterial evenness, but not the richness, of the gut compared to that after consumption of the baseline diet. Macronutrient composition affected taxon abundances, mainly within the predominant phyla, Firmicutes and Bacteroidetes The LPHC diet appeared to favor the growth of Bacteroides uniformis and Clostridium butyricum, while the HPLC diet increased the abundances of Clostridium hiranonis, Clostridium perfringens, and Ruminococcus gnavus and enriched microbial gene networks associated with weight maintenance. In addition, we observed a decrease in the Bacteroidetes to Firmicutes ratio and an increase in the Bacteroides to Prevotella ratio in the HPLC diet-fed dogs compared to these ratios in dogs fed other diets. Finally, analysis of the effect of diet on the predicted microbial gene network was performed using phylogenetic investigation of communities by reconstruction of unobserved states (PICRUSt). *IMPORTANCE*: More than 50% of dogs are either overweight or obese in the United States. A dysbiotic gut microbiota is associated with obesity and other metabolic problems in humans. HPLC diets have been promoted as an effective weight loss strategy for many years, and potential effects were reported for both humans and dogs. In this study, we explored the influence of the protein and carbohydrate ratio on the gut microbiome in dogs with different body conditions. We demonstrated significant dietary effects on the gut

microbiome, with greater changes in obese dogs than in lean dogs. The HPLC diet-fed dogs showed greater abundances of Firmicutes but fewer numbers of Bacteroidetes than other dogs. This knowledge will enable us to use prebiotics, probiotics, and other nutritional interventions to modulate the gut microbiota and to provide an alternative therapy for canine obesity.

Li, S. W., Chen, Y. S., Lee, Y. S., Yang, C. H., Srionnual, S., Wu, H. C., and Chang, C. H. Comparative genomic analysis of bacteriocin-producing Weissella cibaria 110. Appl.Microbiol.Biotechnol. 2017; 101(3):1227-1237; PM: 28058448

ABSTRACT: Weissella cibaria 110 was isolated from plaa-som, a Thai fermented fish product, and known to produce the weissellicin 110 bacteriocin. We carried out comprehensive comparative genomic analysis of W. cibaria 110 with four other non-bacteriocin-producing W. cibaria strains and identified potential antibiotic-resistant genes. We further identified a type III restriction-modification system, a TA system, and a bacteriocin gene cluster that are unique in W. cibaria 110. Genes related to bacteriocin biosynthesis are organized in clusters and are encoded with minimum genetic machinery consisting of structural cognate immunity genes, including ABC transporter and immunity protein. Finally, we predicted W. cibaria 110 to produce a class IId bacteriocin, weissellicin 110, which is 31 amino acids in length and contains a 21-amino-acid N-terminal leader peptide. This is the first bacteriocin-producing sequencing genome in W. cibaria, and we describe the difference between the bacteriocin-producing and non bacteriocin-producing strains from genome point of view.

Lieske, J. C. Probiotics for prevention of urinary stones. Ann.Transl.Med. 2017; 5(2):29; PM: 28217694

ABSTRACT: BACKGROUND: Urinary supersaturation is one key determinant of calcium oxalate (CaOx) urinary stone formation, and urinary excretions of oxalate and citrate are two key determinants. Each is influenced by gastrointestinal processes. *METHODS*: Open label and randomized placebo studies have examined the effect of oral probiotic preparations on urinary supersaturation and oxalate excretion. Cross sectional studies in humans have studied the association of Oxalobacter formigenes colonization status and urinary oxalate excretion and prevalence of urinary stones. The intestinal microbiome of representative animals adapted to a high oxalate diet has been defined. *RESULTS*: The fecal content of O. formigenes, the best studied oxalate-degrader, varies depending on stone status. However, trials with probiotics designed to degrade oxalate including those containing O. formigenes, Lactobacillus, and/or Bifidobacterium spp., have been disappointing. Multiple intestinal segments of animals on a high oxalate diet contains diverse communities of microorganisms that can function together to degrade and detoxify a large oxalate load. *CONCLUSIONS*: Although the intestinal microbiome seems likely to play a role to modify gastrointestinal absorption of lithogenic substances and hence urinary stone risk, whether we can develop tools to manipulate it and decrease this kidney stone risk remains to be determined.

Lim, F. T., Lim, S. M., and Ramasamy, K. Pediococcus acidilactici LAB4 and Lactobacillus plantarum LAB12 assimilate cholesterol and modulate ABCA1, CD36, NPC1L1 and SCARB1 in vitro. Benef.Microbes. 2-7-2017; 8(1):97-109; PM: 27903090

ABSTRACT: There is growing interest in the use of probiotic lactic acid bacteria (LAB) for

prevention of hypercholesterolaemia. This study assessed the cholesterol lowering ability of Pediococcus acidilactici LAB4 and Lactobacillus plantarum LAB12 in growth media. Both LAB yielded >98% (39.2 mug/ml) cholesterol lowering in growth media. Nile Red staining indicated direct assimilation of cholesterol by the LAB. The LAB were then explored for their prophylactic (pre-treatment of HT29 cells with LAB prior to cholesterol exposure) and biotherapeutic (treatment of HT29 cells with LAB after exposure to cholesterol) use against short and prolonged exposure of HT29 cells to cholesterol, respectively. For HT29 cells pre-treated with LAB, cholesterol lowering was accompanied by down-regulation of ATP-binding cassette family transporter-type A1 (ABCA1), cluster of differentiation 36 (CD36) and scavenger receptor class B member 1 (SCARB1). HT29 cells treated with LAB after prolonged exposure to cholesterol source, on the other hand, was associated with up-regulation of ABCA1, restoration of CD36 to basal level and down-regulation of Neimann-Pick C1-Like 1 (NPC1L1). The present findings implied the potential use of LAB4 and LAB12 as part of the strategies in prevention and management of hypercholesterolaemia.

Lim, S. M. and Kim, D. H. Bifidobacterium adolescentis IM38 ameliorates high-fat diet-induced colitis in mice by inhibiting NF-kappaB activation and lipopolysaccharide production by gut microbiota. Nutr.Res. 4-19-2017; PM: 28479226

ABSTRACT: Gut microbiota play essential roles in the regulation of human metabolism via symbiotic interactions with the host. Prolonged consumption of high-fat diet (HFD) elevates the Firmicutes to Bacteroidetes ratio and lipopolysaccharide (LPS) production by gut microbiota, thereby increasing the probability of developing metabolic and immune disorders such as obesity and colitis. The use of probiotics with anti-inflammatory properties has been suggested to counteract this effect. Here, we tested whether Bifidobacterium adolescentis IM38, which inhibited nuclear factor-kappa B (NF-kappaB) activation in Caco-2 cells and peritoneal macrophages and inhibited Escherichia coli LPS production, exerted an anticolitic effect in mice with HFD-induced obesity. Oral administration of IM38 (2x109CFU/mouse per day) for 6 weeks in mice with HFD-induced obesity inhibited whole-body and epididymal fat weight gain. IM38 also increased HFD-suppressed expression of interleukin (IL)-10 and tight junction proteins but significantly downregulated HFD-induced NF-kappaB activation and tumor necrosis factor expression in the colon. IM38 inhibited differentiation into helper T17 cells and reduced IL-17 levels in the colon of mice with HFD-induced obesity but increased HFD-suppressed differentiation into regulatory T cells and IL-10 levels. Furthermore, treatment with IM38 lowered the HFD-induced LPS levels in blood and colonic fluid, as well as the Proteobacteria to Bacteroidetes ratio in gut microbiota. Therefore, we suggest that IM38 can inhibit HFD-induced LPS production in gut microbiota through the regulation of Proteobacteria to Bacteroidetes ratio and NF-kappaB activation in the colon, which ultimately attenuates colitis. Thus, IM38 may be a suitable ingredient of functional foods designed for treating or preventing colitis.

Lima, M. D. S. F., Souza, K. M. S., Albuquerque, W. W. C., Teixeira, J. A. C., Cavalcanti, M. T. H., and Porto, A. L. F. Saccharomyces cerevisiae from Brazilian kefir-fermented milk: An in vitro evaluation of probiotic properties. Microb.Pathog. 5-4-2017; PM: 28478200

ABSTRACT: The therapeutic use of probiotics for supporting the antibiotic action against gastrointestinal disorders is a current trend and emerging applications have gained popularity because of their support for various microbiological activities in digestive

processes. Microorganisms isolated from kefir with great probiotic properties, in addition to high resistance to harsh environmental conditions, have been widely researched. Administration of probiotic yeasts offers a number of advantages, when compared to bacteria, because of particular characteristics as their larger cell size. In the present study, 28 strains of Saccharomyces cerevisiae were isolated, after in vitro digestion of kefir-fermented milk, and identified by molecular based approaches. A screening was performed to determine important quality requirements for probiotics including: antagonistic and antioxidant activities, beta-galactosidase synthesis, autoaggregation, surface hydrophobicity and adhesion to epithelial cells. The results showed strains: with antagonistic activity against microbial pathogens such as Klebsiella pneumoniae, Pseudomonas aeruginosa, Staphylococcus aureus, Bacillus subtilis; able to produce beta-galactosidase; with antioxidant activity levels higher than 90%; with hydrophobicity activity and autoaggregation ability (evaluated by adhesion test, where all the strains presented adhesion to mice ileal epithelial cells). These findings are relevant and the strains are recommended for further in vivo studies as well as for potential therapeutic applications.

Limeiras, S. M., Ogo, F. M., Genez, L. A., Carreira, C. M., Oliveira, E. J., Pessatto, L. R., Neves, S. C., Pesarini, J. R., Schweich, L. C., Silva, R. A., Cantero, W. B., ntoniolli-Silva, A. C., and Oliveira, R. J. Prevention of DNA damage and anticarcinogenic activity of Activia(R) in a preclinical model. Genet.Mol.Res. 3-22-2017; 16(1); PM: 28340269

ABSTRACT: Colorectal cancer is a global public health issue. Studies have pointed to the protective effect of probiotics on colorectal carcinogenesis. Activia(R) is a lacto probiotic product that is widely consumed all over the world and its beneficial properties are related, mainly, to the lineage of traditional yoghurt bacteria combined with a specific bacillus, DanRegularis, which gives the product a proven capacity to intestinal regulation in humans. The aim of this study was to evaluate the antigenotoxic, antimutagenic, and anticarcinogenic proprieties of the Activia product, in response to damage caused by 1,2-dimethylhydrazine (DMH) in Swiss mice. Activia does not have shown antigenotoxic activity. However, the percent of DNA damage reduction, evaluated by the antimutagenicity assay, ranged from 69.23 to 96.15% indicating effective chemopreventive action. Activia reduced up to 79.82% the induction of aberrant crypt foci by DMH. Facing the results, it is inferred that Activia facilitates the weight loss, prevents DNA damage and pre-cancerous lesions in the intestinal mucosa.

Lin, H. L., Shiu, Y. L., Chiu, C. S., Huang, S. L., and Liu, C. H. Screening probiotic candidates for a mixture of probiotics to enhance the growth performance, immunity, and disease resistance of Asian seabass, Lates calcarifer (Bloch), against Aeromonas hydrophila. Fish.Shellfish.Immunol. 2017; 60:474-482; PM: 27838565

ABSTRACT: Six bacteria, including, Lactobacillus casei M15, Lac. plantarum D8, Lac. pentosus BD6, Lac. fermentum LW2, Enterococcus faecium 10-10, and Bacillus subtilis E20, and one yeast, Saccharomyces cerevisiae P13 were selected as probiotics for Asian seabass, Lates calcarifer, by tracking the growth performance and disease resistance of fish against Aeromonas hydrophila in the first trial. The probiotic efficiency screening results showed that B. subtilis E20 and Lac. pentosus BD6, and S. cerevisiae P13 and Lac. fermentum LW2 respectively improved either the growth performance or disease resistance. Therefore, these four probiotics were then selected to prepare a probiotics mixture, and this was incorporated in equal proportions into diets for Asian seabass at

levels of 0 (control), and 106 (MD6), 107 (MD7), 108 (MD8), and 109 (MD9) colony-forming units (cfu) (kg diet)-1. A synergistic effect of the combined probiotics was investigated in this study, and the probiotics mixture was able to improve both the growth performance and health status of fish. After 56 days of feeding, fish fed the MD9 diet had a higher final weight and percentage of weight gain. In addition, protein contents in the dorsal muscle of fish fed the MD8 and MD9 diets were significantly higher compared to the control. For the pathogen challenge test, fish fed the MD7, MD8, and MD9 diets had significantly lower cumulative mortalities after A. hydrophila infection compared to those of fish fed the control and MD6 diets, which might have been due to increased respiratory bursts, decreased superoxide dismutase activity in leucocytes, and increased phagocytic activity. Therefore, we considered that the probiotics mixture could adequately provide probiotic efficiency for Asian seabass, and the diet containing 109 cfu (kg diet)-1 probiotic mixture is recommended to improve the growth and health status of Asian seabass.

Lin, R., Zhang, Y., Long, B., Li, Y., Wu, Y., Duan, S., Zhu, B., Wu, X., and Fan, H. Oral Immunization with Recombinant Lactobacillus acidophilus Expressing espA-Tir-M Confers Protection against Enterohemorrhagic Escherichia coli O157:H7 Challenge in Mice. Front Microbiol. 2017; 8:417; PM: 28360900

ABSTRACT: Enterohemorrhagic Escherichia coli O157:H7 (EHEC O157:H7) causes hemorrhagic colitis and the formation of characteristic attaching and effacing (A/E) lesions in humans. Given the severe sequelae of EHEC O157:H7 infection, it is critical to develop effective vaccines for human use. However, for achieving this goal many hurdles need to be addressed, such as the type or subset of antigens, adjuvant, and the delivery route. We developed a candidate vaccine by inserting the bivalent antigen espA-Tir-M composed of espA and the Tir central domain into Lactobacillus acidophilus. The recombinant L. acidophilus (LA-ET) was safe in a cell model and excluded EHEC O157:H7 from LoVo cells at rates of nearly 94 and 60% in exclusion and competition assays, respectively. LA-ET inhibited the induction of A/E lesions by EHEC O157:H7 cells in vitro. Oral immunization with LA-ET induced higher levels of specific mucosal and systemic antibody responses in mice. Moreover, LA-ET enhanced interferon-gamma and interleukin-4 and -10 production, which was associated with mixed helper T (Th1/Th2) cell responses, and protected against EHEC O157:H7 colonization and infection in mice at a rate of 80%. Histopathological analyses revealed that orally administered LA-ET reduced or inhibited A/E lesions and toxin-induced systemic injury. These findings demonstrate that LA-ET induces both humoral and cellular immune responses in mice and is therefore a promising vaccine against EHEC O157:H7 infection.

Lippi, G., Danese, E., Mattiuzzi, C., and Favaloro, E. J. The Intriguing Link between the Intestinal Microbiota and Cardiovascular Disease. Semin.Thromb.Hemost. 3-14-2017; PM: 28293920

ABSTRACT: Human microbiota is a term conventionally used to define the normal flora of microbes living in all of us, most of which are resident in the gastrointestinal tract. Despite it having been known for some time that the vast majority of intestinal bacteria exert a strong influence on human life, recent technologic breakthroughs have made it possible to more accurately characterize the host microbial communities and explore their relationship with many human diseases. Notably, the evidence accumulated over the past 10 years suggests that a reasonable relationship can now be established between gut microbiota composition and the risk of cardiovascular disease. The most convincing

information comes from data generated by studies involving trimethylamine-N-oxide (TMAO)-producing bacteria. It seems now clear that these bacterial strains may actively contribute to increase the concentration of endogenous TMAO and consequently enhance the risk of ischemic and thrombotic disorders, so opening intriguing scenarios for effective prevention of cardiovascular disease by targeting the intestine by means of diet, probiotics, prebiotics, antibiotics, or even transplantation of gut microbes.

Liu, C., Zhu, Q., Chang, J., Yin, Q., Song, A., Li, Z., Wang, E., and Lu, F. Effects of Lactobacillus casei and Enterococcus faecalis on growth performance, immune function and gut microbiota of suckling piglets. Arch.Anim Nutr. 2017; 71(2):120-133; PM: 28201936

ABSTRACT: This study was carried out to investigate the effects of orally administrated Lactobacillus casei and Enterococcus faecalis on performance, immune function and gut microbiota of suckling piglets. Neonatal piglets (n = 120) were randomly assigned to 4 groups, with 30 suckling piglets in each group. The piglets were from 15 litters, one male and one female piglet were selected for each group in each litter. The Control group was administrated with normal saline, the other groups with L. casei or E. faecalis or a combination of L. casei and E. faecalis at a ratio of 3:1. Each piglet was orally administrated with 1, 2, 3 and 4 ml probiotics or normal saline at the age of 1, 7, 14 and 21 d, respectively. The piglets were weaned at the age of 21 d. The results showed that compared with the Control group, the average daily gain of piglets administrated with probiotics was significantly increased, and the diarrhoea rate and mortality were significantly decreased ($p < 0.05$). After supplementation of the combined probiotics, the protease activity in stomach, duodenum and colon was increased and in all supplemented groups, the immunoglobulin A concentration in plasma was significantly higher ($p < 0.05$). The combined probiotics significantly increased villus length and the expression level of transforming growth factor-beta in the jejunum ($p < 0.05$) but decreased the expression level of the jejunal tumour necrosis factor-alpha ($p < 0.05$). In addition, probiotics could regulate gut microbiota and increase microbial similarity coefficients for keeping piglet gut microbiota stable.

Liu, P. C., Yan, Y. K., Ma, Y. J., Wang, X. W., Geng, J., Wang, M. C., Wei, F. X., Zhang, Y. W., Xu, X. D., and Zhang, Y. C. Probiotics Reduce Postoperative Infections in Patients Undergoing Colorectal Surgery: A Systematic Review and Meta-Analysis. Gastroenterol.Res.Pract. 2017; 2017:6029075; PM: 28484489

ABSTRACT: Background: We performed this meta-analysis to investigate the efficacy of probiotics on prevention of infection-related complications following colorectal resection. Method. PubMed, EMBASE, Cochrane Library, and the Web of Science were searched up to January 2016. According to the results, only randomized controlled trials that compared the efficacy of probiotics on patients with colorectal resection were included for meta-analysis. *Results*: Nine studies including a total of 1146 patients met the criteria (556 received multistrain probiotic bacteria, 590 with non-multistrain probiotic bacteria). The combination of multistrain probiotics was beneficial in the reduction of total infections (OR = 0.30, 95%CI: 0.15-0.61, p = 0.0009), including surgical site infections (SSI) (OR = 0.48, 95%CI: 0.25-0.89, p = 0.02) and nonsurgical site infections (NSSI) (OR = 0.36, 95%CI: 0.23-0.56, p < 0.00001). However, there was no significant reduction in total infections (OR = 0.74, 95%CI: 0.50-1.09, p = 0.13) or SSI (OR = 0.77, 95%CI: 0.52-1.12, p = 0.17) with the application of non-multistrains of probiotics. *Conclusion*: Combinations of multistrain probiotic bacteria showed promise in preventing the incidence of infections

following colorectal surgery. However, the efficacy of one or two strains of probiotics remains undetermined.

Liu, Y., Zhao, F., Liu, J., Wang, H., Han, X., Zhang, Y., and Yang, Z. Selection of Cholesterol-Lowering Lactic Acid Bacteria and its Effects on Rats Fed with High-Cholesterol Diet. Curr.Microbiol. 2017; 74(5):623-631; PM: 28286906

ABSTRACT: High cholesterol level in serum is a major factor of influence for coronary heart disease. The cholesterol-lowering ability of lactic acid bacteria (LAB) without side effects makes them more and more attractive. Seventy-nine strains of LAB isolated from fermented food were screened in vitro for their ability to assimilate cholesterol. Then, ten strains which exhibited higher ability of cholesterol assimilation were investigated with the characteristics of acidic resistance, bile salt tolerance, and cell adhesion. According to the results, the best strain LP96 was picked out, and used to evaluate its effects on the high-cholesterol diet-fed rats. The results demonstrated that the levels of serum triglyceride (TG), total cholesterol (TC), low-density lipoprotein cholesterol, and liver TC and TG were reduced significantly in the groups that received the strain LP96 solution compared with the model group, and that the serum high-density lipoprotein cholesterol levels were increased without any significant difference. Furthermore, LP96 also showed good antioxidative activity and improvement of intestinal microbial balance in the rats. Thus, LP96 may be a promising probiotics with potential cholesterol-lowering ability.

Lloyd-Lavery, A., Rogers, N. K., Hatfield, S. J., Grindlay, D., Barnett, R., and Thomas, K. S. What's new in atopic eczema? An analysis of systematic reviews published in 2014. Part 2. Treatment and prevention. Clin.Exp.Dermatol. 2017; 42(1):3-7; PM: 27868221

ABSTRACT: This review forms part of a series of annual updates that summarize the evidence base for atopic eczema (AE). It provides a summary of key findings from 12 systematic reviews (SRs) that were published or indexed during 2014, and focuses on the treatment and prevention of AE. For an update of SRs on the epidemiology, mechanisms of disease and methodological issues, see Part 1 of this update. Although phototherapy and various systemic medications (including ciclosporin, azathioprine and methotrexate) are commonly used to treat AE, many of these have not been robustly assessed in head-to-head randomized controlled trials. Educational interventions may improve AE severity and quality of life for children and their families. Intake of probiotics prenatally and postnatally may help prevent AE, but there is little evidence to suggest a role in the treatment of AE. Although no benefit was found for allergen avoidance in preventing AE, the use of immunotherapy to treat AE-associated aeroallergen sensitivity requires further evaluation. There is insufficient evidence for Vitamin D supplementation for the treatment of AE This overview of reviews provides a succinct guide for clinicians and patients wishing to remain up to date with the most recent evidence for the treatment and prevention of AE.

Lodemann, U., Amasheh, S., Radloff, J., Kern, M., Bethe, A., Wieler, L. H., Pieper, R., Zentek, J., and Aschenbach, J. R. Effects of Ex Vivo Infection with ETEC on Jejunal Barrier Properties and Cytokine Expression in Probiotic-Supplemented Pigs. Dig.Dis.Sci. 2017; 62(4):922-933; PM: 27995406

ABSTRACT: BACKGROUND AND AIM: Enterotoxigenic Escherichia coli (ETEC) strains are

involved in piglet post-weaning diarrhea. Prophylactic measures including probiotics have been examined in infection experiments with live piglets. In the present study, we have tested whether the early effects of ETEC infection can also be evoked and studied in a model in which ETEC is added to whole mucosal tissues ex vivo, and whether this response can be modulated by prior supplementation of the piglets with probiotics. *METHODS*: Jejunal barrier and transport properties of Enterococcus faecium-supplemented or control piglets were assessed in Ussing chambers. Part of the epithelia was challenged with an ETEC strain at the mucosal side. Fluxes of fluorescein as a marker of paracellular permeability, and the expression of selected tight junction (TJ) proteins and of proinflammatory cytokines were measured. *RESULTS*: The addition of ETEC ex vivo induced an increase in transepithelial resistance peaking in the first 2 h with a concomitant reduction in fluorescein fluxes, indicating tightening effects on barrier function. The response of short-circuit current after stimulation with PGE2 or glucose was reduced in epithelia treated with ETEC. ETEC induced a decrease in the TJ protein claudin-4 in the control diet group after 280 min and an increase in the mRNA expression of the proinflammatory cytokines interleukin-8 and TNF-alpha in both groups after 180 min. *CONCLUSIONS*: The addition of ETEC ex vivo affected barrier function and transport properties of the jejunal tissues and enhanced cytokine expression. The differences in claudin-4 expression in the jejunum might indicate a beneficial effect of E. faecium prefeeding.

Lopes, E. G., Moreira, D. A., Gullon, P., Gullon, B., Cardelle-Cobas, A., and Tavaria, F. K. Topical application of probiotics in skin: adhesion, antimicrobial and antibiofilm in vitro assays. J.Appl.Microbiol. 2017; 122(2):450-461; PM: 27862685

ABSTRACT: AIMS: When skin dysbiosis occurs as a result of skin disorders, probiotics can act as modulators, restoring microbial balance. Several properties of selected probiotics were evaluated so that their topical application could be considered. *METHODS AND RESULTS*: Adhesion, antimicrobial, quorum sensing and antibiofilm assays were carried out with several probiotic strains and tested against selected skin pathogens. All tested strains displayed significant adhesion to keratin. All lactobacilli with the exception of Lactobacillus delbrueckii, showed antimicrobial activity against skin pathogens, mainly due to organic acid production. Most of them also prevented biofilm formation, but only Propioniferax innocua was able to break down mature biofilms. *CONCLUSIONS*: This study demonstrates that although all tested probiotics adhered to human keratin, they showed limited ability to prevent adhesion of some potential skin pathogens. Most of the tested probiotics successfully prevented biofilm formation, suggesting that they may be successfully used in the future as a complement to conventional therapies in the treatment of a range of skin disorders. *SIGNIFICANCE AND IMPACT OF STUDY*: The topically used probiotics may be a natural, targeted treatment approach to several skin disorders and a complement to conventional therapies which present many undesirable side effects.

Lopetuso, L., Graziani, C., Guarino, A., Lamborghini, A., Masi, S., and Stanghellini, V. Gelatin tannate and tyndallized probiotics: a novel approach for treatment of diarrhea. Eur.Rev.Med.Pharmacol.Sci. 2017; 21(4):873-883; PM: 28272692

ABSTRACT: OBJECTIVE: Intestinal permeability impairment is implicated in many gastrointestinal (GI) diseases. Chronic diarrhea, defined as the presence of diarrhea for more than 3 weeks in adults and 2 weeks in children, requires a different diagnostic and therapeutic work-up than acute diarrhea. Gelatin tannate, by reducing the clinical

activity of acute colitis and the proinflammatory effects of lipopolysaccharide (LPS), is emerging as a mucosal barrier protector. *MATERIALS AND METHODS*: New therapeutic strategies focusing on the physiological function of the intestinal barrier, may offer an innovative approach for the clinical improvement of highly debilitating chronic GI diseases. We review the available data on the role of gelatin tannate and tyndallized probiotics in the treatment of diarrhea. *RESULTS*: Gelatin tannate and tyndallized probiotics can be used to re-establish the physiological functions of the gut barrier, as well as for preventing dysbiosis. There is evidence that due to their particular properties, gelatin tannate and tyndallized probiotics are highly effective in the treatment of acute gastroenteritis and may be especially indicated in the management of moderate and prolonged diarrhea. *CONCLUSIONS*: Gelatin tannate and tyndallized probiotics may be effective in the management of chronic diarrhea. Further clinical trials are necessary to further explore their effects in clinical practice.

Lopez-Lopez, A., Camelo-Castillo, A., Ferrer, M. D., Simon-Soro, A., and Mira, A. Health-Associated Niche Inhabitants as Oral Probiotics: The Case of Streptococcus dentisani. Front Microbiol. 2017; 8:379; PM: 28344574

ABSTRACT: Oral diseases, including dental caries and periodontitis, are among the most prevalent diseases worldwide and develop as a consequence of a microbial dysbiosis. Several bacterial strains are being tested as potential oral health-promoting organisms, but usually they are species isolated from niches other than the site where they must exert its probiotic action, typically from fecal samples. We hypothesize that oral inhabitants associated to health conditions will be more effective than traditional, gut-associated probiotic species in key aspects such as colonization of the oral site where disease takes place or the possession of oral health promoting functions, as well as more practical issues like safety and toxicity, and establishing proper doses for administration. As an example of these active colonizers, we describe the case of Streptococcus dentisani, a new streptococcal species isolated from dental plaque of caries-free individuals. We have detected it in 98% of dental plaque samples from healthy individuals and, as expected, it does not produce any toxic secondary metabolite and does not survive a simulated stomach digestion, preventing potential secondary effects. Besides, this species has a double probiotic action, as it inhibits the growth of major oral pathogens through the production of bacteriocins, and also buffers acidic pH (the primary cause of dental caries) through an arginolytic pathway. We propose the use of S. dentisani as a promising probiotic against tooth decay.

Loren, V., Manye, J., Fuentes, M. C., Cabre, E., Ojanguren, I., and Espadaler, J. Comparative Effect of the I3.1 Probiotic Formula in Two Animal Models of Colitis. Probiotics.Antimicrob.Proteins. 2017; 9(1):71-80; PM: 27832441

ABSTRACT: Use of probiotic therapy is an active area of investigation to treat intestinal disorders. The clinical benefits of the I3.1 probiotic formula (Lactobacillus plantarum (CECT7484, CECT7485) and P. acidilactici (CECT7483)) were demonstrated in irritable bowel syndrome (IBS) patients in a randomized, double-blind, placebo-controlled clinical trial. The aim of this study was to evaluate the therapeutic effects of I3.1 in two experimental models of colitis, a dextran sulfate sodium (DSS)-induced colitis model and an interleukin (IL)-10-deficient mice model. Colitis was induced in 32 8-week-old Balb/c mice by administering 3% (w/v) DSS in drinking water for 5 days. Probiotics were administered orally (I3.1 or VSL#3, 1 x 109 CFU daily) for 10 days before the administration

of DSS. Also, probiotics (I3.1 or VSL#3, 1 x 109 CFU daily) were administered orally to 36 6-week-old C57B6J IL-10(-/-) mice for 10 weeks. Body weight was recorded daily. Colon samples were harvested for histological examination and cytokine measurements. Body weight after DSS administration did not change in the I3.1 group, whereas the VSL#3 group had weight loss. Also, I3.1 normalized IL-6 to levels similar to that of healthy controls and significantly increased the reparative histologic score. In the IL-10-deficient model, both VSL#3 and I3.1 reduced the severity of colitis compared to untreated controls, and I3.1 significantly reduced the levels of IFN-gamma compared to the other two groups. In conclusion, I3.1 displays a protective effect on two murine models of experimental colitis. Results suggest that the mechanism of action could be different from VSL#3.

Louh, I. K., Greendyke, W. G., Hermann, E. A., Davidson, K. W., Falzon, L., Vawdrey, D. K., Shaffer, J. A., Calfee, D. P., Furuya, E. Y., and Ting, H. H. Clostridium Difficile Infection in Acute Care Hospitals: Systematic Review and Best Practices for Prevention. Infect.Control Hosp.Epidemiol. 2017; 38(4):476-482; PM: 28300019

ABSTRACT: OBJECTIVE: Prevention of Clostridium difficile infection (CDI) in acute-care hospitals is a priority for hospitals and clinicians. We performed a qualitative systematic review to update the evidence on interventions to prevent CDI published since 2009. DESIGN We searched Ovid, MEDLINE, EMBASE, The Cochrane Library, CINAHL, the ISI Web of Knowledge, and grey literature databases from January 1, 2009 to August 1, 2015. *SETTING*: We included studies performed in acute-care hospitals. *PATIENTS OR PARTICIPANTS*: We included studies conducted on hospitalized patients that investigated the impact of specific interventions on CDI rates. *INTERVENTIONS*: We used the QI-Minimum Quality Criteria Set (QI-MQCS) to assess the quality of included studies. Interventions were grouped thematically: environmental disinfection, antimicrobial stewardship, hand hygiene, chlorhexidine bathing, probiotics, bundled approaches, and others. A meta-analysis was performed when possible. *RESULTS*: Of 3,236 articles screened, 261 met the criteria for full-text review and 46 studies were ultimately included. The average quality rating was 82% according to the QI-MQCS. The most effective interventions, resulting in a 45% to 85% reduction in CDI, included daily to twice daily disinfection of high-touch surfaces (including bed rails) and terminal cleaning of patient rooms with chlorine-based products. Bundled interventions and antimicrobial stewardship showed promise for reducing CDI rates. Chlorhexidine bathing and intensified hand-hygiene practices were not effective for reducing CDI rates. *CONCLUSIONS*: Daily and terminal cleaning of patient rooms using chlorine-based products were most effective in reducing CDI rates in hospitals. Further studies are needed to identify the components of bundled interventions that reduce CDI rates. Infect Control Hosp Epidemiol 2017;38:476-482.

Lu, X., Zheng, Z., Miao, S., Li, H., Guo, Z., Zhang, Y., Zheng, Y., Zheng, B., and Xiao, J. Separation of Oligosaccharides from Lotus Seeds via Medium-pressure Liquid Chromatography Coupled with ELSD and DAD. Sci.Rep. 3-9-2017; 7:44174; PM: 28276495

ABSTRACT: Lotus seeds were identified by the Ministry of Public Health of China as both food and medicine. One general function of lotus seeds is to improve intestinal health. However, to date, studies evaluating the relationship between bioactive compounds in lotus seeds and the physiological activity of the intestine are limited. In the present study, by using medium pressure liquid chromatography coupled with evaporative light-scattering detector and diode-array detector, five oligosaccharides were isolated and

their structures were further characterized by electrospray ionization-mass spectrometry and gas chromatography-mass spectrometry. In vitro testing determined that LOS3-1 and LOS4 elicited relatively good proliferative effects on Lactobacillus delbrueckii subsp. bulgaricus. These results indicated a structure-function relationship between the physiological activity of oligosaccharides in lotus seeds and the number of probiotics applied, thus providing room for improvement of this particular feature. Intestinal probiotics may potentially become a new effective drug target for the regulation of immunity.

Lubbert, C., Salzberger, B., and Mossner, J. [Fecal microbiota transplantation]. Internist (Berl). 2017; 58(5):456-468; PM: 28235986

ABSTRACT: The human intestinal microbiome has important metabolic and immunological functions for the host and is part of the defense against pathogens in the gastrointestinal tract. Antibiotics, probiotics, dietary measures, such as prebiotics, and the relatively newly established method of fecal microbiota transplantation (FMT, also known as fecal microbiome transfer) all influence the intestinal microbiome. The FMT procedure comprises the transmission of fecal microorganisms from a healthy donor into the gastrointestinal tract of a patient. The aim of this intervention is to restore a normal microbiome in patients with diseases associated with dysbiosis. The only indication for FMT is currently multiple recurrence of Clostridium difficile infections. Approximately 85% of affected patients can be successfully treated by FMT compared to only about 30% treated conventionally with vancomycin. Other possible therapeutic applications are chronic inflammatory and functional bowel diseases, insulin resistance and morbid obesity but these have to be evaluated further in clinical trials. Knowledge on the optimal donor, the best dosage and the most appropriate route of administration is still limited. A careful donor selection is necessary. The implementation of FMT in Germany is subject to the Medicines Act (Arzneimittelgesetz, AMG) with a duty of disclosure and personal implementation by the attending physician. By documentation in a central register long-term effects and side effects of FMT have to be evaluated.

Lundelin, K., Poussa, T., Salminen, S., and Isolauri, E. Long-term safety and efficacy of perinatal probiotic intervention: Evidence from a follow-up study of four randomized, double-blind, placebo-controlled trials. Pediatr.Allergy Immunol. 2017; 28(2):170-175; PM: 27779809

ABSTRACT: BACKGROUND: Societies worldwide are faced with a progressive increase in immune-mediated health problems such as allergic, autoimmune, and inflammatory diseases, as well as obesity. Perinatal administration of specific probiotic bacteria is an attractive approach in reducing the risk of these conditions, but long-term efficacy and safety data are lacking. The aim here was to evaluate the clinical benefit and long-term safety of specific probiotics administered during the perinatal period. METHODS: The probiotic strains used were Lactobacillus rhamnosus GG, Bifidobacterium lactis Bb-12, Lactobacillus paracasei ST11, and Bifidobacterium longum BL999. The children involved have subsequently undergone prospective long-term follow-up. In addition to physical examination, data were collected by structured questionnaires on non-communicable diseases and continued probiotic use, and growth data from welfare clinics and school nurses. RESULTS: Altogether 303 mother-infant pairs were included in the analysis. Seventy-six of 163 (47%) children receiving perinatal probiotics had developed allergic disease compared with 79 of 140 (56%) receiving placebo (OR 0.67, 95% confidence intervals [CI] 0.43-1.06, p = 0.09). Fifty-nine of 133 (44%) children receiving L. rhamnosus GG perinatally

had developed allergic disease, OR 0.62, 95% CI 0.38-0.99, p = 0.047, as compared to placebo. We found no differences in growth or non-communicable disease prevalence between children receiving perinatally probiotics or placebo. *CONCLUSIONS*: Perinatal probiotic administration is safe in long-term follow-up. Children receiving L. rhamnosus GG perinatally tended to have decreased allergy prevalence.

Luo, J., Ranadheera, C. S., King, S., Evans, C. A., and Baines, S. K. Potential influence of dairy propionibacteria on the growth and acid metabolism of Streptococcus bovis and Megasphaera elsdenii. Benef.Microbes. 2-7-2017; 8(1):111-119; PM: 27824275

ABSTRACT: Ruminal acidosis is a prevalent disorder among dairy cows and feedlot cattle, which can significantly impair their health and productivity. This study, involving seven different strains of dairy propionibacteria, represents an in vitro investigation of the feasibility of using these organisms as direct-fed microbials to control lactic acid acumulation in the rumen. Interactions between the propionibacteria, Streptococcus bovis and Megasphaera elsdenii were evaluated in terms of effects on lactic, acetic and propionic acid metabolism, following co-incubation. Spot resistance tests showed slight but varying degrees of growth inhibition by S. bovis among the propionibacteria, while no inhibition was observed between M. elsdenii and the different strains of dairy propionibacteria. In the co-culture experiments comprising S. bovis in nutrient broth, significant differences in pH and the levels of production of lactic, acetic and propionic acid, were observed between treatments following inoculation with various propionibacteria and/or M. elsdenii. In general, lactic acid concentrations at the end of the incubation were significantly lower in the cultures containing propionibacteria compared with cultures comprising either S. bovis only or S. bovis + M. elsdenii, although efficacy of lactate metabolism varied between species and strains. Moreover,the accumulation of acetic and propionic acid in the combined cultures, but not in the solo S. bovis culture, indicated that these compounds were produced as a result of the metabolism of lactic acid by the propionibacteria and M. elsdenii.

Ma, S., Sun, Y., Wang, F., Mi, R., Wen, Z., Li, X., Meng, N., Li, Y., Du, X., and Li, S. Effects of tussah immunoreactive substances on growth, immunity, disease resistance against Vibrio splendidus and gut microbiota profile of Apostichopus japonicus. Fish.Shellfish.Immunol. 2017; 63:471-479; PM: 28254498

ABSTRACT: Tussah immunoreactive substance (TIS) comprises a number of active chemicals with various bioactivities. The current study investigated the effects of these substances on the sea cucumber Apostichopus japonicus. The specific growth rate (SGR) of TIS-fed sea cucumbers was significantly enhanced, whereas no significant difference in SGR was observed between those soaked in antibiotics and those fed with basal diet only. TIS also improved the immune response of the animals when given at a dose of 1.0% or 2.0%, as shown by increased phagocytic, lysozyme, superoxide dismutase, alkaline phosphatase, acid phosphatase, and catalase activities following injection with live Vibrio splendidus. At a dose of 1.0% or 2.0%, TIS significantly enhanced the immune ability ($P < 0.05$) of the sea cucumbers, but except for lysozyme activity, other immune indices were reduced one day after the animals were injected with Vibrio splendidus. However, the values of these immune indexes were still significantly higher compared to those of the control groups ($P < 0.05$). Intestinal micro flora counts and high-throughput sequencing showed that dietary TIS could improve the amount of probiotic bacteria, yielding a 6-fold increase in Bacillus and 10-fold increase in Lactobacillus for sea

cucumbers fed with 2.0% TIS diet compared to the control. Furthermore, TIS-containing diet also greatly reduced the number of harmful bacteria, with the number of Vibrio in sea cucumbers fed with 1%TIS diet decreased by 67% compared to the control. The results thus indicated that TIS increased the growth of sea cucumbers and enhanced their resistance to V. splendidus infection by improving the immunity of the animals. TIS also improved the gut microbiota profiles of the animals by increasing the probiotics and reducing the harmful bacteria within their guts.

Mai, V., Waugh, S., Byrd, D., Simpson, D., and Ukhanova, M. Novel encapsulation improves recovery of probiotic strains in fecal samples of human volunteers. Appl.Microbiol.Biotechnol. 2017; 101(4):1419-1425; PM: 27796434

ABSTRACT: Probiotic supplements can contribute to maintaining health and ameliorating various disease symptoms. Probiotics can be delivered in many forms with crucial differences in their survival during gastrointestinal (GI) passage. Previously, a novel encapsulation, Probiotic Pearls Acidophilus, Integrative Therapeutics, LLC, USA (Pearls), was shown to increase survival in vitro after exposure to gastric conditions. Here, we compare fecal recovery in human volunteers consuming Pearls or a conventional hard-shelled gelatin capsule. We performed a randomized double-blinded, two-armed trial, with six healthy subjects in each 12-day study arm. In fecal samples collected at baseline, twice during the intervention period, and after washout, we compared colony counts between the two encapsulation methods. The identity of the colonies was confirmed by colony morphology, strain-specific PCR, and 16S rRNA gene sequencing. We further performed a comprehensive 16S rRNA gene sequencing-based analysis to identify differential effects on overall microbiota composition. We detected an average log increase in bifidobacteria of 0.152 cfu/g with gelatin and 0.651 cfu/g with Pearls capsules ($p > 0.05$). Total lactobacilli counts increased in both groups with no difference between the groups. However, the supplemented Lactobacillus acidophilus NCFM decreased to baseline levels within 7 days after end of supplementation with gelatin capsules while 3.11 log cfu/g higher counts compared to baseline ($p = 0.05$) remained for Pearls. Targeted qPCR largely confirmed the trends observed by viable plate counts. Protecting the probiotic strains by Pearls encapsulation results in higher recovery rates of the supplemented lactobacilli and bifidobacteria in fecal samples and increased persistence, suggesting an improved survival and viability that might increase efficacy towards achieving desired health benefits.

Majidi-Mosleh, A., Sadeghi, A. A., Mousavi, S. N., Chamani, M., and Zarei, A. Ileal MUC2 gene expression and microbial population, but not growth performance and immune response, are influenced by in ovo injection of probiotics in broiler chickens. Br.Poult.Sci. 2017; 58(1):40-45; PM: 27844495

ABSTRACT: 1. The objective of present study was to evaluate the effects of intra-amniotic injection of different probiotic strains (Bacillus subtilis, Enterococcus faecium and Pediococcus acidilactici) on the intestinal MUC2 gene expression, microbial population, growth performance and immune response in broiler chicken. 2. In a completely randomised design, different probiotic strains were injected into the amniotic fluid of the 480 live embryos (d 18 of incubation), with 4 treatments and 5 replicates. Ileal MUC2 gene expression, microbial profile, growth performance and immune response were determined. 3. Injection of probiotic strains, especially B. subtilis, had significant effect on expression of the MUC2 on d 21 of incubation and d 3 post-hatch, but not on d 19 of

incubation. 4. Injection of the probiotic strains decreased significantly the Escherichia coli population and increased the lactic acid bacteria population during the first week post-hatch. 5. Inoculation of probiotics had no significant effect on antibody titres against Newcastle disease virus, antibody titres against sheep red blood cell and cell-mediated immune response of chickens compared to control. 6. In ovo injection of the probiotic strains had no significant effect on growth performance of broiler chickens. 7. It was concluded that injection of probiotic bacteria especially B. subtilis into the amniotic fluid has a beneficial effect on ileal MUC2 gene expression and bacteria population during the first week post-hatch, but has no effect on growth performance and immune response in broiler chickens.

Majlesi, M., Shekarforoush, S. S., Ghaisari, H. R., Nazifi, S., Sajedianfard, J., and Eskandari, M. H. Effect of Probiotic Bacillus Coagulans and Lactobacillus Plantarum on Alleviation of Mercury Toxicity in Rat. Probiotics.Antimicrob.Proteins. 1-13-2017; PM: 28084611

ABSTRACT: The objective of this study was to evaluate the efficiency of probiotics (Lactobacillus plantarum and Bacillus coagulans) against mercury-induced toxicity using a rat model. Mercury (Hg) is a widespread heavy metal and was shown to be associated with various diseases. Forty-eight adult male Wistar rats were randomly divided into six groups (control, mercury-only, each probiotic-only, and mercury plus each probiotic group). Hg-treated groups received 10 ppm mercuric chloride, and probiotic groups were administrated 1 x 109 CFU of probiotics daily for 48 days. Levels of mercury were determined using cold vapor technique, and some biochemical factors (list like glutathione peroxidase (GPx), superoxide dismutase (SOD), creatinine, urea, bilirubin, alanine transaminase (ALT), and aspartate transaminase (AST)) were measured to evaluate changes in oxidative stress. Oral administration of either probiotic was found to provide significant protection against mercury toxicity by decreasing the mercury level in the liver and kidney and preventing alterations in the levels of GPx and SOD. Probiotic treatment generated marked reduction in the levels of creatinine, urea, bilirubin, ALT, and AST indicating the positive influence of the probiotics on the adverse effects of Hg in the body.

Makela, R., Makila, H., and Peltomaa, R. Dietary Therapy in Patients With Inflammatory Arthritis. Altern.Ther.Health Med. 2017; 23(1):34-39; PM: 28160762

ABSTRACT: Context * The exact etiology of rheumatoid disease is currently unknown. Changes in the microbiota of the gastrointestinal (GI) tract, chronic bacterial infection of the upper urinary tract, increased permeability of the GI tract, and food sensitivities have been classified among the factors that may cause or aggravate the disease. Dietary deficiencies also may render patients more susceptible to inflammatory conditions and disorders of the immunological system. Objective * The study intended to determine the effects of a therapy consisting of dietary elimination, dietary supplements, and probiotics, collectively called DDP therapy, which is given either independently or in combination with conventional pharmacological agents. Design * The research team designed a retrospective survey, sending out a detailed questionnaire to determine the outcomes for patients who had received DDP therapy. Setting * The study took place at an antioxidant clinic in Helsinki, Finland. Participants * The participants were 104 patients with inflammatory arthritis who had undergone DDP therapy at the clinic. Intervention * The dietary elimination in DDP therapy included the omission of all animal milks, wheat, rye, barley, and oats, and the patients were asked to avoid added sugar and yeast. The

dietary supplements included multivitamins with the main antioxidants, n-3-omega polyunsaturated fatty acids, and curcuminoids. The probiotic supplement most often used consisted of a mixture of 109 CFU/d of Bifidobacterium lactis and 109 CFU/d of Lactobacillus rhamnosus. Outcome Measures * The physician who had given the DDP therapy analyzed the patients' case histories to form his opinion on the efficacy of the therapy. In addition, a detailed questionnaire was sent to the 104 patients to obtain their evaluations of the outcomes for the DDP therapy. Results * Seventy-nine of the 104 patients (76%) returned their questionnaires. Of those respondents, 72 patients (91%) were taking conventional medication at baseline and 64 (81%) were using disease-modifying antirheumatic drugs. The average duration of their disease was 6.9 y. Seventy patients (88.6%) reported that they had benefited overall from the DDP therapy, expressed as a diminished need for conventional medications and/or an improvement in general health. Sixty-six of the patients (83.5%) reported a moderate or significant improvement in their joint symptoms. Reported adverse effects from DDP therapy were few and mild. Conclusions * This study demonstrates that patients with inflammatory arthritis perceive benefits from DDP therapy, and the risks appear to be low.

Manafi, M., Khalaji, S., Hedayati, M., and Pirany, N. Efficacy of Bacillus subtilis and bacitracin methylene disalicylate on growth performance, digestibility, blood metabolites, immunity, and intestinal microbiota after intramuscular inoculation with Escherichia coli in broilers. Poult.Sci. 5-1-2017; 96(5):1174-1183; PM: 28339520

ABSTRACT: This experiment was conducted to evaluate the effect of Bacillus subtilis (BS) on broiler performance and health after intramuscular inoculation with E. coli and compare its effect with a growth promoter antibiotic. In a completely randomized design manner, 360 male Ross 308 chicks were divided into 6 treatments and 5 replicates of 12 chicks in each replicate. Experimental treatments included control diet, control + E. coli (0.5 mL of culture containing 108 CFU of E. coli/ml), control + 0.1% BS, control + 0.05% bacitracin methylene disalicylate (BMD), control + E. coli and BS, and control + E. coli and BMD in a factorial arrangement (3 x 2). Addition of BMD or BS to the control diet significantly ($P < 0.01$) increased body weight and decreased FCR, but E. coli challenge adversely reduced ($P < 0.01$) body weight and increased FCR, so that the addition of BMD or BS did not compensate growth reduction. E. coli challenged chicks had the lowest vaccine titers for ND, IB, AI, and IBD and the highest were observed in chicks fed BS. The E. coli challenge significantly ($P < 0.01$) increased albumin, globulin, cholesterol, triglyceride, LDL, ALT, and ALP indices. Addition of BMD and BS decreased albumin and globulin in challenged chick's plasma but had no effect on plasma lipid profile concentration. The E. coli challenge decreased villus height and increased crypt depth and goblet cell numbers significantly ($P < 0.01$). In birds subjected to BMD or BS, crypt depth decreased and villus height increased ($P < 0.01$), compared with the control diet. Challenge of E. coli significantly ($P < 0.01$) increased the bacterial population of E. coli, coliforms, and Salmonella in cecal parts of broilers' intestines. In challenged birds receiving BMD or BS, E. coli, coliform, and Salmonella populations of ceca showed a significant ($P < 0.01$) reduction. Both BMD and BS increased the digestibility of nutrients significantly ($P < 0.01$), but a reduction was observed in E. coli challenged groups. Results of the study suggest that spore-forming probiotics are partially effective in unsuitable rearing situations such as colibacillosis in which the load of harmful bacteria is high.

Mandal, S. and Hati, S. Microencapsulation of Bacterial Cells by Emulsion Technique for Probiotic Application. Methods Mol.Biol. 2017; 1479:273-279; PM: 27738944

ABSTRACT: Probiotics are dietary concepts to improve the dynamics of intestinal microbial balance favorably. Careful screening of probiotic strains for their technological suitability can also allow selection of strains with the best manufacturing and food technology characteristics. However, even the most robust probiotic bacteria are currently in the range of food applications to which they can be applied. Additionally, bacteria with exceptional functional heath properties are ruled out due to technological limitations. New process and formulation technologies will enable both expansion of the range of products in to which probiotics can be applied and the use of efficacious stains that currently cannot be manufactured or stored with existing technologies. Viability of probiotics has been both a marketing and technological concern for many industrial produces. Probiotics are difficult to work with, the bacteria often die during processing, and shelf life is unpredictable. Probiotics are extremely susceptible environmental conditions such as oxygen, processing and preservation treatments, acidity, and salt concentration, which collectively affect the overall viability of probiotics. Manufacturers have long been fortifying products with probiotics; they have faced significant processing challenges regarding the stability and survivability of probiotics during processing and preservation treatments, storage as well during their passage through GIT. Application of microencapsulation significantly improves the stability of probiotics during food processing and gastrointestinal transit.

Manes-Lazaro, R., Van Diemen, P. M., Pin, C., Mayer, M. J., Stevens, M. P., and Narbad, A. Administration of Lactobacillus johnsonii FI9785 to chickens affects colonisation by Campylobacter jejuni and the intestinal microbiota. Br.Poult.Sci. 5-12-2017; 1-9; PM: 28318296

ABSTRACT: 1. Campylobacter jejuni is the most common bacterial cause of human food-borne gastroenteritis in the world. A major source of human infection is the consumption of contaminated meat, particularly poultry. New control measures to reduce or eliminate this pathogen from the animal gastrointestinal tract are urgently required, and the use of probiotics as competitive exclusion agents is a promising biocontrol measure to reduce C. jejuni in the food chain. 2. In this study, we assessed the potential of Lactobacillus johnsonii FI9785, which has shown efficacy against Clostridium perfringens, to combat C. jejuni. The effect of prophylactic administration of L. johnsonii on the ability of C. jejuni to colonise chickens was determined. 3. Two doses of L. johnsonii given a week apart led to a reduction in C. jejuni colonisation in the caecal contents, but this biocontrol seemed reliant upon a high level of initial colonisation by the probiotic. 4. The microbial composition in the chicken gut was significantly altered by the probiotic treatment, as shown by denaturing gradient gel electrophoresis of 16S rRNA gene amplicons. 5. Together these results demonstrate the potential of this probiotic strain to be tested further as a competitive exclusion agent in poultry against C. jejuni.

Mangano, A. and Marciano, L. Effect of probiotics on postoperative quality of gastric bypass surgeries: a prospective randomized trial. Surg.Obes.Relat Dis. 2-2-2017; PM: 28284568

No Abstract Available.

Mansour, N. M., Elkhatib, W. F., Aboshanab, K. M., and Bahr, M. M. A. Inhibition of Clostridium difficile in Mice Using a Mixture of Potential Probiotic Strains Enterococcus faecalis

NM815, E. faecalis NM915, and E. faecium NM1015: Novel Candidates to Control C. difficile Infection (CDI). Probiotics.Antimicrob.Proteins. 5-11-2017; PM: 28497217

ABSTRACT: This study is aimed at the isolation, identification, and characterization of potential probiotic strains capable of inhibiting Clostridium difficile in vitro and in vivo. Twenty isolates were isolated from infant fecal samples and screened against C. difficile using their cell-free supernatant. Only three isolates showed maximum inhibition from 56.05 to 60.60%, thus they were characterized for probiotic properties and safety. The results obtained approved their tolerance to the gastrointestinal tract conditions and safety profile. They were identified by sequencing 16S rRNA as Enterococcus faecalis NM815, E. faecalis NM915, and Enterococcus faecium NM1015. For in vivo evaluation, a viable mixture of these three strains (109 CFU/mL) was administrated to a group of mice (treated group) in daily dose for 14 days, then followed by challenge with viable C. difficile (105 CFU/mL) in daily dose for 7 days, then a second administration of a viable mixture of the three strains was done daily for 7 days. In addition, the control group was administered PBS buffer only and the untreated group received PBS buffer instead of the probiotic mixture before and after the challenge with C. difficile. The results obtained from histological analysis confirmed the effectiveness of our three potential probiotic strains which expressed inhibition of C. difficile and maintained the structural integrity of the liver and intestinal cells.

Manzanares, W. and Wischmeyer, P. E. Response to "Reassessing the death risk related to probiotics in critically ill patients". Crit Care. 2-27-2017; 21(1):43; PM: 28241845

No Abstract Available.

Manzanares, W., Langlois, P. L., and Wischmeyer, P. E. Restoring the Microbiome in Critically Ill Patients: Are Probiotics Our True Friends When We Are Seriously Ill? JPEN J.Parenter.Enteral Nutr. 2017; 41(4):530-533; PM: 28445681

No Abstract Available.

Marco, M. L., Heeney, D., Binda, S., Cifelli, C. J., Cotter, P. D., Foligne, B., Ganzle, M., Kort, R., Pasin, G., Pihlanto, A., Smid, E. J., and Hutkins, R. Health benefits of fermented foods: microbiota and beyond. Curr.Opin.Biotechnol. 2017; 44:94-102; PM: 27998788

ABSTRACT: Fermented foods and beverages were among the first processed food products consumed by humans. The production of foods such as yogurt and cultured milk, wine and beer, sauerkraut and kimchi, and fermented sausage were initially valued because of their improved shelf life, safety, and organoleptic properties. It is increasingly understood that fermented foods can also have enhanced nutritional and functional properties due to transformation of substrates and formation of bioactive or bioavailable end-products. Many fermented foods also contain living microorganisms of which some are genetically similar to strains used as probiotics. Although only a limited number of clinical studies on fermented foods have been performed, there is evidence that these foods provide health benefits well-beyond the starting food materials.

Marmol, I., Sanchez-de-Diego, C., Pradilla, Dieste A., Cerrada, E., and Rodriguez Yoldi, M. J. Colorectal Carcinoma: A General Overview and Future Perspectives in Colorectal Cancer. Int.J.Mol.Sci. 1-19-2017; 18(1); PM: 28106826

ABSTRACT: Colorectal cancer (CRC) is the third most common cancer and the fourth most common cause of cancer-related death. Most cases of CRC are detected in Western countries, with its incidence increasing year by year. The probability of suffering from colorectal cancer is about 4%-5% and the risk for developing CRC is associated with personal features or habits such as age, chronic disease history and lifestyle. In this context, the gut microbiota has a relevant role, and dysbiosis situations can induce colonic carcinogenesis through a chronic inflammation mechanism. Some of the bacteria responsible for this multiphase process include Fusobacterium spp, Bacteroides fragilis and enteropathogenic Escherichia coli. CRC is caused by mutations that target oncogenes, tumour suppressor genes and genes related to DNA repair mechanisms. Depending on the origin of the mutation, colorectal carcinomas can be classified as sporadic (70%); inherited (5%) and familial (25%). The pathogenic mechanisms leading to this situation can be included in three types, namely chromosomal instability (CIN), microsatellite instability (MSI) and CpG island methylator phenotype (CIMP). Within these types of CRC, common mutations, chromosomal changes and translocations have been reported to affect important pathways (WNT, MAPK/PI3K, TGF-beta, TP53), and mutations; in particular, genes such as c-MYC, KRAS, BRAF, PIK3CA, PTEN, SMAD2 and SMAD4 can be used as predictive markers for patient outcome. In addition to gene mutations, alterations in ncRNAs, such as lncRNA or miRNA, can also contribute to different steps of the carcinogenesis process and have a predictive value when used as biomarkers. In consequence, different panels of genes and mRNA are being developed to improve prognosis and treatment selection. The choice of first-line treatment in CRC follows a multimodal approach based on tumour-related characteristics and usually comprises surgical resection followed by chemotherapy combined with monoclonal antibodies or proteins against vascular endothelial growth factor (VEGF) and epidermal growth receptor (EGFR). Besides traditional chemotherapy, alternative therapies (such as agarose tumour macrobeads, anti-inflammatory drugs, probiotics, and gold-based drugs) are currently being studied to increase treatment effectiveness and reduce side effects.

Martinez-Martinez, M. I., Calabuig-Tolsa, R., and Cauli, O. The effect of probiotics as a treatment for constipation in elderly people: A systematic review. Arch.Gerontol.Geriatr. 2017; 71:142-149; PM: 28467916

ABSTRACT: PURPOSE: Treating constipation in elderly people remains a challenge; the administration of probiotics may be a valid therapy for this problem as an alternative to traditional drug-based treatments. The objective of this systematic review was to evaluate the efficiency of probiotics in treating constipation in elderly people. *METHODS*: Articles related to this topic and published, without any time limitations, in the Medline, Embase, Scopus, Lilacs, or Cochrane databases were systematically reviewed according to Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines. The primary search terms were 'constipation' and 'probiotics'. The main inclusion criteria were: 1) the article was original and the whole text was published in English or Spanish and 2) included the primary search terms in the title, summary, or body text; 3) the studies had to have included 60 or more participants defined as 'elderly' and 4) have specifically evaluated the effect of the administration of probiotics. *RESULTS*: Of the 475 articles consulted, 9 met the inclusion criteria. Among the selected studies, there

were four randomised and placebo-controlled trials and the remaining five reports were observational. Overall, our analysis of the randomised and placebo-controlled trials suggests that administration of probiotics significantly improved constipation in elderly individuals by 10-40% compared to placebo controls in which no probiotic was administered. The strain of bacteria most commonly tested was Bifidobacterium longum. However, caution is needed when interpreting these reports because of the heterogeneity of the original study designs, populations, and the risk of bias. Therefore, further placebo-controlled trials are necessary to determine the most efficient strains, doses, and the optimal treatment duration.

Martinez, K. B., Leone, V., and Chang, E. B. Western diets, gut dysbiosis, and metabolic diseases: Are they linked? Gut Microbes. 3-4-2017; 8(2):130-142; PM: 28059614

ABSTRACT: Obesity afflicts 36.5% of the US population and 600 million individuals world-wide. Thus, it is imperative to understand the risk factors underlying metabolic disease including diet, activity level, sleep, and genetics. Another key contributory factor is the gut microbiota given its widely reported role in the development of metabolic disease. The gut microbiota, particularly its structure and function, is heavily influenced by Western style diets rich in a complex mixture of fats and high in simple sugars. In this review, the profound impact of obesity and Western diets on the gut microbiota will be illustrated, and the following research questions will be addressed: 1) to what extent do high fat diets (HFDs) alter community membership and function and does this depend upon the amount or type of fat consumed?, 2) how rapidly do dietary shifts alter gut microbial communities?, 3) are these alterations sustained or can the microbiome recover from dietary stress?, 4) how does diet drive host-microbe interactions leading to obesity?, and 5) what can be done to restore the detrimental impact of HFD on the gut microbiota? The goal of this review is to address these questions by parsing out the effects and underlying mechanisms of how Western diets impact the gut microbiota and host. By doing so, potential avenues for further exploration and strategies for microbiome-based interventions to prevent or treat diet-induced obesity may become more apparent.

Mathipa, M. G. and Thantsha, M. S. Probiotic engineering: towards development of robust probiotic strains with enhanced functional properties and for targeted control of enteric pathogens. Gut Pathog. 2017; 9:28; PM: 28491143

ABSTRACT: There is a growing concern about the increase in human morbidity and mortality caused by foodborne pathogens. Antibiotics were and still are used as the first line of defense against these pathogens, but an increase in the development of bacterial antibiotic resistance has led to a need for alternative effective interventions. Probiotics are used as dietary supplements to promote gut health and for prevention or alleviation of enteric infections. They are currently used as generics, thus making them non-specific for different pathogens. A good understanding of the infection cycle of the foodborne pathogens as well as the virulence factors involved in causing an infection can offer an alternative treatment with specificity. This specificity is attained through the bioengineering of probiotics, a process by which the specific gene of a pathogen is incorporated into the probiotic. Such a process will subsequently result in the inhibition of the pathogen and hence its infection. Recombinant probiotics offer an alternative novel therapeutic approach in the treatment of foodborne infections. This review article

focuses on various strategies of bioengineered probiotics, their successes, failures and potential future prospects for their applications.

Matsuyama, M., Harb, T., David, M., Davies, P. S., and Hill, R. J. Effect of fortified milk on growth and nutritional status in young children: a systematic review and meta-analysis. Public Health Nutr. 2017; 20(7):1214-1225; PM: 27938461

ABSTRACT: OBJECTIVE: Adequate nutrition is critical for optimal growth and development. However, young children may be at risk of nutrient deficiencies when transitioning to weaning foods for a variety of reasons. Supplementation with fortified milk may provide potentially lacking essential nutrients, but effects on growth and nutritional status are yet to be established. *DESIGN*: Five databases were searched for randomised controlled trials using fortified milk against control milk in young children. Outcomes were growth, body composition and/or biochemical markers. Pooled differences in means were calculated for continuous outcomes and odds ratios for binary outcomes. *SETTING*: Randomised controlled trials set in any country. *SUBJECTS*: Otherwise healthy children aged 6-47 months. *RESULTS*: Fifteen articles met the eligibility criteria. Fortification varied from Fe, Zn, vitamins, essential fatty acids, to pre- and/or probiotics. Frequently reported outcomes were weight, height and Fe status. Studies varied in geographical location, sample size and duration. Fortified milk had minimal effects on weight gain (mean difference=0.17 kg; 95 % CI 0.02, 0.31 kg) compared with control milk. The risk of anaemia was reduced in fortified milk groups (OR=0.32; 95 % CI 0.15, 0.66) compared with control groups. There were no significant effects on height gain, changes in body composition or Hb concentration. *CONCLUSIONS*: Fortified milk is an effective source of complementary nutrition to supplement children in need when consumed in appropriate amounts in addition to a normal diet. Due to compositional differences, further research on fortified milk is warranted before making global recommendations on benefits for growth and nutritional outcomes in young children.

McClements, D. J. Designing biopolymer microgels to encapsulate, protect and deliver bioactive components: Physicochemical aspects. Adv.Colloid Interface Sci. 2017; 240:31-59; PM: 28034309

ABSTRACT: Biopolymer microgels have considerable potential for their ability to encapsulate, protect, and release bioactive components. Biopolymer microgels are small particles (typically 100nm to 1000mum) whose interior consists of a three-dimensional network of cross-linked biopolymer molecules that traps a considerable amount of solvent. This type of particle is also sometimes referred to as a nanogel, hydrogel bead, biopolymer particles, or microsphere. Biopolymer microgels are typically prepared using a two-step process involving particle formation and particle gelation. This article reviews the major constituents and fabrication methods that can be used to prepare microgels, highlighting their advantages and disadvantages. It then provides an overview of the most important characteristics of microgel particles (such as size, shape, structure, composition, and electrical properties), and describes how these parameters can be manipulated to control the physicochemical properties and functional attributes of microgel suspensions (such as appearance, stability, rheology, and release profiles). Finally, recent examples of the utilization of biopolymer microgels to encapsulate, protect, or release bioactive agents, such as pharmaceuticals, nutraceuticals, enzymes, flavors, and probiotics is given.

McFarland, L. V. Primary prevention of Clostridium difficile infections - how difficult can it be? Expert.Rev.Gastroenterol.Hepatol. 2017; 11(6):507-521; PM: 28347160

ABSTRACT: INTRODUCTION: C. difficile infections (CDI) have been a challenging disease to treat, much less to prevent, for decades. Efforts for primary prevention have mainly focused on improving infection control practices, but CDI outbreaks continue to plague healthcare facilities. Areas covered: A literature search from 1970-December 2016 found 13 facility-level and 2 patient-level strategies that were evidence-based. The aim of this manuscript is to assess the current state of the literature on primary prevention of CDI and offer insights into which strategies may be more effective. *Expert commentary*: The strongest evidence for primary prevention is based on multi-faceted infection control bundles, while there is promising moderate evidence involving facility-wide use of specific probiotics. Moderate-level evidence was found for patient-level use of specific probiotics and low level evidence for vaccines. Future suggestions include use of consistent outcome metrics, measurements of implementation compliance and program sustainability.

McKean, J., Naug, H., Nikbakht, E., Amiet, B., and Colson, N. Probiotics and Subclinical Psychological Symptoms in Healthy Participants: A Systematic Review and Meta-Analysis. J.Altern.Complement Med. 2017; 23(4):249-258; PM: 27841940

ABSTRACT: INTRODUCTION/AIM: Interest in the gut-brain axis and emerging evidence that the intestinal microbiota can influence central nervous system function has led to the hypothesis that probiotic supplementation can have a positive effect on mood and psychological symptoms such as depression and anxiety. Although several human clinical trials have investigated this, results have been inconsistent. Therefore, a systematic review and meta-analytic approach was chosen to examine if probiotic consumption has an effect on psychological symptoms. *METHODS*: The online databases PubMed, Scopus, and the Cochrane Library were searched for relevant studies up to July 2016. Those that were randomized and placebo controlled and measured preclinical psychological symptoms of depression, anxiety, and perceived stress in healthy volunteers pre and post supplementation with a probiotic were included. To control for differences in scales of measurement, data were converted to percentage change, and the standardized mean difference between the probiotic and control groups was investigated using Revman software. A random effects model was used for analysis. Heterogeneity was assessed using the I2 statistic. Quality assessment was undertaken using the Rosendal scale. *RESULTS*: Seven studies met the inclusion criteria and provided data for nine comparisons. All studies passed the quality analysis. The meta-analysis showed that supplementation with probiotics resulted in a statistically significant improvement in psychological symptoms (standardized mean difference 0.34; 95% confidence interval 0.07-0.61, Z = 2.49) compared with placebo. *CONCLUSION*: These results show that probiotic consumption may have a positive effect on psychological symptoms of depression, anxiety, and perceived stress in healthy human volunteers.

Mearin, F., Ciriza, C., Minguez, M., Rey, E., Mascort, J. J., Pena, E., Canones, P., and Judez, J. [Irritable bowel syndrome with constipation and functional constipation in adults: Treatment (Part 2 of 2)]. Semergen. 2017; 43(2):123-140; PM: 28189496

ABSTRACT: In this Clinical practice guide we examine the diagnostic and therapeutic management of adult patients with constipation and abdominal discomfort, at the

confluence of the spectrum of irritable bowel syndrome and functional constipation. Both fall within the framework of functional intestinal disorders and have major personal, health and social impact, altering the quality of life of the patients affected. The former is a subtype of irritable bowel syndrome in which constipation and altered bowel habit predominate, often along with recurring abdominal pain, bloating and abdominal distension. Constipation is characterised by infrequent or hard-to-pass bowel movements, often accompanied by straining during defecation or the sensation of incomplete evacuation. There is no underlying organic cause in the majority of cases; it being considered a functional bowel disorder. There are many clinical and pathophysiological similarities between the two conditions, the constipation responds in a similar way to commonly used drugs, the fundamental difference being the presence or absence of pain, but not in an "all or nothing" way. The severity of these disorders depends not only on the intensity of the intestinal symptoms but also on other biopsychosocial factors: association of gastrointestinal and extraintestinal symptoms, degree of involvement, forms of perception and behaviour. Functional bowel disorders are diagnosed using the Rome criteria. This Clinical practice guide adapts to the Rome IV criteria published at the end of May 2016. The first part (96, 97, 98) examined the conceptual and pathophysiological aspects, alarm criteria, diagnostic test and referral criteria between Primary Care and Gastroenterology. This second part reviews all the available treatment alternatives (exercise, fluid ingestion, diet with soluble fibre-rich foods, fibre supplements, other dietary components, osmotic or stimulating laxatives, probiotics, antibiotics, spasmolytics, peppermint essence, prucalopride, linaclotide, lubiprostone, biofeedback, antdepressants, psychological treatment, acupuncture, enemas, sacral root neurostimulation and surgery), and practical recommendations are made for each.

Mearin, F., Ciriza, C., Minguez, M., Rey, E., Mascort, J. J., Pena, E., Canones, P., and Judez, J. [Irritable bowel syndrome with constipation and functional constipation in adults: Treatment (Part 2 of 2)]. Aten.Primaria. 2017; 49(3):177-194; PM: 28238460

ABSTRACT: In this Clinical practice guide we examine the diagnostic and therapeutic management of adult patients with constipation and abdominal discomfort, at the confluence of the spectrum of irritable bowel syndrome and functional constipation. Both fall within the framework of functional intestinal disorders and have major personal, health and social impact, altering the quality of life of the patients affected. The former is a subtype of irritable bowel syndrome in which constipation and altered bowel habit predominate, often along with recurring abdominal pain, bloating and abdominal distension. Constipation is characterised by infrequent or hard-to-pass bowel movements, often accompanied by straining during defecation or the sensation of incomplete evacuation. There is no underlying organic cause in the majority of cases; it being considered a functional bowel disorder. There are many clinical and pathophysiological similarities between the two conditions, the constipation responds in a similar way to commonly used drugs, the fundamental difference being the presence or absence of pain, but not in an "all or nothing" way. The severity of these disorders depends not only on the intensity of the intestinal symptoms but also on other biopsychosocial factors: association of gastrointestinal and extraintestinal symptoms, degree of involvement, forms of perception and behaviour. Functional bowel disorders are diagnosed using the Rome criteria. This Clinical practice guide adapts to the Rome IV criteria published at the end of May 2016. The first part (96, 97, 98) examined the conceptual and pathophysiological aspects, alarm criteria, diagnostic test and referral criteria between Primary Care and Gastroenterology. This second part reviews all the

available treatment alternatives (exercise, fluid ingestion, diet with soluble fibre-rich foods, fibre supplements, other dietary components, osmotic or stimulating laxatives, probiotics, antibiotics, spasmolytics, peppermint essence, prucalopride, linaclotide, lubiprostone, biofeedback, antdepressants, psychological treatment, acupuncture, enemas, sacral root neurostimulation and surgery), and practical recommendations are made for each.

Meng, F., Yang, S., Wang, X., Chen, T., Wang, X., Tang, X., Zhang, R., and Shen, L. Reclamation of Chinese herb residues using probiotics and evaluation of their beneficial effect on pathogen infection. J.Infect.Public Health. 2-8-2017; PM: 28189509

ABSTRACT: Environmental pollution caused by herb residues and the huge waste of medicinal ingredients contained in herb residues hinder the development of traditional Chinese medicine enterprises. To solve this problem, several probiotics were tested, and Lactobacillus plantarum (HM218749) was finally selected for the reuse of herb residues of Jianweixiaoshi tablets. A mouse model of Helicobacter pylori infection was developed to evaluate the anti-H. pylori infection activity of the herb residue fermentation supernatant using a urease activity test, histological imaging, an enzyme-linked immunosorbent assay (ELISA) and denaturing gel gradient electrophoresis (DGGE). The results demonstrated that the herb residue fermentation supernatant successfully inhibited urease activity, slowed cell infiltration in the gastric area and significantly reduced the production of interleukin-6 (IL-6), IL-8 and TNF-alpha in the treatment group ($p<0.01$). In addition, the DGGE results indicated that the herb residue fermentation supernatant was beneficial for the recovery of the disturbed microbiota in the infected model to the normal condition, in which L. gasseri (GU417842.1) and L. johnsonii (HQ828141.1) were dominant in all groups. Therefore, the probiotics exhibited strong potential for the development of herb residues in this study, and the products showed strong potential in curing H. pylori infections.

Meng, H., Ba, Z., Lee, Y., Peng, J., Lin, J., Fleming, J. A., Furumoto, E. J., Roberts, R. F., Kris-Etherton, P. M., and Rogers, C. J. Consumption of Bifidobacterium animalis subsp. lactis BB-12 in yogurt reduced expression of TLR-2 on peripheral blood-derived monocytes and pro-inflammatory cytokine secretion in young adults. Eur.J.Nutr. 2017; 56(2):649-661; PM: 26621631

ABSTRACT: PURPOSE: Probiotic bacteria modulate immune parameters and inflammatory outcomes. Emerging evidence demonstrates that the matrix used to deliver probiotics may influence the efficacy of probiotic interventions in vivo. The aims of the current study were to evaluate (1) the effect of one species, Bifidobacterium animalis subsp. lactis BB-12 at a dose of log10 +/- 0.5 CFUs/day on immune responses in a randomized, partially blinded, 4-period crossover, free-living study, and (2) whether the immune response to BB-12 differed depending on the delivery matrix. *METHODS*: Healthy adults (n = 30) aged 18-40 years were recruited and received four treatments in a random order: (A) yogurt smoothie alone; smoothie with BB-12 added (B) before or (C) after yogurt fermentation, or (D) BB-12 given in capsule form. At baseline and after each 4-week treatment, peripheral blood mononuclear cells (PBMCs) were isolated, and functional and phenotypic marker expression was assessed. *RESULTS*: BB-12 interacted with peripheral myeloid cells via Toll-like receptor 2 (TLR-2). The percentage of CD14+HLA-DR+ cells in peripheral blood was increased in male participants by all yogurt-containing treatments compared to baseline ($p = 0.0356$). Participants who consumed yogurt smoothie with BB-

12 added post-fermentation had significantly lower expression of TLR-2 on CD14+HLA-DR+ cells (p = 0.0186) and reduction in TNF-alpha secretion from BB-12- (p = 0.0490) or LPS-stimulated (p = 0.0387) PBMCs compared to baseline. *CONCLUSIONS*: These findings not only demonstrate a potential anti-inflammatory effect of BB-12 in healthy adults, but also indicate that the delivery matrix influences the immunomodulatory properties of BB-12.

Mezzasalma, V., Manfrini, E., Ferri, E., Boccarusso, M., Di, Gennaro P., Schiano, I., Michelotti, A., and Labra, M. Orally administered multispecies probiotic formulations to prevent uro-genital infections: a randomized placebo-controlled pilot study. Arch.Gynecol.Obstet. 2017; 295(1):163-172; PM: 27826653

ABSTRACT: PURPOSE: The aim of this study was to evaluate in the vagina of 60 pre-menopausal women the detection of orally administered multispecies probiotic formulations showing anti-microbial properties in test in vitro. *METHODS*: A randomized, double-blind, three-arm parallel pilot study was carried out on 60 pre-menopausal women. Subjects were randomly divided in three groups (F_1, F_2, F_3). Each group received a daily oral administration of probiotic mixtures (for 14 days and at the day 21, 7 days after the wash-out) containing: Lactobacillus acidophilus and Lactobacillus reuteri (F_1), or Lactobacillus plantarum, Lactobacillus rhamnosus and Bifidobacterium animalis subsp. lactis (F_2), or placebo (F_3), respectively. Vaginal swabs were collected at four experimental times, at t0 and at t7, t14 and t21 days, and analyzed by qPCR. At the same time, the anti-microbial activity of the probiotic formulations was verified by assays in vitro against microorganisms as Escherichia coli and Candida albicans. *RESULTS*: L. acidophilus and L. reuteri as well as L. plantarum, L. rhamnosus and B. lactis were significantly increased on 7 days in the groups administered with F_1 and F_2, respectively, compared to group F_3. A similar significant trend was observed on 21 days, 7 days after the wash-out. F_1 and F_2 showed coherent anti-microbial properties. *CONCLUSION*: Both probiotic formulations F_1 and F_2, chosen because of their anti-microbial activity against pathogens responsible for vaginal dysbiosis and infections, led to vaginal detection and enhancement of the amount of species of formulates when orally administered. This work provides the basis for further clinical investigations of the F_1 and F_2 capacity to prevent or treat uro-genital infections.

Minami, N., Matsuura, M., Koshikawa, Y., Yamada, S., Honzawa, Y., Yamamoto, S., and Nakase, H. Maternal and fetal outcomes in pregnant Japanese women with inflammatory bowel disease: our experience with a series of 23 cases. Intest.Res. 2017; 15(1):90-96; PM: 28239318

ABSTRACT: BACKGROUND/AIMS: Our physicians work to expand the possibilities to treat female patients with inflammatory bowel disease (IBD) who wish to become pregnant. Although many drugs, including 5-aminosalicylate (5-ASA), corticosteroids, immunomodulators, and biologics, are used safely during pregnancy, few reports have described the therapeutic regimen throughout pregnancy and the management of patients who relapse during pregnancy precisely. The aim of this study was to assess the management of patients with IBD during pregnancy. *METHODS*: We identified 19 patients (five with Crohn's disease and 14 with ulcerative colitis [UC]) who became pregnant with a total of 23 pregnancies between May 2005 and May 2015 by reviewing the medical records of Kyoto University Hospital. The following data were collected: the maternal variables, the IBD treatment type, the disease activity, the pregnancy outcome, and the

mode of delivery. *RESULTS*: Among the 19 patients, 18 had become pregnant after being diagnosed with IBD, while one had developed UC newly after pregnancy. Throughout the gestation, all patients were treated with probiotics, 5-ASA, prednisolone, cytapheresis, or infliximab. The relapse rate during pregnancy was 21.7% (5/23 cases). The five patients who experienced a relapse were able to pursue their pregnancy after intensification of their treatments. There were no adverse fetal or neonatal problems, except in one case that required an emergency Caesarean section because of placental dysfunction and in which a very low-birth-weight infant was born preterm. *CONCLUSIONS*: Our present data confirmed that even if the disease flares up during pregnancy, good pregnancy outcomes can be achieved with an optimal intensification of the patient's treatment.

Mingmongkolchai, S. and Panbangred, W. In vitro evaluation of candidate Bacillus spp. for animal feed. J.Gen.Appl.Microbiol. 5-12-2017; 63(2):147-156; PM: 28331163

ABSTRACT: The aim of this study was to select aerobic spore-formers for animal feed based on their in vitro probiotic potential, including their enzyme-producing ability and safety assessment. Seven isolates out of 187 spore-forming bacteria were selected for their ability to produce cellulase (89.21-1668.32 U/ml), xylanase (1399.68-4351.10 U/ml), and phytase (2.72-28.70 U/ml). Among seven isolates, five had activities towards a broad range of p-nitrophenyl esters with acyl chain lengths from C2 to C12. The probiotic properties of all selected isolates varied with respect to their acid and bile salt tolerance under simulated gastrointestinal tract (GIT) conditions, and their adherence ability to human intestinal cell lines (Caco-2 and HT-29). The safety assessment revealed that the isolate CM40 was not cytotoxic to Caco-2 and HT-29, did not exhibit hemolytic activity, carried no enterotoxin or emetic toxin genes, and was susceptible to ten antibiotics, including six key antibiotics (chloramphenicol, erythromycin, gentamicin, tetracycline, streptomycin, and kanamycin) as recommended by the European Food Safety Authority (EFSA). Co-incubation of isolate CM40 with enteric bacteria (Salmonella Typhi, Salmonella Enteritidis 1781, and Escherichia coli) demonstrated that CM40 significantly decreased the number of pathogens (about 30-48%) adhering to Caco-2 and HT-29 ($P < 0.05$). Analysis of gene encoding 16*S* rRNA, gyrase A (gyrA) and the cheA histidine kinase revealed that CM40 belongs to Bacillus subtilis. On the basis of probiotic properties and basic safety aspects, the B. subtilis strain CM40 was found to possess desirable in vitro probiotic properties, and may be a potential candidate for supplementation of animal feed.

Miraglia Del, Giudice M., Indolfi, C., Capasso, M., Maiello, N., Decimo, F., and Ciprandi, G. Bifidobacterium mixture (B longum BB536, B infantis M-63, B breve M-16V) treatment in children with seasonal allergic rhinitis and intermittent asthma. Ital.J.Pediatr. 3-7-2017; 43(1):25; PM: 28270216

ABSTRACT: BACKGROUND: Allergic rhinitis (AR) and allergic asthma are caused by an IgE-mediated inflammatory reaction. Probiotics may exert anti-inflammatory and immune-modulatory activity. Thus, this study aimed at investigating whether a Bifidobacteria mixture could be able to relieve nasal symptoms, and affect quality of life (QoL) in children with AR and intermittent asthma due to Parietaria allergy. *MATERIALS AND METHODS*: The present study was conducted as placebo-controlled, double-blinded, and randomized. Globally, 40 children (18 males; mean age 9 +/- 2.2 years) were enrolled. They were treated with probiotics or placebo: 1 sachet/day for 4 weeks. AR

symptoms, and QoL were assessed at baseline and after treatment. Use of rescue medications, such as cetirizine syrup and salbutamol spray, was also permitted and recorded. *RESULTS*: Children treated with probiotic mixture achieved a significant improvement of symptoms ($p < 0.005$), and QoL (($p < 0.001$). Placebo group had worsening of symptoms ($p < 0.005$) and QoL ($p < 0.001$). The use of rescue medications was overlapping in the two groups. The intergroup analysis showed that probiotic mixture was significantly superior than placebo for all parameters. *CONCLUSIONS*: The current study demonstrated that a Bifidobacteria mixture was able of significantly improving AR symptoms and QoL in children with pollen-induced AR and intermittent asthma. *CLINICAL TRIAL REGISTRATION*: ClinicalTrials.gov ID NCT02807064.

Miyazima, T. Y., Ishikawa, K. H., Mayer, M., Saad, S., and Nakamae, A. Cheese supplemented with probiotics reduced the Candida levels in denture wearers-RCT. Oral Dis. 3-27-2017; PM: 28346730

ABSTRACT: OBJECTIVES: The access to probiotics should be facilitated in order to encourage their usage. We evaluated the effect of consumption of two experimental probiotic-containing cheeses on the oral colonization of Candida in denture wearers. *METHODS*: Sixty denture wearers harboring oral Candida were randomly allocated in groups who received cheese supplemented with Lactobacillus acidophilus NCFM (T1) or Lactobacillus rhamnosus Lr-32 (T2), daily for 8 weeks, and a control group (C) who received a control cheese. Oral samples were obtained through a mouthwash, and Candida levels were determined (CFU/mL) at baseline and after the 8-week experimental period. *RESULTS*: At baseline, the mean levels of Candida spp. (log CFU/mL) were similar among the groups. However, the mean levels of Candida were significantly reduced in groups T1 and T2 but not in C (Tukey, $p<.05$). The reduction in Candida oral levels occurred independently on the colonizing Candida species, participant age, and use of bi- or unimaxillary dentures. *CONCLUSIONS*: Daily consumption of cheese supplemented with probiotics, with either L. acidophilus NCFM or L. rhamnosus Lr-32, was able to reduce the colonization of oral Candida in complete denture wearers, suggesting its potential in reducing the risk of oral candidiasis in this highly susceptible population.

Mizoguchi, T., Kasahara, K., Yamashita, T., Sasaki, N., Yodoi, K., Matsumoto, T., Emoto, T., Hayashi, T., Kitano, N., Yoshida, N., Amin, H. Z., and Hirata, K. I. Oral administration of the lactic acid bacterium Pediococcus acidilactici attenuates atherosclerosis in mice by inducing tolerogenic dendritic cells. Heart Vessels. 2-8-2017; PM: 28181012

ABSTRACT: The intestinal microbiota appears to play an important role in the development of atherosclerosis. We investigated the effect of the probiotic lactic acid bacterium Pediococcus acidilactici R037 on atherosclerosis using apolipoprotein E-deficient (ApoE -/-) mice. Six-week-old ApoE -/- mice were orally administered R037 six times a week. Mice treated with R037 for 12 weeks exhibited markedly attenuated atherosclerotic lesions in the aortic root (2.3 +/- 0.15 x 105 microm2 vs. 3.3 +/- 0.29 x 105 microm2, respectively; $P < 0.01$; $n = 15$-17 each group). The expression of Ki-67 in CD4+ T cells, the population of interferon gamma-producing CD4+ T cells in the spleen, and pro-inflammatory cytokine production from splenic lymphocytes were significantly decreased in R037-treated mice. Interestingly, splenic dendritic cells (DCs) isolated from R037-treated mice suppressed CD4+ T-cell proliferation and pro-inflammatory cytokine production ex vivo, suggesting that R037 treatment induced tolerogenic DCs.

Programmed cell death ligand 1 expression in DCs was significantly enhanced in R037-treated mice, which might explain the immunosuppressive effect of DCs at least in part. These results indicate that R037 attenuates atherosclerosis by inducing tolerogenic DCs, which suppress Th1-driven inflammation and the proliferative activity of CD4+ T cells. Our findings may provide a novel therapeutic approach for the prevention of atherosclerosis based on dietary supplementation with probiotics.

Mofidi, F., Poustchi, H., Yari, Z., Nourinayyer, B., Merat, S., Sharafkhah, M., Malekzadeh, R., and Hekmatdoost, A. Synbiotic supplementation in lean patients with non-alcoholic fatty liver disease: a pilot, randomised, double-blind, placebo-controlled, clinical trial. Br.J.Nutr. 2017; 117(5):662-668; PM: 28345499

ABSTRACT: Although non-alcoholic fatty liver disease (NAFLD) is the leading aetiology of liver disorders in the world, there is no proven treatment for NAFLD patients with normal or low BMI. The aim of this study was to evaluate the efficacy of synbiotics supplementation in NAFLD patients with normal or low BMI. In this randomised, double-blind, placebo-controlled, clinical trial, fifty patients with NAFLD were assigned to take either a synbiotic supplement or a placebo capsule for 28 weeks. Both groups were advised to follow a healthy lifestyle. At the end of the study, hepatic steatosis and fibrosis reduced in both groups; however, the mean reduction was significantly greater in the synbiotic group rather than in the placebo group (P<0.001). Furthermore, serum levels of fasting blood sugar, TAG and most of the inflammatory mediators reduced in the synbiotic group significantly compared with the placebo group (P<0.05). Our results provide evidence that synbiotic supplementation improves the main features of NAFLD in patients with normal and low BMI, at least partially through reduction in inflammatory indices. Further studies are needed to address the exact mechanism of action of these effects.

Moggia, E., Koti, R., Belgaumkar, A. P., Fazio, F., Pereira, S. P., Davidson, B. R., and Gurusamy, K. S. Pharmacological interventions for acute pancreatitis. Cochrane.Database.Syst.Rev. 4-21-2017; 4:CD011384; PM: 28431202

ABSTRACT: BACKGROUND: In people with acute pancreatitis, it is unclear what the role should be for medical treatment as an addition to supportive care such as fluid and electrolyte balance and organ support in people with organ failure. *OBJECTIVES*: To assess the effects of different pharmacological interventions in people with acute pancreatitis. *SEARCH METHODS*: We searched the Cochrane Central Register of Controlled Trials (CENTRAL, 2016, Issue 9), MEDLINE, Embase, Science Citation Index Expanded, and trial registers to October 2016 to identify randomised controlled trials (RCTs). We also searched the references of included trials to identify further trials. *SELECTION CRITERIA*: We considered only RCTs performed in people with acute pancreatitis, irrespective of aetiology, severity, presence of infection, language, blinding, or publication status for inclusion in the review. *DATA COLLECTION AND ANALYSIS*: Two review authors independently identified trials and extracted data. We did not perform a network meta-analysis as planned because of the lack of information on potential effect modifiers and differences of type of participants included in the different comparisons, when information was available. We calculated the odds ratio (OR) with 95% confidence intervals (CIs) for the binary outcomes and rate ratios with 95% CIs for count outcomes using a fixed-effect model and random-effects model. *MAIN RESULTS*: We included 84 RCTs with 8234 participants in this review. Six trials (N = 658) did not report any of the outcomes of interest for this review. The remaining 78 trials excluded 210 participants

after randomisation. Thus, a total of 7366 participants in 78 trials contributed to one or more outcomes for this review. The treatments assessed in these 78 trials included antibiotics, antioxidants, aprotinin, atropine, calcitonin, cimetidine, EDTA (ethylenediaminetetraacetic acid), gabexate, glucagon, iniprol, lexipafant, NSAIDs (non-steroidal anti-inflammatory drugs), octreotide, oxyphenonium, probiotics, activated protein C, somatostatin, somatostatin plus omeprazole, somatostatin plus ulinastatin, thymosin, ulinastatin, and inactive control. Apart from the comparison of antibiotics versus control, which included a large proportion of participants with necrotising pancreatitis, the remaining comparisons had only a small proportion of patients with this condition. Most trials included either only participants with severe acute pancreatitis or included a mixture of participants with mild acute pancreatitis and severe acute pancreatitis (75 trials). Overall, the risk of bias in trials was unclear or high for all but one of the trials. *SOURCE OF FUNDING*: seven trials were not funded or funded by agencies without vested interest in results. Pharmaceutical companies partially or fully funded 21 trials. The source of funding was not available from the remaining trials.Since we considered short-term mortality as the most important outcome, we presented only these results in detail in the abstract. Sixty-seven studies including 6638 participants reported short-term mortality. There was no evidence of any differences in short-term mortality in any of the comparisons (very low-quality evidence). With regards to other primary outcomes, serious adverse events (number) were lower than control in participants taking lexipafant (rate ratio 0.67, 95% CI 0.46 to 0.96; N = 290; 1 study; very low-quality evidence), octreotide (rate ratio 0.74, 95% CI 0.60 to 0.89; N = 770; 5 studies; very low-quality evidence), somatostatin plus omeprazole (rate ratio 0.36, 95% CI 0.19 to 0.70; N = 140; 1 study; low-quality evidence), and somatostatin plus ulinastatin (rate ratio 0.30, 95% CI 0.15 to 0.60; N = 122; 1 study; low-quality evidence). The proportion of people with organ failure was lower in octreotide than control (OR 0.51, 95% CI 0.27 to 0.97; N = 430; 3 studies; very low-quality evidence). The proportion of people with sepsis was lower in lexipafant than control (OR 0.26, 95% CI 0.08 to 0.83; N = 290; 1 study; very low-quality evidence). There was no evidence of differences in any of the remaining comparisons in these outcomes or for any of the remaining primary outcomes (the proportion of participants experiencing at least one serious adverse event and the occurrence of infected pancreatic necrosis). None of the trials reported heath-related quality of life. *AUTHORS' CONCLUSIONS*: Very low-quality evidence suggests that none of the pharmacological treatments studied decrease short-term mortality in people with acute pancreatitis. However, the confidence intervals were wide and consistent with an increase or decrease in short-term mortality due to the interventions. We did not find consistent clinical benefits with any intervention. Because of the limitations in the prognostic scoring systems and because damage to organs may occur in acute pancreatitis before they are clinically manifest, future trials should consider including pancreatitis of all severity but power the study to measure the differences in the subgroup of people with severe acute pancreatitis. It may be difficult to power the studies based on mortality. Future trials in participants with acute pancreatitis should consider other outcomes such as complications or health-related quality of life as primary outcomes. Such trials should include health-related quality of life, costs, and return to work as outcomes and should follow patients for at least three months (preferably for at least one year).

Mohd Nor, N. 'N., Abbasiliasi, S., Marikkar, M. N., Ariff, A., Amid, M., Lamasudin, D. U., bdul Manap, M. Y., and Mustafa, S. Defatted coconut residue crude polysaccharides as potential prebiotics: study of their effects on proliferation and acidifying activity of probiotics in vitro. J.Food Sci.Technol. 2017; 54(1):164-173; PM: 28242914

ABSTRACT: This paper reports on the extraction, partial characterization and the potential application of crude polysaccharides from defatted coconut residue as a prebiotic. The coconut residue was defatted and extracted to obtain the crude polysaccharides and its physicochemical properties were determined. The crude polysaccharides were assessed for monosaccharide composition, total carbohydrate content, reducing sugar concentration and protein content determination. The functional group and structural elucidation of crude polysaccharides was also done using Fourier transform infrared spectra analysis. The product was then subjected to artificial human gastric juice treatment to determine digestibility. Finally, an in vitro proliferation and acid production by two probiotic bacteria namely Lactobacillus casei Shirota and Lactobacillus bulgaricus were included in this study. It was found that the defatted coconut residue contained ash (0.54%), moisture (55.42%), protein (1.69%), crude fat (17.26%) and carbohydrate (25.73%). The percentage of crude polysaccharides extracted was 0.73 +/- 0.04. The two fractions of monosaccharides obtained were glucose and fructose. Total carbohydrate content of DCR was 13.35% (w/v). The quantitative value of the reducing sugars obtained was 20.71%. Protein content in the crude polysaccharides was 0.009% and the peaks which indicated the presence of protein were observed at around 1640 cm-1 (amide I) and 1530 cm-1 (amide II). DCR crude polysaccharides were highly resistant (88%) to hydrolysis when subjected to artificial human gastric juice. The product was found to markedly stimulate two tested probiotics to proliferate and produce organic acids. All the above findings are supportive of the fact that polysaccharides extracted from DCR, an industrial waste, have a vast potential to be exploited as novel prebiotics.

Mokhtari, S., Jafari, S. M., Khomeiri, M., Maghsoudlou, Y., and Ghorbani, M. The cell wall compound of Saccharomyces cerevisiae as a novel wall material for encapsulation of probiotics. Food Res.Int. 2017; 96:19-26; PM: 28528098

ABSTRACT: Yeast cell wall is known as a food grade ingredient which is recently being used increasingly as a novel coating for encapsulation of different materials in the food industry. This application is limited to core materials smaller than yeast in size. In this study, we have tried to encapsulate larger particles by crushing yeast cells. Hence, probiotic bacteria of Lactobacillus acidophilus and Bifidobacterium bifidum were encapsulated firstly by calcium alginate using the emulsion method and these microbeads were coated again by Saccharomyces cerevisiae cell wall compound and another layer of calcium alginate. The average diameter of microcapsules for single layer microbeads (M), microbeads coated by two layers of alginate (MCA), and microbeads coated by a layer of yeast cell and two layers of alginate (MCYA) were 54.25+/-0.18, 77.43+/-8.24 and 103.66+/-13.33mum, respectively. In simulated gastrointestinal conditions, there was a significant (P<0.05) enhancement in resistance of L. acidophilus when applying a layer of S. cerevisiae cell wall compound. For MCA and MCYA after 2h exposure to simulated gastric juice, it was revealed a log reduction of 1.53+/-0.1 and 1.1+/-0.02 with pH1.55 and in simulated intestinal juice, 2.92+/-0.04 and 2.42+/-0.06 with 0.6% bile after previous 1h incubation in gastric conditions, respectively. It can be concluded that the cell wall compound of S. cerevisiae is a suitable protective coating for probiotics and it can improve the survival of probiotics within food products.

Mokhtari, Z., Gibson, D. L., and Hekmatdoost, A. Nonalcoholic Fatty Liver Disease, the Gut Microbiome, and Diet. Adv.Nutr. 2017; 8(2):240-252; PM: 28298269

ABSTRACT: Nonalcoholic fatty liver disease (NAFLD) is the most common liver disorder in the world, yet the pathogenesis of the disease is not well elucidated. Due to the close anatomic and functional association between the intestinal lumen and the liver through the portal system, it is speculated that the gut microbiome may play a pivotal role in the pathogenesis of NAFLD. Furthermore, diet, which can modulate the gut microbiome and several metabolic pathways involved in NAFLD development, shows a potential tripartite relation between the gut, diet, and the liver. In this review, we summarize the current evidence that supports the association between NAFLD, the gut microbiome, and the role of diet.

Mokkala, K., Roytio, H., Ekblad, U., and Laitinen, K. Opportunities for probiotics and polyunsaturated fatty acids to improve metabolic health of overweight pregnant women. Benef.Microbes. 2-7-2017; 8(1):3-15; PM: 27936867

ABSTRACT: Overweight during pregnancy predisposes both the mother and foetus to health complications. Maternal complications include gestational diabetes, obstetric problems and type 2 diabetes later in life. Complications for the offspring are not only restricted to the foetal period or birth, such as prematurity and foetal macrosomia, but may also have long-term metabolic health implications through the mechanism of early nutrition programming. One of the key metabolic components characterising overweight in the non-pregnant state is low-grade inflammation manifested by elevated levels of circulatory pro-inflammatory cytokines. In pregnancy, in addition to adipose tissue and placenta, inflammatory response may originate from the gut. The extent to which overweight induces metabolic maladaptation during pregnancy and further compromises maternal and child health is currently poorly understood. In this review, we evaluate recent scientific literature and describe the suggested links between overweight, gut and low-grade inflammation associated metabolic disorders. We focus on overweight pregnant women and gestational diabetes, and discuss how specific dietary factors, probiotics and long-chain polyunsaturated fatty acids (fish oil), might confer health benefits in combatting against metabolic risk factors.

Moller, C. M., Olsa, E. J. A., Ginty, A. T., Rapelje, A. L., Tindall, C. L., Holesh, L. A., Petersen, K. L., and Conklin, S. M. Influence of acute multi-species and multi-strain probiotic supplementation on cardiovascular function and reactivity to psychological stress in young adults: a double-blind, randomized, placebo-controlled trial. Psychosom.Med. 5-12-2017; PM: 28498275

ABSTRACT: OBJECTIVE: The potential influence of probiotic supplementation on cardiovascular health and stress responsivity remains largely unexplored. Some evidence suggests the possibility that probiotics may influence blood pressure. A separate body of research suggests that exaggerated cardiovascular reactions to acute psychological stress in the laboratory predict cardiovascular morbidity and mortality. The current investigation explored the effect of acute probiotic use on: 1) resting cardiovascular measures in healthy young adults and 2) cardiovascular and psychological reactions to an acute psychological stressor in the laboratory. *METHOD*: Participants (N = 105, M age = 20.17 SD = 1.26, 84.8% white) completed a two-week, double blind and placebo-controlled trial of a multi-species and multi-strain probiotic. Exclusion criteria included prior probiotic use, diagnosed GI disorder, and/or current antibiotic use. At visit one and two, participants completed the Paced Auditory Serial Addition Test, a widely-used psychological stress task. Participants were randomly assigned to a probiotic blend or

matched placebo. *RESULTS*: Compared to placebo, two-week probiotic supplementation did not affect resting measures of cardiovascular function, cardiovascular responses during or recovery from stress, or psychological reactions to acute psychological stress. *CONCLUSIONS*: Contrary to expectations, short term use of a probiotic supplement in healthy participants did not influence measures of cardiovascular function or responsivity to psychological stress. Future research is needed to determine species and strain specific effects of probiotics in healthy participants with various degrees of stress responsiveness, as well as in diseased populations.

Moller, M. S., Goh, Y. J., Rasmussen, K. B., Cypryk, W., Celebioglu, H. U., Klaenhammer, T. R., Svensson, B., and Abou, Hachem M. An extracellular cell-attached pullulanase confers branched alpha-glucan utilization in human gut Lactobacillus acidophilus. Appl.Environ.Microbiol. 4-14-2017; PM: 28411221

ABSTRACT: Of the few predicted extracellular glycan-active enzymes, glycoside hydrolase family 13 subfamily 14 (GH13_14) pullulanases are the most common in human gut lactobacilli. These enzymes share a unique modular organization, not observed in other bacteria, featuring a catalytic module, two starch binding modules, a domain of unknown function, and a C-terminal surface layer association protein (SLAP) domain. Here we explore the specificity of a representative of this group of pullulanases, LaPul13_14 and its role in branched alpha-glucans metabolism in the well characterized Lactobacillus acidophilus NCFM that is widely used as a probiotic. Growth experiments of L. acidophilus NCFM on starch-derived branched substrates revealed preference for alpha-glucans with short branches of about two to three glucosyl moieties over amylopectin with longer branches. Cell-attached debranching activity was measurable in the presence of alpha-glucans but was repressed by glucose. The debranching activity is conferred exclusively by LaPul13_14 and is abolished in a mutant strain lacking a functional LaPul13_14 gene. Hydrolysis kinetics of recombinant LaPul13_14 confirmed the preference for short branched alpha-glucan oligomers consistent with the growth data. Curiously, this enzyme displayed the highest catalytic efficiency and the lowest Km reported for a pullulanase. Inhibition kinetics revealed mixed inhibition by beta-cyclodextrin suggesting the presence of additional glucan binding sites besides the active site of the enzyme, which may contribute to the unprecedented substrate affinity. The enzyme also displays high thermostability and higher activity in the acidic pH range reflecting adaptation to the physiologically challenging conditions in the human gut.IMPORTANCE Starch is one of the most abundant glycans in human diet. Branched alpha-1,6-glucans in dietary starch and glycogen are non-degradable by human enzymes and constitute a metabolic resource for the gut microbiota. The role of health-beneficial lactobacilli prevalent in the human small intestine in starch metabolism remains unexplored in contrast to colonic bacterial residents.This study highlights the pivotal role of debranching enzymes in the break-down of starchy branched alpha-glucan oligomers (alpha-limit dextrins) by human gut lactobacilli exemplified by Lactobacillus acidophilus NCFM, which is one of the best characterized strains used as probiotics.Our data bring novel insight into the metabolic preference of L. acidophilus for alpha-glucans with short alpha-1,6-branches. The unprecedented affinity of the debranching enzyme that confers growth on these substrates reflects its adaptation to the nutrient-competitive gut ecological niche and constitutes a potential advantage in cross-feeding from human and bacterial dietary starch metabolism.

Mongardini, C., Pilloni, A., Farina, R., Di, Tanna G., and Zeza, B. Adjunctive efficacy of probiotics in the treatment of experimental peri-implant mucositis with mechanical and photodynamic therapy: a randomized, cross-over clinical trial. J.Clin.Periodontol. 2017; 44(4):410-417; PM: 28032908

ABSTRACT: AIM: To evaluate the adjunctive clinical efficacy of probiotics in the treatment of peri-implant mucositis (p-iM) with professionally administered plaque removal (PAPR) and photodynamic therapy (PDT). *MATERIALS AND METHODS*: Following p-iM induction, patients underwent PAPR + PDT and were randomly assigned to receive the professional and home-based administration of probiotics (Lactobacillus plantarum and Lactobacillus brevis) (test treatment) or placebo preparation (control treatment) according to a cross-over design. Clinical parameters were assessed at six sites for each implant before as well as at 2 and 6 weeks after professional treatment administration. *RESULTS*: Twenty patients contributing one dental implant each were included. Immediately before treatment and at 6 weeks, the median number of sites with bleeding on probing (BoP+) sites per implant unit was 4 (3-6) and 2 (0-2) ($p < 0.001$), respectively, for test treatment, and 3.5 (2-4) and 2 (0-3) ($p = 0.03$), respectively, for control treatment. No significant difference in clinical outcomes was observed between treatment groups. *CONCLUSION*: The combination of PAPR and PDT either alone or associated with probiotics determined a significant reduction in the number of BoP+ sites at 2 and 6 weeks around implants with p-iM. The adjunctive use of probiotics did not significantly enhance the clinical outcomes of PAPR + PDT.

Morrow, L. E. and Wischmeyer, P. Blurred Lines: Dysbiosis and Probiotics in the ICU. Chest. 2017; 151(2):492-499; PM: 27771302

ABSTRACT: Clinicians have traditionally dichotomized bacteria as friendly commensals or harmful pathogens. However, the line separating the two has become blurred with the recognition that the intestinal microbiome is a complex entity in which species can shift sides-from friend to foe and back again-based on crucial factors in their local environment. Significant disruptions in the homeostasis of the microbiome, a phenomenon called dysbiosis, is increasingly associated with a host of untoward effects. Patients in the ICU are at high risk for dysbiosis given the high rate of antibiotic use, acute changes in diet, and the stress of critical illness. Probiotics are living microbes of human origin that when ingested in sufficient quantities, can colonize sites such as the oropharynx and GI tract and provide benefits to the host. In recent years, we have increasingly explored the utility of using probiotics to reverse the intestinal dysbiosis associated with critical illness, thereby reducing select ICU complications associated with increased morbidity and mortality. Although these preliminary efforts have demonstrated varying degrees of success, our present studies suffer from a host of limitations that hinder the strength of their conclusions and the generalizability of their results. Probiotic investigations have been further hobbled by current regulatory requirements, which were designed to serve as the framework for pharmaceutical research. Although such measures are intended to ensure patient safety, they inadvertently impose barriers that stifle innovation regarding nutraceuticals. This review strives to summarize the current evidence regarding the efficacy and safety of probiotics in the ICU as well as to provide an overview of the obstacles probiotic researchers face going forward.

Moshiri, M., Dallal, M. M. S., Rezaei, F., Douraghi, M., Sharifi, L., Noroozbabaei, Z., Gholami, M., and Mirshafiey, A. The Effect of Lactobacillus acidophilus PTCC 1643 on Cultured Intestinal

Epithelial Cells Infected with Salmonella enterica serovar Enteritidis. Osong.Public Health Res.Perspect. 2017; 8(1):54-60; PM: 28443224

ABSTRACT: OBJECTIVES: Gastrointestinal disorders caused by Salmonella enterica serovar Enteritidis (SesE) are a significant health problem around the globe. Probiotic bacteria have been shown to have positive effects on the immune responses. Lactobacillus acidophilus was examined for its capability to influence the innate immune response of HT29 intestinal epithelial cells towards SesE. The purpose of this work was to assess the effect of L. acidophilus PTCC 1643 on cultured intestinal epithelial cells infected with SesE. *METHODS*: HT29 cells were cultured in Roswell Park Memorial Institute medium supplemented with 10% fetal bovine serum and 1% penicillin/streptomycin. The cells were treated with L. acidophilus PTCC 1643 after or before challenge with SesE. At 2 and 4 hours post-infection, we measured changes in the expression levels of TLR2 and TLR4 via real-time polymerase chain reaction. RESULTS: Treatment with L. acidophilus inhibited SesE-induced increases in TLR2 and TLR4 expression in the infected HT29 cells. Moreover, the expression of TLR2 and TLR4 in cells that were pretreated with L. acidophilus and then infected with SesE was significantly higher than that in cells infected with SesE without pretreatment. Taken together, the results indicated that L. acidophilus had an anti-inflammatory effect and modulated the innate immune response to SesE by influencing TLR2 and TLR4 expression. *CONCLUSION*: Our findings suggested that L. acidophilus PTCC 1643 was able to suppress inflammation caused by SesE infection in HT29 cells and reduce TLR2 and TLR4 expression. Additional in vivo and in vitro studies are required to further elucidate the mechanisms underlying this anti-inflammatory effect.

Mourand, G., Paboeuf, F., Fleury, M. A., Jouy, E., Bougeard, S., Denamur, E., and Kempf, I. Escherichia coli Probiotic Strain ED1a in Pigs Has a Limited Impact on the Gut Carriage of Extended-Spectrum-beta-Lactamase-Producing E. coli. Antimicrob.Agents Chemother. 2017; 61(1); PM: 27795372

ABSTRACT: Four trials were conducted to evaluate the impact of Escherichia coli probiotic strain ED1a administration to pigs on the gut carriage or survival in manure of extended-spectrum-beta-lactamase-producing E. coli Groups of pigs were orally inoculated with strain E. coli M63 carrying the blaCTX-M-1 gene (n = 84) or used as a control (n = 26). In the first two trials, 24 of 40 E. coli M63-inoculated pigs were given E. coli ED1a orally for 6 days starting 8 days after oral inoculation. In the third trial, 10 E. coli M63-inoculated pigs were given either E. coli ED1a or probiotic E. coli Nissle 1917 for 5 days. In the fourth trial, E. coli ED1a was given to a sow and its 12 piglets, and these 12 piglets plus 12 piglets that had not received E. coli ED1a were then inoculated with E. coli M63. Fecal shedding of cefotaxime-resistant Enterobacteriaceae (CTX-RE) was studied by culture, and blaCTX-M-1 genes were quantified by PCR. The persistence of CTX-RE in manure samples from inoculated pigs or manure samples inoculated in vitro with E. coli M63 with or without probiotics was studied. The results showed that E. coli M63 and ED1a were good gut colonizers. The reduction in the level of fecal excretion of CTX-RE in E. coli ED1a-treated pigs compared to that in nontreated pigs was usually less than 1 log10 CFU and was mainly observed during the probiotic administration period. The results obtained with E. coli Nissle 1917 did not differ significantly from those obtained with E. coli ED1a. CTX-RE survival did not differ significantly in manure samples with or without probiotic treatment. In conclusion, under our experimental conditions, E. coli ED1a and E. coli Nissle 1917 could not durably prevent CTX-RE colonization of the pig gut.

Mousa, H. A. Prevention and Treatment of Influenza, Influenza-Like Illness, and Common Cold by Herbal, Complementary, and Natural Therapies. J.Evid.Based.Complementary.Altern.Med. 2017; 22(1):166-174; PM: 27055821

ABSTRACT: In recent years viral respiratory tract infections, especially influenza viruses, have had a major impact on communities worldwide as a result of unavailability of effective treatment or vaccine. The frequent alterations in the antigenic structures of respiratory viruses, particularly for RNA viruses, pose difficulties in production of effective vaccines. The unavailability of optimal medication and shortage of effective vaccines suggests the requirement for alternative natural therapies. Several herbal remedies were used for prevention and treatment viral respiratory illnesses. Among those that were found effective included maoto, licorice roots, antiwei, North American ginseng, berries, Echinacea, plants extracted carnosic acid, pomegranate, guava tea, and Bai Shao. There is scientific evidence regarding the effectiveness of several complementary therapies for colds. Oral zinc may reduce the length and severity of a cold. Taking vitamin C supplements on a regular basis only slightly reduces the length and severity of colds. Probiotics were found better than placebo in reducing the number episodes of acute upper respiratory tract infections, the rate of episodes of acute upper respiratory tract infection and reducing antibiotic use. Alkaline diets or drinks might have antiviral properties as in vitro studies demonstrated inactivation effect of alkaline medium on respiratory virus. Earthing might have a natural anti-inflammatory effect for human body. It is now accepted that an overwhelming inflammatory response is the cause of human deaths from avian H5N1 influenza infection. Earthing accelerates immune response following vaccination, as demonstrated by increases of gamma globulin concentration. No in vivo or clinical studies were found that investigate the role of alkalization or earthing on respiratory viral infections. Thus, future studies are recommended to reveal any potential curative effects.

Moya-Perez, A., Luczynski, P., Renes, I. B., Wang, S., Borre, Y., Anthony, Ryan C., Knol, J., Stanton, C., Dinan, T. G., and Cryan, J. F. Intervention strategies for cesarean section-induced alterations in the microbiota-gut-brain axis. Nutr.Rev. 4-1-2017; PM: 28379454

ABSTRACT: Microbial colonization of the gastrointestinal tract is an essential process that modulates host physiology and immunity. Recently, researchers have begun to understand how and when these microorganisms colonize the gut and the early-life factors that impact their natural ecological establishment. The vertical transmission of maternal microbes to the offspring is a critical factor for host immune and metabolic development. Increasing evidence also points to a role in the wiring of the gut-brain axis. This process may be altered by various factors such as mode of delivery, gestational age at birth, the use of antibiotics in early life, infant feeding, and hygiene practices. In fact, these early exposures that impact the intestinal microbiota have been associated with the development of diseases such as obesity, type 1 diabetes, asthma, allergies, and even neurodevelopmental disorders. The present review summarizes the impact of cesarean birth on the gut microbiome and the health status of the developing infant and discusses possible preventative and restorative strategies to compensate for early-life microbial perturbations.

Mueller, M., Cavarkapa, A., Unger, F. M., Viernstein, H., and Praznik, W. Prebiotic potential of neutral oligo- and polysaccharides from seed mucilage of Hyptis suaveolens. Food Chem. 4-15-2017; 221:508-514; PM: 27979234

ABSTRACT: Prebiotics are selectively fermented by the gastrointestinal microflora, resulting in benefits to human health. The seed mucilage of Hyptis suaveolens contains neutral and acidic polysaccharides in a ratio of 1:1. The neutral polysaccharides consist of galactose, glucose and mannose whereas the acidic polysaccharides contain fucose, xylose and 4-O-methylglucuronic acid -residues. The growth of probiotics in the presence of total, acidic or neutral polysaccharides and oligosaccharides was tested using turbidity measurements. The majority (11 out of 14) of the tested probiotic strains significantly grew in the neutral fraction. Growth occurred with some time delay, but may be longer lasting than with other lower molecular prebiotics. The extent of growth increased with neutral polysaccharides from H. suaveolens corresponding to the externally available galactose units (20%). In conclusion, neutral poly- and oligosaccharides from H. suaveolens have a prebiotic potential characterized by a delayed but long lasting effect.

Muniz, F. W., Friedrich, S. A., Silveira, C. F., and Rosing, C. K. The impact of chewing gum on halitosis parameters: a systematic review. J.Breath.Res. 2-17-2017; 11(1):014001; PM: 28212110

ABSTRACT: This study aimed to analyze the impact of chewing gum on halitosis parameters. Three databases were searched with the following focused question: 'Can chewing gum additionally reduce halitosis parameters, such as organoleptic scores and volatile sulfur compounds (VSC), when compared to a control treatment'? Controlled clinical trials presenting at least two halitosis measurements (organoleptic scores and/or VSC) were included. Ten studies were included, and different active ingredients were used. One study was performed using a chewing gum without any active ingredient. Chewing gum containing probiotic bacterium was shown to significantly reduce the organoleptic scores. Chewing gums containing zinc acetate and magnolia bark extract as well as allylisothiocyanate (AITC) with zinc lactate significantly reduced the levels of VSC in comparison to a placebo chewing gum. Furthermore, a sodium bicarbonate-containing chewing gum significantly reduced the VSC levels in comparison to rinsing with water. Furthermore, eucalyptus-extract chewing gum showed significant reductions in both organoleptic scores and VSC when compared with a control chewing gum. Chewing gum containing sucrose was able to reduce the VSC levels, in comparison to xylitol and zinc citrate chewing gum, but only for 5 min. It was concluded that chewing gums containing probiotics Lactobaccilus, zinc acetate and magnolia bark extract, eucalyptus-extract, and AITC with zinc lactate may be suitable for halitosis management. However, the low number of included studies and the high heterogeneity among the selected studies may limit the clinical applications of these findings.

Murphy, T. K., Brennan, E. M., Johnco, C., Parker-Athill, E. C., Miladinovic, B., Storch, E. A., and Lewin, A. B. A Double-Blind Randomized Placebo-Controlled Pilot Study of Azithromycin in Youth with Acute-Onset Obsessive-Compulsive Disorder. J.Child Adolesc.Psychopharmacol. 3-30-2017; PM: 28358599

ABSTRACT: OBJECTIVES: Sudden and severe onset of obsessive-compulsive disorder (OCD) may present secondary to infectious and/or immune-mediated triggers. We assessed the preliminary efficacy, tolerability, and safety of azithromycin compared with placebo in the treatment of OCD and associated symptoms in children with pediatric acute-onset neuropsychiatric syndrome (PANS). *METHODS*: Thirty-one youth aged 4-14

years (M = 8.26 +/- 2.78 years, 62.5% male) were randomized to receive either placebo or azithromycin for 4 weeks (10 mg/kg up to 500 mg per day). Both groups were administered twice daily probiotics. The primary outcome, obsessive-compulsive symptom severity, was assessed using the OCD Clinical Global Impressions Severity (CGI-S OCD) and Children's Yale-Brown Obsessive Compulsive Scale (CY-BOCS). *RESULTS*: Participants in the azithromycin group (n = 17) showed significantly greater reductions in OCD severity on the CGI-S OCD than the placebo group (n = 14) posttreatment (p = 0.003), although there were no significant differences on the CY-BOCS. Significantly more participants in the azithromycin condition met treatment responder criteria on the CGI-I OCD at the end of week 4 (41.2%, n = 7) in comparison to the placebo group (7.1%, n = 1; p = 0.045). Tic severity moderated treatment response, with greater tic severity being associated with enhanced treatment response on the CGI-S OCD. Azithromycin was well tolerated with minimal adverse effects and no study dropouts due to side effects. However, the azithromycin group showed a trend toward significantly greater electrocardiography QTc (p = 0.060) at the end of week 4, and significantly more reports of loose or abnormal stools (p = 0.009). *CONCLUSION*: This double blind pilot study suggests that azithromycin may be helpful in treating youth meeting the PANS diagnosis, especially those with elevated levels of both OCD and tic symptoms. Azithromycin was well tolerated, but the potential for cardiac risks suggests that additional monitoring may be needed to ensure safety

Murray, K. A., Belanger, A., Devine, L. T., Lane, A., and Condren, M. E. Emergency department discharge prescription errors in an academic medical center. Proc.(Bayl.Univ Med.Cent.). 2017; 30(2):143-146; PM: 28405061

ABSTRACT: This study described discharge prescription medication errors written for emergency department patients. This study used content analysis in a cross-sectional design to systematically categorize prescription errors found in a report of 1000 discharge prescriptions submitted in the electronic medical record in February 2015. Two pharmacy team members reviewed the discharge prescription list for errors. Open-ended data were coded by an additional rater for agreement on coding categories. Coding was based upon majority rule. Descriptive statistics were used to address the study objective. Categories evaluated were patient age, provider type, drug class, and type and time of error. The discharge prescription error rate out of 1000 prescriptions was 13.4%, with "incomplete or inadequate prescription" being the most commonly detected error (58.2%). The adult and pediatric error rates were 11.7% and 22.7%, respectively. The antibiotics reviewed had the highest number of errors. The highest within-class error rates were with antianginal medications, antiparasitic medications, antacids, appetite stimulants, and probiotics. Emergency medicine residents wrote the highest percentage of prescriptions (46.7%) and had an error rate of 9.2%. Residents of other specialties wrote 340 prescriptions and had an error rate of 20.9%. Errors occurred most often between 10:00 am and 6:00 pm.

Musilova, S., Modrackova, N., Hermanova, P., Hudcovic, T., Svejstil, R., Rada, V., Tejnecky, V., and Bunesova, V. Assessment of the synbiotic properites of human milk oligosaccharides and Bifidobacterium longum subsp. infantis in vitro and in humanised mice. Benef.Microbes. 4-26-2017; 8(2):281-289; PM: 28116928

ABSTRACT: The mode of delivery plays a crucial role in infant gastrointestinal tract colonisation, which in the case of caesarean section is characterised by the presence of clostridia and low bifidobacterial counts. Gut colonisation can be modified by probiotics,

prebiotics or synbiotics. Human milk oligosaccharides (HMOs) are infant prebiotics that show a bifidogenic effect. Moreover, genome sequencing of Bifidobacterium longum subsp. infantis within the infant microbiome revealed adaptations for milk utilisation. This study aimed to evaluate the synbiotic effect of B. longum subsp. infantis, HMOs and human milk (HM) both in vitro and in vivo (in a humanised mouse model) in the presence of faecal microbiota from infants born by caesarean section. The combination of B. longum and HMOs or HM reduced the clostridia and G-bacteria counts both in vitro and in vivo. The bifidobacterial population in vitro significantly increased and produce high concentrations of acetate and lactate. In vitro competition assays confirmed that the tested bifidobacterial strain is a potential probiotic for infants and, together with HMOs or HM, acts as a synbiotic. It is also able to inhibit potentially pathogenic bacteria. The synbiotic effects identified in vitro were not observed in vivo. However, there was a significant reduction in clostridia counts in both experimental animal groups (HMOs + B. longum and HM + B. longum), and a specific immune response via increased interleukin (IL)-10 and IL-6 production. Animal models do not perfectly mimic human conditions; however, they are essential for testing the safety of functional foods.

Myintzu, Hlaing M., Wood, B., McNaughton, D., Ying, D., and Augustin, M. A. Raman spectroscopic analysis of Lactobacillus rhamnosus GG in response to dehydration reveals DNA conformation changes. J.Biophotonics. 2017; 10(4):589-597; PM: 27244082

ABSTRACT: Dehydration of bacterial cells elicits cellular stress responses in bacteria. Microencapsulation has been used to protect cells against the environmental stress. In this study, Confocal Raman Spectroscopy was used to examine DNA changes in the chemical composition of non-encapsulated and microencapsulated Lactobacillus rhamnosus GG and the reversibility of these changes upon freeze drying and rehydration. The viability of cells upon freeze drying was also enumerated using culture methods and membrane integrity was measured using BacLight Live/Dead staining. Raman analyses show changes in the spectral features associated with various biochemical compounds, which are interpreted as the result of detrimental freeze drying effects on the bacterial cells. Specifically, analyses based on Principal Components Analysis (PCA) of Raman spectra, confirm that microencapsulation protects cells from environmental stress. The results also reveal a B- to A-like DNA conformation change in dormant cells that provided insights into the extent of reversibility of this transition upon rehydration. The extent of this reversibility is less in non-encapsulated than in microencapsulated cells. These findings indicate the potential application of Raman spectroscopy in rapid sensing of microbial dehydration stress responses.

Nacher-Vazquez, M., Iturria, I., Zarour, K., Mohedano, M. L., Aznar, R., Pardo, M. A., and Lopez, P. Dextran production by Lactobacillus sakei MN1 coincides with reduced autoagglutination, biofilm formation and epithelial cell adhesion. Carbohydr.Polym. 7-15-2017; 168:22-31; PM: 28457443

ABSTRACT: In this work we have investigated two dextran-producing lactic acid bacteria, Lactobacillus sakei MN1 and Leuconostoc mesenteroides RTF10, isolated from fermented meat products. These bacteria synthesise dextran when sucrose, but not glucose, is present in the growth medium. The influence of dextran on bacterial aggregation, adhesion and biofilm formation was investigated in cultures challenged with sucrose or glucose. For Lb. sakei MN1, the synthesis of the dextran drastically impaired the three

processes; in contrast it had no effect on Lc. mesenteroides RTF10. Therefore, the influence of dextran on probiotic properties of Lb. sakei MN1 was tested in vivo using gnotobiotic zebrafish models. The bacterium efficiently colonised the fish gut and inhibited the killing activity of Vibrio anguillarum NB10[pOT11]. Furthermore, under conditions of dextran synthesis, the adhesion of Lb. sakei MN1 to the epithelial cells decreased, without greatly affecting its anti V. anguillarum activity.

Nandi, A., Dan, S. K., Banerjee, G., Ghosh, P., Ghosh, K., Ringo, E., and Ray, A. K. Probiotic Potential of Autochthonous Bacteria Isolated from the Gastrointestinal Tract of Four Freshwater Teleosts. Probiotics.Antimicrob.Proteins. 2017; 9(1):12-21; PM: 27557836

ABSTRACT: In this study, a total of 121 bacterial strains were isolated from the gastrointestinal tract of four teleostean species, namely striped snakehead (Channa striatus), striped dwarf catfish (Mystus vittatus), orangefin labeo (Labeo calbasu) and mrigal carp (Cirrhinus mrigala), among which 8 isolates showed promising antibacterial activity against four potential fish pathogens, Aeromonas hydrophila, Aeromonas salmonicida, Aeromonas sobria and Pseudomonas fluorescens and were non-hemolytic. The isolates were further screened in response to fish bile tolerance and extracellular digestive enzyme activity. Two bacterial strains MVF1 and MVH7 showed highest tolerance and extracellular enzymes activities, and selected for further studies. Antagonistic activity of these two isolates was further confirmed by in vitro growth inhibition assay against four selected fish pathogens in liquid medium. Finally, these two bacterial strains MVF1 and MVH7 were selected as potential probiotic candidates and thus identification by partial 16S rRNA gene sequence analysis. The bacterial isolates MVF1 and MVH7 were identified as two strains of Bacillus sp.

Napolitano, L. M. and Edmiston, C. E., Jr. Clostridium difficile disease: Diagnosis, pathogenesis, and treatment update. Surgery. 3-3-2017; PM: 28267992

ABSTRACT: Clostridium difficile infections are the leading cause of health care-associated infectious diarrhea, posing a significant risk for both medical and surgical patients. Because of the significant morbidity and mortality associated with C difficile infections, knowledge of the epidemiology of C difficile in combination with a high index of suspicion and susceptible patient populations (including surgical, postcolectomy, and inflammatory bowel disease patients) is warranted. C difficile infections present with a wide spectrum of disease, ranging from mild diarrhea to fulminant colitis or small bowel enteritis and recurrent C difficile infections. Early implementation of medical and operative treatment strategies for C difficile infections is imperative for optimal patient outcomes. National and international guidelines recommend early operative consultation and total abdominal colectomy with end ileostomy and preservation of rectum. Diverting loop ileostomy and colonic lavage followed by intravenous metronidazole and intracolonic vancomycin administered via the efferent limb of the ileostomy should be considered as an alternative to total colectomy in selected patients. New and emerging strategies for C difficile infection treatment include monoclonal antibodies, vaccines, probiotics, biotherapeutics, and new antibiotics. A successful C difficile prevention and eradication program requires a multidisciplinary approach that includes early disease recognition, implementation of guidelines for monitoring adherence to environmental control, judicious hand hygiene, evidence-based treatment and management strategies, and a focused antibiotic stewardship program.

Surgeons are an important part of the clinical team in the management of C difficile infection prevention and treatment.

Naqash, F., Masoodi, F. A., Rather, S. A., Wani, S. M., and Gani, A. Emerging concepts in the nutraceutical and functional properties of pectin-A Review. Carbohydr.Polym. 7-15-2017; 168:227-239; PM: 28457445

ABSTRACT: Pectin is a structural heteropolysaccharide found ubiquitously in terrestrial plants. It finds diverse food applications such as that of a gelling agent, stabilizer, and fat replacer. In the pharmaceutical arena, pectin exhibits a number of functions, from decreasing blood fat to combating various types of cancers. This review shows the shift of pectin from its conventional roles to its progressive applications. Insights into the advances in the production of pectin, the role it plays as a nutraceutical, possible prebiotic potential and a delivery vehicle for probiotics, and food applications are highlighted. Bioactive and functional properties of pectin are discussed and how the structural built up defines them, is emphasized. As a biopolymer, the applications of pectin in active packaging are also mentioned.

Nascimento, M. M., Zaura, E., Mira, A., Takahashi, N., and Ten Cate, J. M. Second Era of OMICS in Caries Research: Moving Past the Phase of Disillusionment. J.Dent.Res. 4-1-2017; 22034517701902; PM: 28384412

ABSTRACT: Novel approaches using OMICS techniques enable a collective assessment of multiple related biological units, including genes, gene expression, proteins, and metabolites. In the past decade, next-generation sequencing (NGS) technologies were improved by longer sequence reads and the development of genome databases and user-friendly pipelines for data analysis, all accessible at lower cost. This has generated an outburst of high-throughput data. The application of OMICS has provided more depth to existing hypotheses as well as new insights in the etiology of dental caries. For example, the determination of complete bacterial microbiomes of oral samples rather than selected species, together with oral metatranscriptome and metabolome analyses, supports the viewpoint of dysbiosis of the supragingival biofilms. In addition, metabolome studies have been instrumental in disclosing the contributions of major pathways for central carbon and amino acid metabolisms to biofilm pH homeostasis. New, often noncultured, oral streptococci have been identified, and their phenotypic characterization has revealed candidates for probiotic therapy. Although findings from OMICS research have been greatly informative, problems related to study design, data quality, integration, and reproducibility still need to be addressed. Also, the emergence and continuous updates of these computationally demanding technologies require expertise in advanced bioinformatics for reliable interpretation of data. Despite the obstacles cited above, OMICS research is expected to encourage the discovery of novel caries biomarkers and the development of next-generation diagnostics and therapies for caries control. These observations apply equally to the study of other oral diseases.

Nath, D. Complementary and Alternative Medicine in the School-Age Child With Autism. J.Pediatr.Health Care. 2017; 31(3):393-397; PM: 28017488

ABSTRACT: This case study examines some common complementary and alternative

treatments used in the management of behavioral and gastrointestinal symptoms associated with autism including food selectivity, abdominal pain, nausea, gastroesophageal reflux, constipation, and diarrhea. The current literature on the safety and efficacy of these treatments for pediatric patients is reviewed. This study examines therapies including gluten-free and casein-free diet, probiotics, vitamin B12, omega-3 fatty acid supplementation, chelation therapy, acupuncture, and chiropractic manipulations used in treating these core symptoms of autism.

Navarro, J. B., Mashburn-Warren, L., Bakaletz, L. O., Bailey, M. T., and Goodman, S. D. Enhanced Probiotic Potential of Lactobacillus reuteri When Delivered as a Biofilm on Dextranomer Microspheres That Contain Beneficial Cargo. Front Microbiol. 2017; 8:489; PM: 28396655

ABSTRACT: As with all orally consumed probiotics, the Gram-positive bacterium Lactobacillus reuteri encounters numerous challenges as it transits through the gastrointestinal tract of the host, including low pH, effectors of the host immune system, as well as competition with commensal and pathogenic bacteria, all of which can greatly reduce the availability of live bacteria for therapeutic purposes. Recently we showed that L. reuteri, when adhered in the form of a biofilm to a semi-permeable biocompatible dextranomer microsphere, reduces the incidence of necrotizing enterocolitis by 50% in a well-defined animal model following delivery of a single prophylactic dose. Herein, using the same semi-permeable microspheres, we showed that providing compounds beneficial to L. reuteri as diffusible cargo within the microsphere lumen resulted in further advantageous effects including glucosyltransferase-dependent bacterial adherence to the microsphere surface, resistance of bound bacteria against acidic conditions, enhanced adherence of L. reuteri to human intestinal epithelial cells in vitro, and facilitated production of the antimicrobial compound reuterin and the anti-inflammatory molecule histamine. These data support continued development of this novel probiotic formulation as an adaptable and effective means for targeted delivery of cargo beneficial to the probiotic bacterium.

Nealon, N. J., Yuan, L., Yang, X., and Ryan, E. P. Rice Bran and Probiotics Alter the Porcine Large Intestine and Serum Metabolomes for Protection against Human Rotavirus Diarrhea. Front Microbiol. 2017; 8:653; PM: 28484432

ABSTRACT: Human rotavirus (HRV) is a leading cause of severe childhood diarrhea, and there is limited vaccine efficacy in the developing world. Neonatal gnotobiotic pigs consuming a prophylactic synbiotic combination of probiotics and rice bran (Pro+RB) did not exhibit HRV diarrhea after challenge. Multiple immune, gut barrier protective, and anti-diarrheal mechanisms contributed to the prophylactic efficacy of Pro+RB when compared to probiotics (Pro) alone. In order to understand the molecular signature associated with diarrheal protection by Pro+RB, a global non-targeted metabolomics approach was applied to investigate the large intestinal contents and serum of neonatal gnotobiotic pigs. The ultra-high performance liquid chromatography-tandem mass spectrometry platform revealed significantly different metabolites (293 in LIC and 84 in serum) in the pigs fed Pro+RB compared to Pro, and many of these metabolites were lipids and amino acid/peptides. Lipid metabolites included 2-oleoylglycerol (increased 293.40-fold in LIC of Pro+RB, p = 3.04E-10), which can modulate gastric emptying, andhyodeoxycholate (decreased 0.054-fold in the LIC of Pro+RB, p = 0.0040) that can increase colonic mucus production to improve intestinal barrier function. Amino acid metabolites included cysteine (decreased 0.40-fold in LIC, p = 0.033, and 0.62-fold in

serum, p = 0.014 of Pro+RB), which has been found to reduce inflammation, lower oxidative stress and modulate mucosal immunity, and histamine (decreased 0.18-fold in LIC, p = 0.00030, of Pro+RB and 1.57-fold in serum, p = 0.043), which modulates local and systemic inflammatory responses as well as influences the enteric nervous system. Alterations to entire LIC and serum metabolic pathways further contributed to the anti-diarrheal and anti-viral activities of Pro+RB such as sphingolipid, mono/diacylglycerol, fatty acid, secondary bile acid, and polyamine metabolism. Sphingolipid and long chain fatty acid profiles influenced the ability of HRV to both infect and replicate within cells, suggesting that Pro+RB created a protective lipid profile that interferes with HRV activity. Polyamines act on enterocyte calcium-sensing receptors to modulate intracellular calcium levels, and may directly interfere with rotavirus replication. These results support that multiple host and probiotic metabolic networks, notably those involving lipid and amino acid/peptide metabolism, are important mechanisms through which Pro+RB protected against HRV diarrhea in neonatal gnotobiotic pigs.

Newlove-Delgado, T. V., Martin, A. E., Abbott, R. A., Bethel, A., Thompson-Coon, J., Whear, R., and Logan, S. Dietary interventions for recurrent abdominal pain in childhood. Cochrane.Database.Syst.Rev. 3-23-2017; 3:CD010972; PM: 28334433

ABSTRACT: BACKGROUND: This is an update of the original Cochrane review, last published in 2009 (Huertas-Ceballos 2009). Recurrent abdominal pain (RAP), including children with irritable bowel syndrome, is a common problem affecting between 4% and 25% of school-aged children. For the majority of such children, no organic cause for their pain can be found on physical examination or investigation. Many dietary inventions have been suggested to improve the symptoms of RAP. These may involve either excluding ingredients from the diet or adding supplements such as fibre or probiotics. *OBJECTIVES*: To examine the effectiveness of dietary interventions in improving pain in children of school age with RAP. *SEARCH METHODS*: We searched CENTRAL, Ovid MEDLINE, Embase, eight other databases, and two trials registers, together with reference checking, citation searching and contact with study authors, in June 2016. *SELECTION CRITERIA*: Randomised controlled trials (RCTs) comparing dietary interventions with placebo or no treatment in children aged five to 18 years with RAP or an abdominal pain-related, functional gastrointestinal disorder, as defined by the Rome III criteria (Rasquin 2006). *DATA COLLECTION AND ANALYSIS*: We used standard methodological procedures expected by Cochrane. We grouped dietary interventions together by category for analysis. We contacted study authors to ask for missing information and clarification, when needed. We assessed the quality of the evidence for each outcome using the GRADE approach. *MAIN RESULTS*: We included 19 RCTs, reported in 27 papers with a total of 1453 participants. Fifteen of these studies were not included in the previous review. All 19 RCTs had follow-up ranging from one to five months. Participants were aged between four and 18 years from eight different countries and were recruited largely from paediatric gastroenterology clinics. The mean age at recruitment ranged from 6.3 years to 13.1 years. Girls outnumbered boys in most trials. Fourteen trials recruited children with a diagnosis under the broad umbrella of RAP or functional gastrointestinal disorders; five trials specifically recruited only children with irritable bowel syndrome. The studies fell into four categories: trials of probiotic-based interventions (13 studies), trials of fibre-based interventions (four studies), trials of low FODMAP (fermentable oligosaccharides, disaccharides, monosaccharides and polyols) diets (one study), and trials of fructose-restricted diets (one study).We found that children treated with probiotics reported a greater reduction in pain frequency at zero to three months postintervention than those given placebo (standardised mean difference (SMD) -0.55,

95% confidence interval (CI) -0.98 to -0.12; 6 trials; 523 children). There was also a decrease in pain intensity in the intervention group at the same time point (SMD -0.50, 95% CI -0.85 to -0.15; 7 studies; 575 children). However, we judged the evidence for these outcomes to be of low quality using GRADE due to an unclear risk of bias from incomplete outcome data and significant heterogeneity.We found that children treated with probiotics were more likely to experience improvement in pain at zero to three months postintervention than those given placebo (odds ratio (OR) 1.63, 95% CI 1.07 to 2.47; 7 studies; 722 children). The estimated number needed to treat for an additional beneficial outcome (NNTB) was eight, meaning that eight children would need to receive probiotics for one to experience improvement in pain in this timescale. We judged the evidence for this outcome to be of moderate quality due to significant heterogeneity.Children with a symptom profile defined as irritable bowel syndrome treated with probiotics were more likely to experience improvement in pain at zero to three months postintervention than those given placebo (OR 3.01, 95% CI 1.77 to 5.13; 4 studies; 344 children). Children treated with probiotics were more likely to experience improvement in pain at three to six months postintervention compared to those receiving placebo (OR 1.94, 95% CI 1.10 to 3.43; 2 studies; 224 children). We judged the evidence for these two outcomes to be of moderate quality due to small numbers of participants included in the studies.We found that children treated with fibre-based interventions were not more likely to experience an improvement in pain at zero to three months postintervention than children given placebo (OR 1.83, 95% CI 0.92 to 3.65; 2 studies; 136 children). There was also no reduction in pain intensity compared to placebo at the same time point (SMD -1.24, 95% CI -3.41 to 0.94; 2 studies; 135 children). We judged the evidence for these outcomes to be of low quality due to an unclear risk of bias, imprecision, and significant heterogeneity.We found only one study of low FODMAP diets and only one trial of fructose-restricted diets, meaning no pooled analyses were possible.We were unable to perform any meta-analyses for the secondary outcomes of school performance, social or psychological functioning, or quality of daily life, as not enough studies included these outcomes or used comparable measures to assess them.With the exception of one study, all studies reported monitoring children for adverse events; no major adverse events were reported. *AUTHORS' CONCLUSIONS*: Overall, we found moderate- to low-quality evidence suggesting that probiotics may be effective in improving pain in children with RAP. Clinicians may therefore consider probiotic interventions as part of a holistic management strategy. However, further trials are needed to examine longer-term outcomes and to improve confidence in estimating the size of the effect, as well as to determine the optimal strain and dosage. Future research should also explore the effectiveness of probiotics in children with different symptom profiles, such as those with irritable bowel syndrome.We found only a small number of trials of fibre-based interventions, with overall low-quality evidence for the outcomes. There was therefore no convincing evidence that fibre-based interventions improve pain in children with RAP. Further high-quality RCTs of fibre supplements involving larger numbers of participants are required. Future trials of low FODMAP diets and other dietary interventions are also required to facilitate evidence-based recommendations.

Nguyen, T. H. and Nguyen, V. D. Characterization and Applications of Marine Microbial Enzymes in Biotechnology and Probiotics for Animal Health. Adv.Food Nutr.Res. 2017; 80:37-74; PM: 28215328

ABSTRACT: Marine microorganisms have been recognized as potential sources of novel enzymes because they are relatively more stable than the corresponding enzymes derived from plants and animals. Enzymes from marine microorganisms also differ from

homologous enzymes in terrestrial microorganisms based on salinity, pressure, temperature, and lighting conditions. Marine microbial enzymes can be used in diverse industrial applications. This chapter will focus on the biotechnological applications of marine enzymes and also their use as a tool of marine probiotics to improve host digestion (food digestion, food absorption, and mucus utilization) and cleave molecular signals involved in quorum sensing in pathogens to control disease in aquaculture.

Ni, Y., Wong, V. H., Tai, W. C., Li, J., Wong, W. Y., Lee, M. M., Fong, F. L., El-Nezami, H., and Panagiotou, G. A metagenomic study of the preventive effect of Lactobacillus rhamnosus GG on intestinal polyp formation in ApcMin/+ mice. J.Appl.Microbiol. 2017; 122(3):770-784; PM: 28004480

ABSTRACT: AIMS: To investigate the in vivo effects of Lactobacillus rhamnosus GG (LGG) on intestinal polyp development and the interaction between this single-organism probiotic and the gut microbiota therein. *METHODS AND RESULTS*: The ApcMin/+ mouse model was used to study the potential preventive effect of LGG on intestinal polyposis, while shotgun metagenomic sequencing was employed to characterize both taxonomic and functional changes within the gut microbial community. We found that the progression of intestinal polyps in the control group altered the community functional profile remarkably despite small variation in the taxonomic diversity. In comparison, the consumption of LGG helped maintain the overall functional potential and taxonomic profile in the resident microbes, thereby leading to a 25% decrease of total polyp counts. Furthermore, we found that LGG enriched those microbes or microbial activities related to short-chain fatty acid production (e.g. Roseburia and Coprococcus), as well as suppressed the ones that can lead to inflammation (e.g. Bilophila wadsworthia). *CONCLUSIONS*: Our study using shotgun metagenomics highlights how single probiotic LGG may exert its beneficial effects and decrease polyp formation in mice by maintaining gut microbial functionality. *SIGNIFICANCE AND IMPACT OF THE STUDY*: This probiotic intervention targeting microbiota may be used in conjugation with other dietary supplements or drugs as part of prevention strategies for early-stage colon cancer, after further clinical validations in human.

Nikniaz, Z., Nikniaz, L., Bilan, N., Somi, M. H., and Faramarzi, E. Does probiotic supplementation affect pulmonary exacerbation and intestinal inflammation in cystic fibrosis: a systematic review of randomized clinical trials. World J.Pediatr. 4-29-2017; PM: 28470579

ABSTRACT: BACKGROUND: Patients with cystic fibrosis (CF) usually have abnormal intestinal microbiota due to massive exposure to antibiotics. Probiotics could modify the gut microbiota and hence may affect CF management. So the aim of present systematic review was evaluation of the efficacy and safety of probiotic supplementation for the management of cystic fibrosis. *DATA SOURCES*: We searched PubMed, Science Direct, Google Scholar, Springer Cochrane Library Databases until January 2016 for randomized controlled trials (RCTs) performed in pediatric or adult populations related to the study aim. Key words were selected based on Mesh terms. Based on the Critical Appraisal Skills Programme checklist, eligibility of included articles was evaluated. *RESULTS*: Five studies included in this review represent 188 participants with a follow up period ranging from 1 month to 6 months. The results of the included studies supporting the use of probiotics in management of pulmonary exacerbation and intestinal calprotectin in patients with cystic fibrosis. However the level of evidence was limited. *CONCLUSIONS*: The lack of high quality RCTs makes it impossible to support a

general recommendation about the use of probiotics in the treatment of CF pulmonary exacerbation and intestinal inflammation.

nis-Wall, J. C., Culpepper, T., Nieves, C., Jr., Rowe, C. C., Burns, A. M., Rusch, C. T., Federico, A., Ukhanova, M., Waugh, S., Mai, V., Christman, M. C., and Langkamp-Henken, B. Probiotics (Lactobacillus gasseri KS-13, Bifidobacterium bifidum G9-1, and Bifidobacterium longum MM-2) improve rhinoconjunctivitis-specific quality of life in individuals with seasonal allergies: a double-blind, placebo-controlled, randomized trial. Am.J.Clin.Nutr. 2017; 105(3):758-767; PM: 28228426

ABSTRACT: Background: Rhinoconjunctivitis-specific quality of life is often reduced during seasonal allergies. The Mini Rhinoconjunctivitis Quality of Life Questionnaire (MRQLQ) is a validated tool used to measure quality of life in people experiencing allergies (0 = not troubled to 6 = extremely troubled). Probiotics may improve quality of life during allergy season by increasing the percentage of regulatory T cells (Tregs) and inducing tolerance.*Objective*: The objective of this study was to determine whether consuming Lactobacillus gasseri KS-13, Bifidobacterium bifidum G9-1, and B. longum MM-2 compared with placebo would result in beneficial effects on MRQLQ scores throughout allergy season in individuals who typically experience seasonal allergies. Secondary outcomes included changes in immune markers as part of a potential mechanism for changes in MRQLQ scores.*Design*: In this double-blind, placebo-controlled, parallel, randomized clinical trial, 173 participants (mean +/- SEM: age 27 +/- 1 y) who self-identified as having seasonal allergies received either a probiotic (2 capsules/d, 1.5 billion colony-forming units/capsule) or placebo during spring allergy season for 8 wk. MRQLQ scores were collected weekly throughout the study. Fasting blood samples were taken from a subgroup (placebo, n = 37; probiotic, n = 35) at baseline and week 6 (predicted peak of pollen) to determine serum immunoglobulin (Ig) E concentrations and Treg percentages.*Results*: The probiotic group reported an improvement in the MRQLQ global score from baseline to pollen peak (-0.68 +/- 0.13) when compared with the placebo group (-0.19 +/- 0.14; P = 0.0092). Both serum total IgE and the percentage of Tregs increased from baseline to week 6, but changes were not different between groups.*Conclusions*: This combination probiotic improved rhinoconjunctivitis-specific quality of life during allergy season for healthy individuals with self-reported seasonal allergies; however, the associated mechanism is still unclear. This trial was registered at clinicaltrials.gov as NCT02349711.

Nishida, S., Ishii, M., Nishiyama, Y., Abe, S., Ono, Y., and Sekimizu, K. Lactobacillus paraplantarum 11-1 Isolated from Rice Bran Pickles Activated Innate Immunity and Improved Survival in a Silkworm Bacterial Infection Model. Front Microbiol. 2017; 8:436; PM: 28373863

ABSTRACT: Lactic acid bacteria (LAB) have high immune system-stimulating activity and are considered beneficial for human health as probiotics in the gut. The innate immune system is highly conserved between mammals and insects. Microbe-associated molecular patterns (e.g., peptidoglycan and beta-glucan) induce cytokine maturation, which, in silkworm larvae, leads to muscle contraction. The purpose of this study is to find a novel probiotic by using silkworm muscle contraction assay. In the present study, we isolated LAB derived from rice bran pickles. We selected highly active LAB to activate the innate immune system of the silkworm, which was assayed based on silkworm muscle contraction. Of various LAB, L. paraplantarum 11-1 strongly stimulated innate immunity in

the silkworm, leading to stronger silkworm contraction than a dairy-based LAB. Silkworms fed a diet containing L. paraplantarum 11-1 exhibited tolerance against the pathogenicity of Pseudomonas aeruginosa. These findings suggest that L. paraplantarum 11-1 could be a useful probiotic for activating innate immunity.

Nobili, V. and Cucchiara, S. The Use of Probiotics in Pediatric Nonalcoholic Fatty Liver Disease: Teachable Moment or Missed Opportunity? J.Pediatr.Gastroenterol.Nutr. 2017; 64(3):336-337; PM: 27749611

No Abstract Available.

Noble, E. E., Hsu, T. M., and Kanoski, S. E. Gut to Brain Dysbiosis: Mechanisms Linking Western Diet Consumption, the Microbiome, and Cognitive Impairment. Front Behav.Neurosci. 2017; 11:9; PM: 28194099

ABSTRACT: Consumption of a Western Diet (WD) that is high in saturated fat and added sugars negatively impacts cognitive function, particularly mnemonic processes that rely on the integrity of the hippocampus. Emerging evidence suggests that the gut microbiome influences cognitive function via the gut-brain axis, and that WD factors significantly alter the proportions of commensal bacteria in the gastrointestinal tract. Here we review mechanisms through which consuming a WD negatively impacts neurocognitive function, with a particular focus on recent evidence linking the gut microbiome with dietary- and metabolic-associated hippocampal impairment. We highlight evidence linking gut bacteria to altered intestinal permeability and blood brain barrier integrity, thus making the brain more vulnerable to the influx of deleterious substances from the circulation. WD consumption also increases production of endotoxin by commensal bacteria, which may promote neuroinflammation and cognitive dysfunction. Recent findings also show that diet-induced alterations in gut microbiota impair peripheral insulin sensitivity, which is associated with hippocampal neuronal derrangements and associated mnemonic deficits. In some cases treatment with specific probiotics or prebiotics can prevent or reverse some of the deleterious impact of WD consumption on neuropsychological outcomes, indicating that targeting the microbiome may be a successful strategy for combating dietary- and metabolic-associated cognitive impairment.

Nobutani, K., Sawada, D., Fujiwara, S., Kuwano, Y., Nishida, K., Nakayama, J., Kutsumi, H., Azuma, T., and Rokutan, K. The effects of administration of the Lactobacillus gasseri strain CP2305 on quality of life, clinical symptoms and changes in gene expression in patients with irritable bowel syndrome. J.Appl.Microbiol. 2017; 122(1):212-224; PM: 27761980

ABSTRACT: *AIMS*: To clarify the effects of Lactobacillus gasseri CP2305 (CP2305) on quality of life and clinical symptoms and its functional mechanisms in patients with irritable bowel syndrome (IBS). *METHODS AND RESULTS*: After the patients were administered CP2305 daily for 4 weeks, the IBS-severity index score was significantly improved compared with that of the placebo group, and this improvement was accompanied by a reduction in health-related worry and changes in intestinal microbiota. The gene expression profiling of the peripheral blood leucocytes showed that CP2305 treatment significantly up-regulated genes related to eukaryotic initiation factor 2 (EIF2) signalling. Eighty-two genes were down-regulated in IBS patients compared with healthy controls.

The expression of 23 of these genes exhibited a CP2305-dependent increase associated with an improvement in IBS severity. The majority of the restored genes were related to EIF2 signalling. *CONCLUSIONS*: CP2305 administration is a potential candidate therapeutic option for patients with IBS. *SIGNIFICANCE AND IMPACT OF THE STUDY*: Although probiotics have been proposed to benefit IBS patients, objective clinical evidence and elucidation of the functional mechanism remain insufficient. Our study demonstrated that CP2305 administration beneficially influences IBS patients in both subjective and objective evaluations, and gene expression profiling provided insights into the functional mechanism.

Nocerino, R., Paparo, L., Terrin, G., Pezzella, V., Amoroso, A., Cosenza, L., Cecere, G., De, Marco G., Micillo, M., Albano, F., Nugnes, R., Ferri, P., Ciccarelli, G., Giaccio, G., Spadaro, R., Maddalena, Y., Berni, Canani F., and Berni, Canani R. Cow's milk and rice fermented with Lactobacillus paracasei CBA L74 prevent infectious diseases in children: A randomized controlled trial. Clin.Nutr. 2017; 36(1):118-125; PM: 26732025

ABSTRACT: BACKGROUND & AIM: Fermented foods have been proposed for the prevention of infectious diseases. We evaluated the efficacy of fermented foods in reducing common infectious diseases (CIDs) in children attending daycare. *METHODS*: Prospective randomized, double-blind, placebo-controlled trial (registered under Clinical Trials.gov identifier NCT01909128) on healthy children (aged 12-48 months) consuming daily cow's milk (group A) or rice (group B) fermented with Lactobacillus paracasei CBA L74, or placebo (group C) for three months during the winter season. The main study outcome was the proportion of children who experienced at least one CID. All CIDs were diagnosed by family pediatricians. Fecal concentrations of innate (alpha- and beta-defensins and cathelicidin LL-37) and acquired immunity biomarkers (secretory IgA) were also evaluated. *RESULTS*: 377 children (193 males, 51%) with a mean (SD) age of 32 (10) months completed the study: 137 in group A, 118 in group B and 122 in group C. Intention-to-treat analysis showed that the proportion of children who experienced at least one CID was lower in group A (51.8%) and B (65.9%) compared to group C (80.3%). Per-protocol analysis showed that the proportion of children presenting upper respiratory tract infections was lower in group A (48.2%) and group B (58.5%) compared with group C (70.5%). The proportion of children presenting acute gastroenteritis was also lower in group A (13.1%) and group B (19.5%) compared with group C (31.1%). A net increase of all fecal biomarkers of innate and acquired immunity was observed for groups A and B compared to group C. Moreover, there was a negative association between fecal biomarkers and the occurrence of CID. *CONCLUSION*: Dietary supplementation with cow's milk or rice fermented with L. paracasei CBA L74 prevents CIDs in children attending daycare possibly by means of a stimulation of innate and acquired immunity.

Nomoto, K. PROBIOTICS AND ALLERGY. Arerugi. 2017; 66(2):82-85; PM: 28331108

No Abstract Available.

Norena, I., Cabrera-Marante, O., and Fernandez-Ruiz, M. Endocarditis due to Lactobacillus rhamnosus in a patient with bicuspid aortic valve: Potential role for the consumption of probiotics? Med.Clin.(Barc.). 5-2-2017; PM: 28476455

No Abstract Available.

Nowak-Wegrzyn, A. and Chatchatee, P. Mechanisms of Tolerance Induction. Ann.Nutr.Metab. 2017; 70 Suppl 2:7-24; PM: 28521317

ABSTRACT: Food allergy results from failure in oral tolerance that usually occurs in infancy or early childhood. Exposure to peanut and hen's egg via the inflamed and disrupted epithelial barrier in children with severe atopic dermatitis is a risk factor for the development of allergy to these foods and supports the hypothesis that epicutaneous exposure in the absence of oral feeding is an important pathway of allergic IgE sensitization in infants. In recent years, the collective evidence has pointed toward the protective effect of an early feeding with peanut and egg in children with eczema, taking advantage of the pathways underlying oral tolerance to counteract epicutaneous exposure. An addendum to the NIAID food allergy guidelines recommends introduction of peanut into the diet of 4- to 6-month-old infants with severe eczema or egg allergy as an effective strategy to prevent peanut allergy. Strategies aimed at restoring the skin barrier are currently explored as an alternative approach of prevention of eczema and allergic sensitization. Manipulation of the diet via supplementation with probiotics and prebiotics to restore the healthy gut microbiota represents another potential pathway to induction of tolerance in the gut. Oral, epicutaneous, and sublingual routes of food immunotherapy are promising and induce desensitization in the majority of the treated subjects with food allergy but are not proven to restore permanent oral tolerance. Rigorous multicenter randomized clinical trials are necessary to elucidate the optimal timing, dose, duration, as well as the preventive and therapeutic effects of these diverse approaches.

Nunez-Acuna, G., Detree, C., Gallardo-Escarate, C., and Goncalves, A. T. Functional Diets Modulate lncRNA-Coding RNAs and Gene Interactions in the Intestine of Rainbow Trout Oncorhynchus mykiss. Mar.Biotechnol.(NY). 5-12-2017; PM: 28500613

ABSTRACT: The advent of functional genomics has sparked the interest in inferring the function of non-coding regions from the transcriptome in non-model species. However, numerous biological processes remain understudied from this perspective, including intestinal immunity in farmed fish. The aim of this study was to infer long non-coding RNA (lncRNAs) expression profiles in rainbow trout (Oncorhynchus mykiss) fed for 30 days with functional diets based on pre- and probiotics. For this, whole transcriptome sequencing was conducted through Illumina technology, and lncRNAs were mined to evaluate transcriptional activity in conjunction with known protein sequences. To detect differentially expressed transcripts, 880 novels and 9067 previously described O. mykiss lncRNAs were used. Expression levels and genome co-localization correlations with coding genes were also analyzed. Significant differences in gene expression were primarily found in the probiotic diet, which had a twofold downregulation of lncRNAs compared to other treatments. Notable differences by diet were also evidenced between the coding genes of distinct metabolic processes. In contrast, genome co-localization of lncRNAs with coding genes was similar for all diets. This study contributes novel knowledge regarding lncRNAs in fish, suggesting key roles in salmons fed with in-feed additives with the capacity to modulate the intestinal homeostasis and host health.

O'Toole, P. W., Marchesi, J. R., and Hill, C. Next-generation probiotics: the spectrum from probiotics to live biotherapeutics. Nat.Microbiol. 4-25-2017; 2:17057; PM: 28440276

ABSTRACT: The leading probiotics currently available to consumers are generally drawn

from a narrow range of organisms. Knowledge of the gut microbiota and its constituent actors is changing this paradigm, particularly given the phylogenetic range and relatively unknown characteristics of the organisms under investigation as novel therapeutics. For this reason, and because their development is likely to be more amenable to a pharmaceutical than a food delivery route, these organisms are often operationally referred to as next-generation probiotics, a concept that overlaps with the emerging concept of live biotherapeutic products. The latter is a class of organisms developed exclusively for pharmaceutical application. In this Perspective, we discuss what lessons have been learned from working with traditional probiotics, explore the kinds of organisms that are likely to be used as novel microbial therapeutics, discuss the regulatory framework required, and propose how scientists may meet this challenge.

Oh, J. K., Pajarillo, E. A., Chae, J. P., Kim, I. H., Yang, D. S., and Kang, D. K. Effects of Bacillus subtilis CSL2 on the composition and functional diversity of the faecal microbiota of broiler chickens challenged with Salmonella Gallinarum. J.Anim Sci.Biotechnol. 2017; 8:1; PM: 28070331

ABSTRACT: BACKGROUND: The chicken gastrointestinal tract contains a diverse microbiota whose composition and structure play important roles in gut functionality. In this study, microbial shifts resulting from feed supplementation with Bacillus subtilis CSL2 were evaluated in broilers challenged and unchallenged with Salmonella Gallinarum. To analyse bacterial community composition and functionality, 454 GS-FLX pyrosequencing of 16*S* rRNA gene amplicons was performed. *RESULTS*: The Quantitative Insights into Microbial Ecology (QIIME) pipeline was used to analyse changes in the faecal microbiota over a 24-h period. A total of 718,204 sequences from broiler chickens were recorded and analysed. At the phylum level, Firmicutes, Bacteroidetes, and Proteobacteria were the predominant bacterial taxa. In Salmonella-infected chickens (SC), Bacteroidetes were more highly abundant compared to control (NC) and Bacillus-treated (BT) chickens. At the genus level, in the NC and BT groups, Lactobacillus was present at high abundance, and the abundance of Turicibacter, unclassified Enterobacteriaceae, and Bacteroides increased in SC broilers. Furthermore, taxon-independent analysis showed that the SC and BT groups were compositionally distinct at the end of the 24-h period. Further analysis of functional properties showed that B. subtilis CSL2 administration increased gut-associated energy supply mechanisms (i.e. carbohydrate transport and metabolism) to maintain a stable microbiota and protect gut integrity. *CONCLUSIONS*: This study demonstrated that S. Gallinarum infection and B. subtilis CSL2 supplementation in the diet of broiler chickens influenced the diversity, composition, and functional diversity of the faecal microbiota. Moreover, the findings offer significant insights to understand potential mechanisms of Salmonella infection and the mode of action of probiotics in broiler chickens.

Oh, J. K., Pajarillo, E. A. B., Chae, J. P., Kim, I. H., and Kang, D. K. Protective effects of Bacillus subtilis against Salmonella infection in the microbiome of Hy-Line Brown layers. Asian-Australas.J.Anim Sci. 4-19-2017; PM: 28423869

ABSTRACT: Objective: This study investigated the effects of Bacillus subtilis CSL2 administration before Salmonella challenge on the fecal microbiota and microbial functionality of Hy-line Brown (HLB) laying hens. Methods: Fecal samples were collected from control (CON), Salmonella-infected (SAL) and Salmonella-infected, probiotic-treated (PRO) groups before and after Salmonella challenge for microbiome analysis

using 16S rRNA gene pyrosequencing. *Results*: Infection with Salmonella led to decreased microbial diversity in hen feces; diversity was recovered with Bacillus administration. In addition, Salmonella infection triggered significant alterations in the composition of the fecal microbiota. The abundance of the phylum Firmicutes decreased while that of Proteobacteria, which includes a wide variety of pathogens, increased significantly. Bacillus administration resulted in normal levels of abundance of Firmicutes and Proteobacteria. Analysis of bacterial genera showed that Salmonella challenge decreased the population of Lactobacillus, the most abundant genus, and increased populations of Pseudomonas and Flavobacterium genera by a factor of 3-5. On the other hand, Bacillus administration caused the abundance of the Lactobacillus genus to recover to control levels and decreased the population of Pseudomonas significantly. Further analysis of operational taxonomic units (OTUs) revealed a high abundance of genes associated with two-component systems and secretion systems in the SAL group, whereas the PRO group had more genes associated with ribosomes. *Conclusion*: The results of this study indicate that B. subtilis CSL2 administration can modulate the microbiota in HLB laying hens, potentially acting as a probiotic to protect against S. Gallinarum infection.

Oh, N. S., Lee, J. Y., Lee, J. M., Lee, K. W., and Kim, Y. Mulberry leaf extract fermented with Lactobacillus acidophilus A4 ameliorates 5-fluorouracil-induced intestinal mucositis in rats. Lett.Appl.Microbiol. 2017; 64(6):459-468; PM: 28378512

ABSTRACT: The objective of the present study was to evaluate the effect of mulberry leaf extract (ME) fermented with Lactobacillus acidophilus A4 (A4) on intestinal mucositis induced by 5-fluorouracil (5-FU) in a rat model. Male Wistar rats were gavaged with A4, ME, fermented mulberry leaf extract FME) or lafutidine (LAF) for 10 days and injected intraperitoneally with 5-FU (150 mg kg-1) or saline (normal control) on day 7 to induce mucositis. After euthanizing the animals, their small and large intestines were removed for evaluation of histopathologic parameters, myeloperoxidase (MPO) activity, mucin content, and mRNA expression of the mucin gene and pro-inflammatory cytokine interleukin (IL)-1beta. 5-FU induced significant weight loss, shortened villi height, and increased histological severity, IL-1beta expression, and MPO activity compared to the normal control group. These pathological changes were markedly ameliorated by treatment with A4, ME and FME. These treatments also stimulated MUC2 and MUC5AC gene expression and mucin production, and reduced IL-1beta expression and MPO level. Interestingly, FME had the greatest protective effect on 5-FU-induced mucositis in rats. SIGNIFICANCE AND IMPACT OF THE STUDY: Our results suggest that fermented mulberry leaf extract (ME) may provide synergistic therapeutic benefits of both probiotics and natural plant extracts in prevention of 5-fluorouracil-induced mucositis. These impacts are particularly significant given the induction of MUC2 and MUC5AC gene expressions for production of mucins and the reduction of pro-inflammatory cytokine interleukin-1beta in gut environments. Therefore, we proposed that enhanced functionality of ME by fermentation of Lactobacillus acidophilus A4 can be applied as food-grade adjuncts for mucositis therapy and prevention in food industry.

Oka, S. Potential synergistic effects of a mixture of mineral trioxide aggregate (MTA) cement and Bacillus subtilis in dental caries treatment. Odontology. 3-24-2017; PM: 28342006

ABSTRACT: Bacillus subtilis is nonpathogenic in humans and produces a number of useful substances and, therefore, this bacterium is used in probiotic therapy. There have been

trials of B. subtilis for patients with periodontitis, but not for patients with caries. Similarly, mineral trioxide aggregate (MTA) cement has been widely used for endodontic treatment, but there are few reports of its use for caries. Therefore, examinations were performed regarding the benefits of addition of B. subtilis to MTA cement for treatment of dental caries. Indirect pulp capping with a mixture of MTA cement and B. subtilis spore powder is effective for avoiding pulpectomy or tooth extraction in such cases (personal communication). This study was planned to examine the scientific basis of this clinical finding, with examination of possible synergistic effects of MTA cement and B. subtilis. From these experiments, the following five results were obtained: (1) B. subtilis did not proliferate in liquid-culture media at pH >/=10. (2) B. subtilis proliferated when mixed with MTA cement. (3) There was no significant difference in proliferation of B. subtilis under aerobic and microaerobic conditions. (4) B. subtilis exhibited antibacterial effects on Staphylococcus aureus and Lactobacillus casei. (5) MTA cement exhibited antibacterial effects on S. aureus and Streptococcus mutans, but not on B. subtilis. These results support the hypothesis that a combination of B subtilis and MTA cement is likely to be clinically useful for treatment of dental caries.

Olek, A., Woynarowski, M., Ahren, I. L., Kierkus, J., Socha, P., Larsson, N., and Onning, G. Efficacy and Safety of Lactobacillus plantarum DSM 9843 (LP299V) in the Prevention of Antibiotic-Associated Gastrointestinal Symptoms in Children-Randomized, Double-Blind, Placebo-Controlled Study. J.Pediatr. 4-21-2017; PM: 28438377

ABSTRACT: OBJECTIVES: To determine if Lactobacillus plantarum DSM9843 (LP299V) reduces the frequency of antibiotic-associated loose/watery stools and gastrointestinal symptoms, and can be administered safely to children who are prescribed antibiotics. *STUDY DESIGN*: We performed a prospective, double-blind, randomized, placebo-controlled, multicenter, parallel-group study in children receiving outpatient antibiotic therapy in primary healthcare settings. The children were given LP299V/placebo during the antibiotic therapy and for 1 week after the end of treatment. The primary outcome measure was the incidence of at least 1 loose/watery stool (type 6 or 7 according to the Bristol Stool Form Scale). Gastrointestinal symptoms (abdominal pain, abdominal distention, vomiting, and flatulence) were followed up until 1 week after the last intake of the study product. *RESULTS*: A total of 438 children (male: 235, female: 203) aged 1-11 years (mean +/- SD: 5.2 +/- 2.7) were randomized to receive LP299V (N = 218) or placebo (N = 220). The incidence of loose/watery stools in the 2 study groups (LP299V and placebo) was similar, 39% vs 44.5% respectively (P = .26) as was the mean number of loose/watery stools (3.9 +/- 3.5 vs 4.7 +/- 6.3; P = .9). Antibiotic-associated diarrhea (defined as >/=3 loose/watery stools/24 hours starting from 2 hours after initiation of antibiotic treatment until the end of the study) occurred in 2.8% of the subjects receiving LP299V compared with 4.1% in the placebo arm (P = .4). The number of children with abdominal symptoms did not differ between the groups. *CONCLUSIONS*: No beneficial effect of LP299V compared with placebo was observed for the incidence of loose/watery stools, mean number of loose/watery stools, or the incidence of abdominal symptoms. LP299V had a satisfactory safety profile. *TRIAL REGISTRATION*: ClinicalTrials.gov: NCT01940913.

Oleskin, A. V., Shenderov, B. A., and Rogovsky, V. S. Role of Neurochemicals in the Interaction between the Microbiota and the Immune and the Nervous System of the Host Organism. Probiotics.Antimicrob.Proteins. 2-22-2017; PM: 28229287

ABSTRACT: This work is concerned with the role of evolutionary conserved substances, neurotransmitters, and neurohormones, within the complex framework of the microbial consortium-immune system-nervous system axis in the human or animal organism. Although the operation of each of these systems per se is relatively well understood, their combined effects on the host organism still await further research. Drawing on recent research on host-produced and microbial low-molecular-weight neurochemicals such as biogenic amines, amino acids, and short-chain fatty acids (SCFAs), we suggest that these mediators form a part of a universal neurochemical "language." It mediates the whole gamut of harmonious and disharmonious interactions between (a) the intestinal microbial consortium, (b) local and systemic immune cells, and (c) the central and peripheral nervous system. Importantly, the ongoing microbiota-host interactivity is bidirectional. We present evidence that a large number of microbially produced low-molecular-weight compounds are identical or homologous to mediators that are synthesized by immune or nervous cells and, therefore, can bind to the corresponding host receptors. In addition, microbial cells specifically respond to host-produced neuromediators/neurohormones because they have adapted to them during the course of many millions of years of microbiota-host coevolution. We emphasize that the terms "microbiota" and "microbial consortium" are to be used in the broadest sense, so as to include, apart from bacteria, also eukaryotic microorganisms. These are exemplified by the mycobiota whose role in the microbial consortium-immune system-nervous system axis researchers are only beginning to elucidate. In light of the above, it is imperative to reform the current strategies of using probiotic microorganisms and their metabolites for treating and preventing dysbiosis-related diseases. The review demonstrates, in the example of novel probiotics (psychobiotics), that many target-oriented probiotic preparations produce important side effects on a wide variety of processes in the host organism. In particular, we should take into account probiotics' capacity to produce mediators that can considerably modify the operation of the microecological, immune, and nervous system of the human organism.

Oliveira, L. F., Salvador, S. L., Silva, P. H., Furlaneto, F. A., Figueiredo, L., Casarin, R., Ervolino, E., Palioto, D. B., Souza, S. L., Taba, M., Jr., Novaes, A. B., Jr., and Messora, M. R. Benefits of Bifidobacterium animalis subsp. lactis Probiotic in Experimental Periodontitis. J.Periodontol. 2017; 88(2):197-208; PM: 27660886

ABSTRACT: BACKGROUND: This study evaluates effects of topical administration of probiotic bacteria of the genus Bifidobacterium on experimental periodontitis (EP) in rats. *METHODS*: Thirty-two rats were divided into groups C (control; without EP), EP (EP only), C-HN019 (control+probiotic), and EP-HN019 (EP+probiotic). On day 0 of the experiment, animals of groups EP and EP-HN019 received cotton ligatures around mandibular first molars (MFMs). In groups C-HN019 and EP-HN019, 1 mL of suspensions containing Bifidobacterium animalis subsp. lactis (B. lactis) HN019 was topically administered in the subgingival region of MFMs on days 0, 3, and 7. In groups C and EP, topical administrations were performed using a sham suspension (without probiotic). All animals were euthanized at day 14. Gingival tissue, hemimandibles, and oral biofilm were collected. Data were statistically analyzed ($P < 0.05$). *RESULTS*: Group EP presented greater bone porosity, trabecular separation, and connective tissue attachment loss (CTAL) as well as reduced bone volume than all other groups ($P < 0.05$). In group EP-HN019, there were greater proportions of Actinomyces and Streptococcus-like species and lower proportions of Veillonella parvula, Capnocytophaga sputigena, Eikenella corrodens, and Prevotella intermedia-like species than group EP. Group EP-HN019

presented greater expressions of osteoprotegerin and beta-defensins than group EP (P <0.05). Group EP presented greater levels of interleukin-1beta and receptor activator of nuclear factor-kappa B ligand than group EP-HN019 (P <0.05). *CONCLUSION*: Topical use of B. lactis HN019 promotes a protective effect against alveolar bone loss and CTALs attributable to EP in rats, modifying immunoinflammatory and microbiologic parameters.

Olmos, Soto J. Bacillus Probiotic Enzymes: External Auxiliary Apparatus to Avoid Digestive Deficiencies, Water Pollution, Diseases, and Economic Problems in Marine Cultivated Animals. Adv.Food Nutr.Res. 2017; 80:15-35; PM: 28215324

ABSTRACT: Exploitation of marine fishes is the main source of several life-supporting feed compounds such as proteins, lipids, and carbohydrates that maintain the production of most trading marine organisms by aquaculture. However, at this rate the marine inventory will go to the end soon, since fishery resources are finite. In this sense, the availability of the principal ingredients obtained from marine fishes is going to decrease considerably, increasing the diet prices and affecting the economy of this activity. Therefore, aquaculture industry needs to find nonexpensive land unconventional resources of protein, carbohydrates, and lipids and use bacterial probiotics to improve digestion-assimilation of these unfamiliar compounds. Bacillus subtilis is a cosmopolitan probiotic bacterium with a great enzymatic profile that could improve nutrient digestion-assimilation, induce healthy growth, and avoid water pollution, decreasing economic problems and increasing yields in the aquaculture industry. In this chapter, we present how Bacillus enzymes can help marine animals to assimilate nutrients from unconventional and economic plant resources.

Omar, A., Wright, J. B., Schultz, G., Burrell, R., and Nadworny, P. Microbial Biofilms and Chronic Wounds. Microorganisms. 3-7-2017; 5(1); PM: 28272369

ABSTRACT: Background is provided on biofilms, including their formation, tolerance mechanisms, structure, and morphology within the context of chronic wounds. The features of biofilms in chronic wounds are discussed in detail, as is the impact of biofilm on wound chronicity. Difficulties associated with the use of standard susceptibility tests (minimum inhibitory concentrations or MICs) to determine appropriate treatment regimens for, or develop new treatments for use in, chronic wounds are discussed, with alternate test methods specific to biofilms being recommended. Animal models appropriate for evaluating biofilm treatments are also described. Current and potential future therapies for treatment of biofilm-containing chronic wounds, including probiotic therapy, virulence attenuation, biofilm phenotype expression attenuation, immune response suppression, and aggressive debridement combined with antimicrobial dressings, are described.

Opara, E. C. Applications of Cell Microencapsulation. Methods Mol.Biol. 2017; 1479:23-39; PM: 27738924

ABSTRACT: The goal of this chapter is to provide an overview of the different purposes for which the cell microencapsulation technology can be used. These include immunoisolation of non-autologous cells used for cell therapy; immobilization of cells for localized (targeted) delivery of therapeutic products to ablate, repair, or regenerate tissue; simultaneous delivery of multiple therapeutic agents in cell therapy; spatial

compartmentalization of cells in complex tissue engineering; expansion of cells in culture; and production of different probiotics and metabolites for industrial applications. For each of these applications, specific examples are provided to illustrate how the microencapsulation technology can be utilized to achieve the purpose. However, successful use of the cell microencapsulation technology for whatever purpose will ultimately depend upon careful consideration for the choice of the encapsulating polymers, the method of fabrication (cross-linking) of the microbeads, which affects the permselectivity, the biocompatibility and the mechanical strength of the microbeads as well as environmental parameters such as temperature, humidity, osmotic pressure, and storage solutions.The various applications discussed in this chapter are illustrated in the different chapters of this book and where appropriate relevant images of the microencapsulation products are provided. It is hoped that this outline of the different applications of cell microencapsulation would provide a good platform for tissue engineers, scientists, and clinicians to design novel tissue constructs and products for therapeutic and industrial applications.

Ornellas, R. M., Santos, T. T., Arcucio, L. B., Sandes, S. H., Oliveira, M. M., Dias, C. V., de Carvalho, Silva S., Uetanabaro, A. P., Vinderola, G., and Nicoli, J. R. Selection of Lactic Acid Bacteria with Probiotic Potential Isolated from the Fermentation Process of "Cupuacu" (Theobroma grandiflorum). Adv.Exp.Med.Biol. 2-22-2017; PM: 28224483

ABSTRACT: In the present study, nine lactic acid bacteria isolated from the fermentation process of "cupuacu" (Theobroma grandiflorum) were selected for probiotic use. In vitro (resistance to gastrointestinal environment, in vitro antagonism and co-aggregation with pathogens) and in vivo (intestinal colonization and ex vivo antagonism in germ-free mice, cumulative mortality, translocation to liver and spleen, histopathological examination of liver and ileum and mRNA cytokine gene expression during an experimental infection with S. Typhimurium) assays were used. Among the nine Lactobacillus strains isolated from the "cupuacu" fermentation, L. plantarum 81 and L. plantarum 90 were selected as potential probiotics based on better results obtained in in vitro evaluations (production of diffusible inhibitory compounds and co-aggregation) as well as in vivo experiments (resistance to gastrointestinal environment, ex vivo antagonism, higher survival after enteropathogen challenge, lower hepatic translocation of enteropathogen, lower histopathological lesions in ileum and liver and anti-inflammatory pattern of immunological response). Concluding, L. plantarum 81 and L. plantarum 90 showed in vitro and in vivo capacities for probiotic use through different mechanisms of protection and its origin would allow an easier adaptation in an alimentary matrix for its administration.

Otani, K., Tanigawa, T., Watanabe, T., Shimada, S., Nadatani, Y., Nagami, Y., Tanaka, F., Kamata, N., Yamagami, H., Shiba, M., Tominaga, K., Fujiwara, Y., and Arakawa, T. Microbiota Plays a Key Role in Non-Steroidal Anti-Inflammatory Drug-Induced Small Intestinal Damage. Digestion. 2017; 95(1):22-28; PM: 28052268

ABSTRACT: BACKGROUND: Non-steroidal anti-inflammatory drugs (NSAIDs) damage the small intestine by causing multiple erosions and ulcers. However, to date, no established therapies and prophylactic agents are available to treat such damages. We reviewed the role of intestinal microbiota in NSAID-induced intestinal damage and identified potential therapeutic candidates. *SUMMARY*: The composition of the intestinal microbiota is an important factor in the pathophysiology of NSAID-induced small

intestinal damage. Once mucosal barrier function is disrupted due to NSAID-induced prostaglandin deficiency and mitochondrial malfunction, lipopolysaccharide from luminal gram-negative bacteria and high mobility group box 1 from the injured epithelial cells activate toll-like receptor 4-signaling pathway and nucleotide-binding oligomerization domain-like receptor family, pyrin domain-containing 3 inflammasome; this leads to the release of proinflammatory cytokines such as tumor necrosis factor-alpha and interleukin-1beta. Proton pump inhibitors (PPIs) are often used for the prevention of NSAID-induced injuries to the upper gastrointestinal tract. However, several studies indicate that PPIs may induce dysbiosis, which may exacerbate the NSAID-induced small intestinal damage. Our recent research suggests that probiotics and rebamipide could be used to prevent NSAID-induced small intestinal damage by regulating the intestinal microbiota. Key Messages: Intestinal microbiota plays a key role in NSAID-induced small intestinal damage, and modulating the composition of the intestinal microbiota could be a new therapeutic strategy for treating this damage.

Ouwehand, A. C. A review of dose-responses of probiotics in human studies. Benef.Microbes. 4-26-2017; 8(2):143-151; PM: 28008787

ABSTRACT: The probiotic definition requires the administration of an 'adequate amount' in order to obtain a health benefit. What that amount should be is not indicated. Here, an overview is given of studies that investigated the dose-response relation of probiotics in human interventions. Studies were divided in; meta-analyses, meta-analyses on specific probiotic strains, and studies testing two or more doses of a probiotic (combination) in the same study. Meta-analyses on the effect of probiotics on antibiotic associated diarrhoea (AAD) suggest a dose-response effect; for Clostridium difficile-associated diarrhoea on the other hand no dose-response was observed. For other end-points; such as necrotising enterocolitis, prevention of atopic dermatitis and slow intestinal transit, no dose-response relation was identified in meta-analyses. For prophylaxis in colorectal cancer and relief of irritable bowel syndrome, no dose-response relation was determined. However, for blood pressure, a meta-analysis observed that higher doses (greater than 1011 cfu) were more effective than lower doses. Meta-analyses of specific strains suggest a break-point for effectiveness of Lactobacillus rhamnosus GG in the treatment of acute gastroenteritis in children; no dose-response was observed for two other probiotics assessed. Studies comparing two or more doses indicate that faecal recovery and risk reduction of AAD follow a positive dose-response relationship. Other end-points such as immune markers, general health, and bowel function did not exhibit clear dose-response relations. For AAD, the findings are very compelling; both meta-analyses and dedicated dose-response studies observe a positive correlation between dose and AAD risk. These findings do not allow for extrapolation, but suggest that studying higher doses for this end-point would be worthwhile. The lack of a clear dose-response for other end-points, does not mean it does not exist; present data does just not allow drawing any conclusions.

Pacifici, S., Song, J., Zhang, C., Wang, Q., Glahn, R. P., Kolba, N., and Tako, E. Intra Amniotic Administration of Raffinose and Stachyose Affects the Intestinal Brush Border Functionality and Alters Gut Microflora Populations. Nutrients. 3-19-2017; 9(3); PM: 28335485

ABSTRACT: This study investigates the effectiveness of two types of prebiotics-stachyose and raffinose-which are present in staple food crops that are widely consumed in regions where dietary Fe deficiency is a health concern. The hypothesis is that these prebiotics

will improve Fe status, intestinal functionality, and increase health-promoting bacterial populations in vivo (Gallus gallus). By using the intra-amniotic administration procedure, prebiotic treatment solutions were injected in ovo (day 17 of embryonic incubation) with varying concentrations of a 1.0 mL pure raffinose or stachyose in 18 MOmega H(2)O. Four treatment groups (50, 100 mg.mL-1 raffinose or stachyose) and two controls (18 MOmega H(2)O and non-injected) were utilized. At hatch the cecum, small intestine, liver, and blood were collected for assessment of the relative abundance of the gut microflora, relative expression of Fe-related genes and brush border membrane functional genes, hepatic ferritin levels, and hemoglobin levels, respectively. The prebiotic treatments increased the relative expression of brush border membrane functionality proteins ($p < 0.05$), decreased the relative expression of Fe-related proteins ($p < 0.05$), and increased villus surface area. Raffinose and stachyose increased the relative abundance of probiotics ($p < 0.05$), and decreased that of pathogenic bacteria. Raffinose and stachyose beneficially affected the gut microflora, Fe bioavailability, and brush border membrane functionality. Our investigations have led to a greater understanding of these prebiotics' effects on intestinal health and mineral metabolism.

Palacios, T., Vitetta, L., Coulson, S., Madigan, C. D., Denyer, G. S., and Caterson, I. D. The effect of a novel probiotic on metabolic biomarkers in adults with prediabetes and recently diagnosed type 2 diabetes mellitus: study protocol for a randomized controlled trial. Trials. 1-9-2017; 18(1):7; PM: 28069054

ABSTRACT: BACKGROUND: Shifts in the gastrointestinal microbiome have been shown to contribute to the progression of metabolic diseases including prediabetes and type 2 diabetes mellitus. Research suggests that in-vivo modulation of the gut microbiome by specific probiotic microorganisms may improve insulin sensitivity and blood sugar management, preventing or delaying the development of type 2 diabetes mellitus. However, further research is needed to understand the effect of probiotics as a therapy for the treatment of metabolic diseases. An evidence-based multi-species probiotic was developed to encourage a shift in the gastrointestinal bacterial cohort from a disease-prone to a balanced state with the aim of improving metabolic markers associated with type 2 diabetes mellitus. *METHODS*: Sixty adults with a body mass index >/=25 kg/m2 with prediabetes or type 2 diabetes mellitus (diagnosed within the previous 12 months) will be enrolled in a double-blind, placebo-controlled pilot study. Participants will be randomized to a multi-species probiotic or placebo for 12 weeks. Both groups will receive lifestyle and nutritional advice. The primary outcome measure is the change between groups in fasting plasma glucose levels from baseline to 12 weeks. Secondary outcome measures include, but are not limited to, the change in lipid profile, systemic inflammation, gut permeability, and faecal microbial and metabolomic profiles. Blood and stool samples are collected at baseline and 12 weeks after treatment. *DISCUSSION*: Intentional manipulation of gastrointestinal microbial profiles may be useful for preventing and controlling type 2 diabetes mellitus and its associated metabolic complications. *TRIAL REGISTRATION*: Australian New Zealand Clinical Trials Registry, ACTRN12613001378718 . Registered on 16 December 2013.

Palaniswamy, S. K. and Govindaswamy, V. A Zymogram technique for preliminary screening and characterization of feruloyl esterases. Enzyme Microb.Technol. 2017; 101:57-59; PM: 28433192

ABSTRACT: We report here, for the first time, a zymogram technique designed for rapid

screening of feruloyl esterase using ethyl ferulate as enzyme substrate and casein precipitation as enzyme activity indicator.

Pan, M., Kumaree, K. K., and Shah, N. P. Physiological Changes of Surface Membrane in Lactobacillus with Prebiotics. J.Food Sci. 2017; 82(3):744-75; PM: 28199749

ABSTRACT: Synbiotics are always considered to be beneficial in healthy manipulation of gut environment; however, the purpose of this research was to investigate the dominance of synbiotic over the individual potential of probiotics and prebiotics. Four different types of prebiotics, fructo-oligosaccharides, raffinose, inulin, and cellobiose, were evaluated based on their varying degree of polymerization, combined each with 2 different Lactobacilli strains, including Lactobacillus paracasei 276 and Lactobacillus plantarum WCFS1. The effects of synbiotics combination on the surface structure were evaluated by analyzing auto-aggregation, membrane hydrophobicity, and adhesion to Caco-2 cells. Our results showed that both Lactobacilli exhibited significantly greater degree of attachment to Caco-2 cells (23.31% and 16.85%, respectively) when using cellobiose as a substrate than with other prebiotics ($P < 0.05$). Intestinal adhesion ability was in correlation with the percent of auto-aggregation, both Lactobacillus exhibited higher percent of auto-aggregation in cellobiose compared to other prebiotics. These behavioral changes in terms of attachment and auto-aggregation were further supported with the changes noticed from infrared spectra (FT-IR).

Panahi, Y., Ghanei, M., Vahedi, E., Mousavi, S. H., Imani, S., and Sahebkar, A. Efficacy of probiotic supplementation on quality of life and pulmonary symptoms due to sulfur mustard exposure: a randomized double-blind placebo-controlled trial. Drug Chem.Toxicol. 2017; 40(1):24-29; PM: 27079636

ABSTRACT: OBJECTIVE: This study investigated the efficacy and safety of supplementation with probiotics in improving chronic pulmonary symptoms due to sulfur mustard (SM) exposure. *METHODS*: In a randomized double-blind placebo-controlled study, 65 subjects suffering from chronic pulmonary complications of SM were assigned to one probiotic capsule (1 x 109 CFU containing seven strains of lactic acid-producing bacteria) every 12 h or an identical placebo for six weeks. Serum high-sensitivity C-reactive protein (CRP) concentrations, pulmonary function tests (FEV1, FEV1/FVC and MMEF 25-75%) and COPD assessment test (CAT) were assessed at baseline and at the end of trial. *RESULTS*: The groups were comparable in baseline characteristics. There were significant improvements in FEV1/FVC in the probiotic but not in placebo group. CAT scores were decreased in both study groups. However, between-group comparison of changes in the assessed parameters reached statistical significance only for CAT score ($p < 0.001$). There was no report of adverse events during the course of trial. *CONCLUSIONS*: Findings of the present trial favor the efficacy of probiotic supplementation in improving the pulmonary symptoms of SM-exposed subjects.

Parashar, A. and Udayabanu, M. Gut microbiota: Implications in Parkinson's disease. Parkinsonism.Relat Disord. 2017; 38:1-7; PM: 28202372

ABSTRACT: Gut microbiota (GM) can influence various neurological outcomes, like cognition, learning, and memory. Commensal GM modulates brain development and behavior and has been implicated in several neurological disorders like Alzheimer's disease, multiple sclerosis, amyotrophic lateral sclerosis, anxiety, stress and much more. A

recent study has shown that Parkinson's disease patients suffer from GM dysbiosis, but whether it is a cause or an effect is yet to be understood. In this review, we try to connect the dots between GM and PD pathology using direct and indirect evidence.

Parcina, Amizic, I, Cigic, L., Gavic, L., Radic, M., Biocina, Lukenda D., Tonkic, M., and Goic, Barisic, I. Antimicrobial efficacy of probiotic-containing toothpastes: an in vitro evaluation. Med.Glas.(Zenica.). 2-1-2017; 14(1):139-144; PM: 28165440

ABSTRACT: *Aim*: To evaluate, in vitro antimicrobial ability of two probiotic toothpastes (one containing Lactobacillus paracasei, other containing Lactobacillus acidophilus) and one toothpaste without probiotic separately, and in a combination with two different mouthrinses (one containing essential oils and the other containing hexitidine). *Methods*: Antimicrobial susceptibility was checked by using the ditch method and Clinical Laboratory Standard Institute (CLSI) guidelines. Two different toothpastes with probiotic, toothpaste without probiotic and two different mouthrinses were tested against the following selected microorganisms: Candida albicans, Candida tropicalis, Enterococcus faecalis, Streptococcus salivarius and Staphylococcus aureus. Kruskal-Wallis test and MannWhitney U test were used for the statistical analysis (p</= 0.05). *Results*: Probiotic toothpastes had better inhibitory effect than toothpaste without probiotic in the case of Candida albicans (p=0.043) and Streptococcus salivarius (p=0.043). In all cases, toothpastes had stronger inhibition capacity than mouthrinses (p</=0.05). *Conclusion*: Probiotic toothpastes, as a relatively new concept in the prevention of oral infectious diseases such as caries and periodontal disease, can contribute to the prevention of oral infectious diseases.

Parois, S., Calandreau, L., Kraimi, N., Gabriel, I., and Leterrier, C. The influence of a probiotic supplementation on memory in quail suggests a role of gut microbiota on cognitive abilities in birds. Behav.Brain Res. 5-11-2017; PM: 28502731

ABSTRACT: The gut microbiota is involved in host behaviour and memory in mammals. Consequently, it may also influence emotional behaviour and memory in birds. Quail from two genetic lines with different fearfulness (LTI: long tonic immobility, n=37; STI: short tonic immobility, n=32) were either or not supplemented with a probiotic (Pediococcus acidilactici) from hatching. Emotional reactivity was measured in a tonic immobility test (d6 and 7 of age) and two open-field tests (d13 to 15; d22 to 24). Memory was measured in a test rewarded with mealworms, where quail had to remember the cups previously visited (d34 to 36). Quail endured a 5-days stress period from days 17 to 21 to help revealing the potentially beneficial effect of the probiotic. As expected, STI quail were less fearful compared to the LTI quail (p<0.05). Probiotic supplementation had no effect on most measures of emotional reactivity (p > 0.05), except in the tonic immobility test where supplemented STI quail had lower immobility duration (p=0.0001). Regarding the memory test, the two lines had similar performances. Quail fed with probiotics made fewer errors (p=0.040). There was no significant correlation between traits of emotional reactivity and of memory. In conclusion, the supplementation with Pediococcus acidilactici as a probiotic, affected a specific trait of emotional reactivity in STI quail, and improved memory in both lines, whichstrengthens the idea that the influence of gut microbiota on the host behaviour and memory seen in mammals is shared by birds.

Partty, A., Kalliomaki, M., Salminen, S., and Isolauri, E. Infantile Colic Is Associated With Low-grade Systemic Inflammation. J.Pediatr.Gastroenterol.Nutr. 2017; 64(5):691-695; PM: 27478897

ABSTRACT: OBJECTIVES: Dysbiosis, an imbalance in the taxonomic composition of the gut bacteria occurring during the critical stages of development, induces lasting shifts in the immunological and metabolic phenotype if accompanied by an inflammatory response. Because altered gut microbiota and successful treatment with probiotics have both been demonstrated in cases of colic, we hypothesized here that infants with colic might have low-grade inflammation. *METHODS*: In 28 infants with colic and in 12 healthy controls at the age of 1 month, we measured the following serum immunological biomarkers: cytokines interleukin 1beta (IL-1beta); IL-6; IL-10; tumor necrosis factor alpha; interferon gamma (IFN-gamma); chemokines IL-8; monocyte chemotactic protein-1 (MCP-1); macrophage inflammatory protein 1beta (MIP-1beta) and chemokine (C-X-C motif) ligand 16; and intestinal fatty acid-binding protein, a biomarker of enterocyte damage and zonulin, a biomarker of intestinal permeability. In addition, intestinal microbiota composition was correlated with immunological biomarkers. *RESULTS*: Infants with colic had increased concentrations of IL-8, MCP-1, and MIP-1beta in serum as compared with healthy children. All the other immunological biomarkers were comparable between the groups. Fecal levels of Clostridium leptum correlated negatively with the proinflammatory markers MCP-1 ($r = -0.44$, $P = 0.02$), MIP-1beta ($r = -0.43$, $P = 0.02$), and tumor necrosis factor alpha ($r = -0.38$, $P = 0.04$). In addition, C coccoides group levels correlated negatively with MCP-1 ($r = -0.43$, $P = 0.02$) and Bifidobacterium breve levels positively with chemokine (C-X-C motif) ligand 16 ($r = 0.38$, $P = 0.04$). *CONCLUSIONS*: In addition to gut microbiota alterations, colic in infants is associated with low-grade systemic inflammation. Specific bacterial species beyond conventional probiotics may have anti-inflammatory properties that may help to modulate microbiota and alleviate colic-related inflammation.

Pawar, M. M., Pattanaik, A. K., Sinha, D. K., Goswami, T. K., and Sharma, K. Effect of dietary mannanoligosaccharide supplementation on nutrient digestibility, hindgut fermentation, immune response and antioxidant indices in dogs. J.Anim Sci.Technol. 2017; 59:11; PM: 28507766

ABSTRACT: BACKGROUND: Use of prebiotics in companion animal nutrition is often considered advantageous over probiotics because of the ease of handling, ability to withstand processing and storage etc. While most of the studies on prebiotic use in dogs have been done with processed food as basal diet, the response in relation to homemade diet feeding is not very well explored. *METHODS*: The study was conducted to evaluate the effects of dietary mannanoligosaccharide (MOS) supplementation on nutrient digestibility, hindgut fermentation, immune response and antioxidant indices in dogs. Ten Spitz pups were divided into two groups: control (CON) with no supplementation, and experimental (MOS) wherein the basal diet was supplemented with MOS at 15 g/kg diet. All dogs were fed on a home-prepared diet for a period of 150 days. The study protocol included a digestion trial, periodic blood collection and analysis for lipid profile and erythrocytic antioxidants. Immune response of the animals was assessed towards the end of the feeding period. *RESULTS*: Results revealed no significant ($P > 0.05$) variations in palatability score, intake and apparent digestibility of nutrients between the groups. Faecal score, faeces voided, faecal pH, concentrations of ammonia, lactate and short-chain fatty acids were comparable ($P > 0.05$) between the

two groups. Cell-mediated immune response, assessed as delayed-type of hypersensitivity response, was significantly higher ($P < 0.05$) in the MOS group. The percent of lymphocyte sub-populations CD4+ and ratio of CD4+:CD8+ were also significantly ($P < 0.05$) higher in MOS group. The serum IgG levels were similar ($P > 0.05$) in both the groups. Supplementation of MOS lowered ($P < 0.05$) serum total- and LDL-cholesterol levels, when compared with the control group. The erythrocytic antioxidant indices were similar ($P > 0.05$) between the two groups. *CONCLUSIONS*: The results indicated that supplementation of MOS at the rate of 15 g/kg in the diet of dog augmented the cell-mediated immune response and serum lipid profile without any influences on digestibility of nutrients, hindgut fermentation and antioxidants indices.

Payandeh, S., Kafilzadeh, F., Juarez, M., de la Fuente, M. A., Ghadimi, D., and Martinez Marin, A. L. Probiotic supplementation effects on milk fatty acid profile in ewes. J.Dairy Res. 2017; 84(2):128-131; PM: 28524013

ABSTRACT: We hypothesised that probiotic feeding would alter the fatty acid (FA) profile of sheep's milk. Sixteen lactating ewes, kept under the same feeding and management practices, were randomly allocated to receive either a control diet or the same diet supplemented with a commercial multi-strain bacterial probiotic. Milk fat FA contents were monitored fortnightly for eight consecutive weeks from 14 d after lambing. Probiotic supplementation increased the contents of butyric and caproic acids in milk fat and had no negative effects on other relevant FA from the human's health point of view (i.e., no differences in branched chain, vaccenic, rumenic and n-3 FA were observed). Under the conditions assayed in the present work, the contents of milk FA originated from rumen microbial metabolism were scantly altered, which suggests that the rumen conversion pathways of FA were not substantially modified by the probiotics.

Pazzini, C. A., Pereira, L. J., da Silva, T. A., Montalvany-Antonucci, C. C., Macari, S., Marques, L. S., and de Paiva, S. M. Probiotic consumption decreases the number of osteoclasts during orthodontic movement in mice. Arch.Oral Biol. 2017; 79:30-34; PM: 28282515

ABSTRACT: AIMS: The aim of the present study was to investigate the effect of probiotic (Bacillus Subtilis) supplementation on bone remodelling induced by mechanical loading. *METHODS*: C57BL/6 mice were divided in two groups: (1) Probiotic and (2) Vehicle (water). The probiotic (1.5x108CFU/mL) was administered orally for 14 days, starting two days before the induction of orthodontic tooth movement (OTM). OTM was determined by histomorphometric analysis by comparing the right to the left side of the maxilla. The number of osteoclasts was determined by counting TRAP-positive cells. Osteoblasts were counted on Masson's trichrome-stained slides. *RESULTS*: OTM was similar between groups (with and without probiotic supplementation) ($p=0.46$). The number of TRAP-positive cells increased ($p<0.01$) on the experimental side (where the spring coil was installed) in comparison to the control side in both groups. However, the number of osteoclasts decreased ($p<0.01$) in the probiotic group, in comparison to the vehicle group. There was an increase in the number of osteoblasts ($p<0.05$) in both the Vehicle and Probiotic groups on the side under OTM, independent of probiotic supplementation. *CONCLUSION*: Oral Supplementation with a probiotic influenced the number of osteoclasts adjacent to the tooth root during orthodontic movement in mice.

Pearson, J. S. and Whorwell, P. J. Progress with treating the microbial dysbiosis associated with irritable bowel syndrome. Curr.Opin.Gastroenterol. 2017; 33(1):21-25; PM: 28134688

ABSTRACT: PURPOSE OF REVIEW: Microbial dysbiosis is receiving increasing attention as possibly being important in the pathophysiology of irritable bowel syndrome. This review will summarize the most recent literature addressing attempts to explore and target the microbiome in patients with irritable bowel syndrome. *RECENT FINDINGS*: Manipulation of the intestinal microbiota in irritable bowel syndrome is receiving increasing attention. Traditionally, dietary manipulation has been utilized. There is now evidence that a low fermentable oligosaccharides, disaccharides, monosaccharides and polyols diet has not only been able to improve symptoms, but may have an effect on the gut microbiota. Probiotics are a safe and attractive option for the manipulation of the microbiota. There have been a number of well-designed trials examining the efficacy of certain strains of bacteria, and even yeasts are receiving attention. The role of antibiotics remains controversial and it seems likely that their use should currently be limited to those individuals with small intestinal bacterial overgrowth. Interest in the role of faecal microbiota transplantation for the treatment of a number of gastrointestinal conditions has intensified and irritable bowel syndrome is no exception. *SUMMARY*: The manipulation of the microbial dysbiosis is gaining momentum. Further research, however, is required in order to identify the most appropriate treatment option for each individual patient.

Peixoto, R. S., Rosado, P. M., Leite, D. C., Rosado, A. S., and Bourne, D. G. Beneficial Microorganisms for Corals (BMC): Proposed Mechanisms for Coral Health and Resilience. Front Microbiol. 2017; 8:341; PM: 28326066

ABSTRACT: The symbiotic association between the coral animal and its endosymbiotic dinoflagellate partner Symbiodinium is central to the success of corals. However, an array of other microorganisms associated with coral (i.e., Bacteria, Archaea, Fungi, and viruses) have a complex and intricate role in maintaining homeostasis between corals and Symbiodinium. Corals are sensitive to shifts in the surrounding environmental conditions. One of the most widely reported responses of coral to stressful environmental conditions is bleaching. During this event, corals expel Symbiodinium cells from their gastrodermal tissues upon experiencing extended seawater temperatures above their thermal threshold. An array of other environmental stressors can also destabilize the coral microbiome, resulting in compromised health of the host, which may include disease and mortality in the worst scenario. However, the exact mechanisms by which the coral microbiome supports coral health and increases resilience are poorly understood. Earlier studies of coral microbiology proposed a coral probiotic hypothesis, wherein a dynamic relationship exists between corals and their symbiotic microorganisms, selecting for the coral holobiont that is best suited for the prevailing environmental conditions. Here, we discuss the microbial-host relationships within the coral holobiont, along with their potential roles in maintaining coral health. We propose the term BMC (Beneficial Microorganisms for Corals) to define (specific) symbionts that promote coral health. This term and concept are analogous to the term Plant Growth Promoting Rhizosphere (PGPR), which has been widely explored and manipulated in the agricultural industry for microorganisms that inhabit the rhizosphere and directly or indirectly promote plant growth and development through the production of regulatory signals, antibiotics and nutrients. Additionally, we propose and discuss the potential mechanisms of the effects of BMC on corals, suggesting strategies for the use of this knowledge to manipulate the microbiome, reversing dysbiosis to restore and protect coral reefs. This may include

developing and using BMC consortia as environmental "probiotics" to improve coral resistance after bleaching events and/or the use of BMC with other strategies such as human-assisted acclimation/adaption to shifting environmental conditions.

Peldan, P., Kukkonen, A. K., Savilahti, E., and Kuitunen, M. Perinatal probiotics decreased eczema up to 10 years of age, but at 5-10 years, allergic rhino-conjunctivitis was increased. Clin.Exp.Allergy. 3-17-2017; PM: 28316095

No Abstract Available.

Pender, C. M., Kim, S., Potter, T. D., Ritzi, M. M., Young, M., and Dalloul, R. A. In ovo supplementation of probiotics and its effects on performance and immune-related gene expression in broiler chicks. Poult.Sci. 5-1-2017; 96(5):1052-1062; PM: 28158826

ABSTRACT: Probiotics are live, nonpathogenic microorganisms known to have a positive effect on the host by improving the natural balance of gut microbiota. The objective of this study was to determine the effects of administering probiotics (Primalac W/S) in ovo on hatchability, early post-hatch performance, and intestinal immune-related gene expression of broiler chicks. At embryonic day eighteen, 360 Cobb 500 eggs were injected with sterile water (sham), 1 x 105, 1 x 106, or 1 x 107 (P1, P2, and P3 respectively) probiotic bacteria. Another 90 eggs remained non-injected to serve as a negative control. Measurements and tissue samples were taken on day of hatch (DOH) and days 4, 6, 8, 15, and 22. No significant differences were seen among groups for hatchability, feed intake, feed conversion ratios, or mortality. Body weight of P2 was significantly greater than that of the negative control, sham and P1 on d 4, and that of the negative control and P1 on d 6. A similar pattern was observed for BW gain (BWG) from DOH to d 4. Real-time PCR was used to investigate the expression of immune-related genes in the ileum and cecal tonsils. Other than an initial upregulation of inducible nitric oxide synthase on DOH, in ovo probiotic supplementation was associated with downregulated expression of Toll-like receptors-2 and -4, inducible nitric oxide synthase, trefoil factor-2, mucin-2, interferon-gamma, and interleukins-4 and -13 in both the ileum and cecal tonsils, though expression patterns differed based on treatment, tissue, and time point evaluated. Taken together, these results indicate that in ovo supplementation of the probiotic product Primalac does not impact hatchability, can improve performance during the first week post-hatch, and is capable of modulating gene expression in the ileum and cecal tonsils.

Pepoyan, A. Z., Balayan, M. H., Manvelyan, A. M., Mamikonyan, V., Isajanyan, M., Tsaturyan, V. V., Kamiya, S., Netrebov, V., and Chikindas, M. L. Lactobacillus acidophilus INMIA 9602 Er-2 strain 317/402 probiotic regulates growth of commensal Escherichia coli in gut microbiota of familial Mediterranean fever disease subjects. Lett.Appl.Microbiol. 2017; 64(4):254-260; PM: 28140472

ABSTRACT: Previously, we reported a positive effect the probiotic formulation, Lactobacillus acidophilus INMIA 9602 Er-2 strain 317/402 (Narine strain), had on the blood characteristics of patients with familial Mediterranean fever disease (FMF). The aim of this investigation was to evaluate the effect of the Narine probiotic on growth characteristics in the predominant commensal Escherichia coli isolates from the gut microbiota in FMF-positive study participants. Bacterial growth of 192 prevalent commensal E. coli isolates

found in the volunteer participants' guts was evaluated using Verhulst's logistic function. This study showed that the duration of the preparatory growth phase for the E. coli isolates collected from FMF-positive volunteers was significantly shorter, whereas the duration of the logarithmic growth phase was significantly longer ($P < 0.03$) than that of the isolates collected from healthy participants. The Narine probiotic formulation caused a significant extension ($P < 0.001$) of the preparatory growth phase in the commensal E. coli isolated from FMF subjects a month after the Narine probiotic administration was terminated. The data suggest that the mathematical model characterizes the growth of commensal E. coli isolates from FMF-positive participants and it can be useful in a decision-making process on the practical use of probiotics during FMF. *SIGNIFICANCE AND IMPACT OF THE STUDY*: This is the first study to demonstrate the effects of Narine, containing the probiotic Lactobacillus acidophilus, on the growth of gut commensal Escherichia coli from study participants with familial Mediterranean fever disease (FMF). Verhulst's logistic function was demonstrated to act as a possible tool for the evaluation and quantification of effects produced by the probiotic formulation in FMF participants.

Perez-Gregorio, R. and Simal-Gandara, J. A Critical Review of Bioactive Food Components, and of their Functional Mechanisms, Biological Effects and Health Outcomes. Curr.Pharm.Des. 3-17-2017; PM: 28317483

ABSTRACT: BACKGROUND: Eating behaviours are closely related to some medical conditions potentially leading to death such as cancer, cardiovascular disease and diabetes. Healthy eating practices, maintaining a normal weight, and regular physical activity could prevent up to 80% of coronary heart disease, 90% of type-2 diabetes and one-third of all cancers[1]. *METHOD*: Over the last two decades, the food industry has invested much effort in research and development of healthier, more nutritious foods. These foods are frequently designated "functional" when they contain nutritional components required for healthy living or "nutraceuticals" when intended to treat or prevent disease or disorders through a variety of bioactive (e.g., antioxidant, antimicrobial, immunomodulatory, hypocholesterolaemic) functions that are performed by functional enzymes, probiotics, prebiotics, fibres, phytosterols, peptides, proteins, isoflavones, saponins or phytic acid, among other substances. *RESULTS*: Some agricultural and industrial residues have proven to be excellent choices as raw materials for producing bioactive compounds and have been proposed as potentially safe natural sources of antimicrobials and/or antioxidants for the food industry. Functional food ingredients containing bioactive compounds could be used as plant extracts by pharmaceutical and food industries. *CONCLUSION*: Bioactive food components influence health outcomes.

Pericolini, E., Gabrielli, E., Ballet, N., Sabbatini, S., Roselletti, E., Cayzeele, Decherf A., Pelerin, F., Luciano, E., Perito, S., Justen, P., and Vecchiarelli, A. Therapeutic activity of a Saccharomyces cerevisiae-based probiotic and inactivated whole yeast on vaginal candidiasis. Virulence. 1-2-2017; 8(1):74-90; PM: 27435998

ABSTRACT: Vulvovaginal candidiasis is the most prevalent vaginal infection worldwide and Candida albicans is its major agent. Vulvovaginal candidiasis is characterized by disruption of the vaginal microbiota composition, as happens following large spectrum antibiotic usage. Recent studies support the effectiveness of oral and local probiotic treatment for prevention of recurrent vulvovaginal candidiasis. Saccharomyces cerevisiae is a safe yeast used as, or for, the production of ingredients for human nutrition

and health. Here, we demonstrate that vaginal administration of probiotic Saccharomyces cerevisiae live yeast (GI) and, in part, inactivated whole yeast Saccharomyces cerevisiae (IY), used as post-challenge therapeutics, was able to positively influence the course of vaginal candidiasis by accelerating the clearance of the fungus. This effect was likely due to multiple interactions of Saccharomyces cerevisiae with Candida albicans. Both live and inactivated yeasts induced coaggregation of Candida and consequently inhibited its adherence to epithelial cells. However, only the probiotic yeast was able to suppress some major virulence factors of Candida albicans such as the ability to switch from yeast to mycelial form and the capacity to express several aspartyl proteases. The effectiveness of live yeast was higher than that of inactivated whole yeast suggesting that the synergy between mechanical effects and biological effects were dominant over purely mechanical effects. The protection of epithelial cells to Candida-induced damage was also observed. Overall, our data show for the first time that Saccharomyces cerevisiae-based ingredients, particularly the living cells, can exert beneficial therapeutic effects on a widespread vaginal mucosal infection.

Piechota, H. [Recurrent and catheter-associated urinary tract infections : Prophylaxis and prevention]. Urologe A. 4-19-2017; PM: 28424831

ABSTRACT: Urinay tract infection (UTI) as one of the most frequent bacterial infections in humans is of utmost relevance. Because of the rising prevalence of antimicrobial resistance, urinalysis should always include urine culture and a resistogram in order to avoid an unspecific selection and overuse of antibiotics. Prevention of recurrent UTI must first of all rule out predisposing uropathogenic conditions. Nowadays, a great variety of drugs, behavioral, and supportive treatment options can effectively minimize UTI recurrence. The growing importance of vaccines (immunotherapy), probiotics (lactobacilli), and standardized herbal preparations meets the need of reducing antibiotic use and the development of antimicrobial resistance. Around 80% of all nosocomial UTIs (nUTIs) are associated with indwelling urinary catheters. It is estimated that up to 70% of all nUTIs occurring in Germany may be avoided by using appropriate preventative measures. Therefore, profound knowledge about the basics of catheter-associated nUTIs and the correct management of urinary catheters are of utmost individual and socioeconomic importance.

Pina-Perez, M. C., Martinez, A., and Rodrigo, D. New Advances in Infant Feeding: New Products and Novel Technologies. Recent Pat Food Nutr.Agric. 3-28-2017; PM: 28355995

ABSTRACT: BACKGROUND: Breastfeeding is the best way to provide ideal food for infants. However, there are many situations in which breastfeeding is unviable (maternal illness, hygiene problems, intravenous feeding requirement, storage). Safe, efficient, and nutritious products should be offered by the industry to mothers and healthcare professionals as an alternative. *OBJECTIVE*: The present review aims to update the state of the art regarding the most innovative developments in infant feeding formulation and, the promising novel technologies that are being investigated to achieve a balance between the microbiological stability, organoleptic and nutritional value of babyfood. *METHODS*: The research lines included in the present systematic review are focused on both, the most innovative ingredients and emergent technologies applied increasing the offer of tailor-made nutritional profiled products with improved quality and safety. *RESULTS*: According to the reviewed research and recently published patents it is

remarkable the current emergence of a new generation of infant products, with specific product lines aimed at infants at different stages of development and affected by several disorders (low-weight babies, premature neonates, allergenic patients), with special emphasis on the application of novel technologies (e.g. High Hydrostatic Pressure (HHP) and microencapsulation) as potential techniques to ensure the microbiological safety of developed products, and the improvement of their nutritional value, complementary to the addition of functional ingredients such as omega 3 and 6 fatty acids, amino acids, prebiotics and probiotics, and medicinal herb supplementation (e.g. lemon balm, royal jelly). *CONCLUSION*: The present research work provides a general view of recent advances in infant products processing and formulation focusing on the technological effects and quality/safety developments.

Pinto-Sanchez, M. I., Hall, G. B., Ghajar, K., Nardelli, A., Bolino, C., Lau, J. T., Martin, F. P., Cominetti, O., Welsh, C., Rieder, A., Traynor, J., Gregory, C., De, Palma G., Pigrau, M., Ford, A. C., Macri, J., Berner, B., Bergonzelli, G., Surette, M. G., Collins, S. M., Moayyedi, P., and Bercik, P. Probiotic Bifidobacterium longum NCC3001 Reduces Depression Scores and Alters Brain Activity: a Pilot Study in Patients With Irritable Bowel Syndrome. Gastroenterology. 5-5-2017; PM: 28483500

ABSTRACT: BACKGROUND & AIMS: Probiotics can reduce symptoms of irritable bowel syndrome (IBS), but little is known about their effects on psychiatric comorbidities. We performed a prospective study to evaluate the effects of Bifidobacterium longum NCC3001 (BL) on anxiety and depression in patients with IBS. *METHODS*: We performed a randomized, double-blind, placebo-controlled study of 44 adults with IBS and diarrhea or a mixed-stool pattern (based on Rome III criteria) and mild to moderate anxiety and/or depression (based on the Hospital Anxiety and Depression scale) at McMaster University in Canada, from March 2011 to May 2014. At the screening visit, clinical history and symptoms were assessed and blood samples were collected. Patients were then randomly assigned to groups and given daily BL (n=22) or placebo (n=22) for 6 weeks. At week 0, 6 and 10, we determined patients' levels of anxiety and depression, IBS symptoms, quality of life, and somatization using validated questionnaires. At week 0 and 6, stool, urine and blood samples were collected, and functional magnetic resonance imaging (fMRI) test was performed. We assessed brain activation patterns, fecal microbiota, urine metabolome profiles, serum markers of inflammation, neurotransmitters and neurotrophin levels. *RESULTS*: At week 6, 14/22 patients in the BL group had reduction in depression scores of 2 points or more on the Hospital Anxiety and Depression scale, vs 7/22 patients in the placebo group (P=.04). BL had no significant effect on anxiety or IBS symptoms. Patients in the BL group had a mean increase in quality of life score compared with the placebo group. The fMRI analysis showed that BL reduced responses to negative emotional stimuli in multiple brain areas, including amygdala and fronto-limbic regions, compared with placebo. The groups had similar fecal microbiota profiles, serum markers of inflammation, and levels of neurotrophins and neurotransmitters, but the BL group had reduced urine levels of methylamines and aromatic amino acids metabolites. At week 10, depression scores were reduced in patients given BL vs placebo. *CONCLUSION*: In a placebo-controlled trial, we found that the probiotic BL reduces depression but not anxiety scores and increases quality of life in patients with IBS. These improvements were associated with changes in brain activation patterns that indicate that this probiotic reduces limbic reactivity. ClinicalTrials.gov no. NCT01276626.

Podolsky, S. H. Historical Perspective on the Rise and Fall and Rise of Antibiotics and Human Weight Gain. Ann.Intern.Med. 1-17-2017; 166(2):133-138; PM: 28114473

ABSTRACT: In recent medical and popular literature, audiences have been asked to consider whether antibiotics have contributed to the rising obesity epidemic. Prominent magazines have stated that weight may be adversely affected by antibiotics that destroy existing microbiomes and replace them with less helpful ones. However, there is a long history of efforts to investigate the relationship between antibiotics and human weight gain. In the early 1950s, amid initial findings that low doses of antibiotics served as growth promoters in animal livestock, investigators explored the role of antibiotics as magic bullets for human malnutrition. Nevertheless, early enthusiasm was tempered by controlled studies showing that antibiotics did not serve as useful, nonspecific growth promoters for humans. In subsequent decades, against the backdrop of rising concern over antibiotic resistance, investigators studying the role of antibiotics in acute malnutrition have had to navigate a more complicated public health calculus. In a related historical stream, scientists since the 1910s have explored the role of the intestinal microflora in human health. By the 2000s, as increasing resources and more sophisticated tools were devoted to understanding the microbiome (a term coined in 2001), attention would turn to the role of antibiotics and the intestinal microflora in the rising obesity epidemic. Despite scientific and commercial enthusiasm, easy answers (whether about antibiotics or probiotics) have again given way to an appreciation for the complexity of human growth. History encourages caution about our hopes for simplistic answers for presumed "fat drugs" and slimming probiotics alike.

Ponziani, F. R., Binda, C., and Gasbarrini, A. How to modulate gut microbiota: diet, pre-probiotics or antibiotics? Minerva Gastroenterol.Dietol. 2-17-2017; PM: 28215066

ABSTRACT: The gut microbiota is involved in the maintenance of humans' health and its alterations have been associated to several intestinal and extra intestinal disorders. For this reason, there is increasing interest on gut microbiota modulation as both a preventive strategy or as a therapeutic option in different gastrointestinal, hepatic and systemic diseases. Many studies have tried to find out the impact of diet, prebiotic, probiotic and antibiotics on gut microbiota composition and function, obtaining very heterogeneous and sometimes conflicting results, especially as regards the effect on clinical outcomes. However, these preliminary data represent a promising premise for further studies that will provide a more comprehensive knowledge about the role of gut microbiota as a therapeutic target.

Porto, M. C., Kuniyoshi, T. M., Azevedo, P. O., Vitolo, M., and Oliveira, R. P. Pediococcus spp.: An important genus of lactic acid bacteria and pediocin producers. Biotechnol.Adv. 2017; 35(3):361-37; PM: 28284993

ABSTRACT: Probiotics have gained increasing attention due to several health benefits related to the human digestive and immune systems. Pediococcus spp. are lactic acid bacteria (LAB) that are widely described as probiotics and characterized as coccus-shaped bacteria (arranged in tetrads), Gram-positive, non-motile, non-spore forming, catalase-negative, and facultative anaerobes. There are many Pediococcus strains that produce pediocin, an effective antilisterial bacteriocin. Pediocins are small, cationic molecules consisting of a conserved hydrophilic N-terminal portion containing the YGNGV motif and an amphiphilic or hydrophobic C-terminal variable portion. A number

of studies have been developed with Pediococcus isolated from multiple biological niches to conduct fermentation processes for pediocin or Pediococcus cell production. This review gathers the most significant information about the cultivation, mode of action, and variability of bacteriocins produced by Pediococcus spp., emphasizing their applications in the areas of food and clinical practice. This updated panorama assists in delimiting the challenges that still need to be overcome for pediocin use to be approved for human consumption and the food industry.

Poutsiaka, D. D., Mahoney, I. J., McDermott, L. A., Stern, L. L., Thorpe, C. M., Kane, A. V., Baez-Giangreco, C., McKinney, J., Davidson, L. E., Leyva, R., Goldin, B., and Snydman, D. R. Selective method for identification and quantification of Bifidobacterium animalis subspecies lactis BB-12 (BB-12) from the gastrointestinal tract of healthy volunteers ingesting a combination probiotic of BB-12 and Lactobacillus rhamnosus GG. J.Appl.Microbiol. 2017; 122(5):1321-1332; PM: 28256070

ABSTRACT: AIM: To develop a novel validated method for the isolation of Bifidobacterium animalis ssp. lactis BB-12 (BB-12) from faecal specimens and apply it to studies of BB-12 and Lactobacillus rhamnosus GG (LGG) recovered from the healthy human gastrointestinal (GI) tract. *METHODS AND RESULTS*: A novel method for isolating and enumerating BB-12 was developed based on its morphologic features of growth on tetracycline-containing agar. The method identified BB-12 correctly from spiked stool close to 100% of the time as validated by PCR confirmation of identity, and resulted in 97-104% recovery of BB-12. The method was then applied in a study of the recovery of BB-12 and LGG from the GI tract of healthy humans consuming ProNutrients(R) Probiotic powder sachet containing BB-12 and LGG. Viable BB-12 and LGG were recovered from stool after 21 days of probiotic ingestion compared to baseline. In contrast, no organisms were recovered 21 days after baseline in the nonsupplemented control group. *CONCLUSIONS*: We demonstrated recovery of viable BB-12, using a validated novel method specific for the isolation of BB-12, and LGG from the GI tract of healthy humans who consumed the probiotic supplement. *SIGNIFICANCE AND IMPACT OF THE STUDY*: This method will enable more detailed and specific studies of BB-12 in probiotic supplements, including when in combination with LGG.

Pujia, A. M., Costacurta, M., Fortunato, L., Merra, G., Cascapera, S., Calvani, M., and Gratteri, S. The probiotics in dentistry: a narrative review. Eur.Rev.Med.Pharmacol.Sci. 2017; 21(6):1405-1412; PM: 28387884

ABSTRACT: The total number of microbes that colonize the human body is far greater than the number of cells that make it up. In recent years, it has been shown that bacteria play an essential role in the body; in fact, they are essential for the maturation of the intestine, the development and control of the immune system, the development of the brain, the metabolism of macronutrients, the synthesis of vitamins, and the energy balance. Bacteria play an essential role in defense of their territory against the entry of other bacteria that may be pathogenic to health. Metchnikoff, about a century ago, invented probiotics, assuming that the use of certain bacteria could be beneficial to maintaining health. Bacteria colonize our body from birth and breastfeeding, using the bacterial flora of the mother by accessing newborns through the mouth. Antibiotic therapies in pregnancy or cesarean section prevent this flow of probiotics to infants and open the way for very important diseases, such as diabetes and obesity. The alterations

of oral bacterial flora are responsible for numerous diseases of the oral cavity and the idea of the use of probiotics is leading the way to new therapeutic perspectives.

Puyol, D., Batstone, D. J., Hulsen, T., Astals, S., Peces, M., and Kromer, J. O. Resource Recovery from Wastewater by Biological Technologies: Opportunities, Challenges, and Prospects. Front Microbiol. 2016; 7:2106; PM: 28111567

ABSTRACT: Limits in resource availability are driving a change in current societal production systems, changing the focus from residues treatment, such as wastewater treatment, toward resource recovery. Biotechnological processes offer an economic and versatile way to concentrate and transform resources from waste/wastewater into valuable products, which is a prerequisite for the technological development of a cradle-to-cradle bio-based economy. This review identifies emerging technologies that enable resource recovery across the wastewater treatment cycle. As such, bioenergy in the form of biohydrogen (by photo and dark fermentation processes) and biogas (during anaerobic digestion processes) have been classic targets, whereby, direct transformation of lipidic biomass into biodiesel also gained attention. This concept is similar to previous biofuel concepts, but more sustainable, as third generation biofuels and other resources can be produced from waste biomass. The production of high value biopolymers (e.g., for bioplastics manufacturing) from organic acids, hydrogen, and methane is another option for carbon recovery. The recovery of carbon and nutrients can be achieved by organic fertilizer production, or single cell protein generation (depending on the source) which may be utilized as feed, feed additives, next generation fertilizers, or even as probiotics. Additionlly, chemical oxidation-reduction and bioelectrochemical systems can recover inorganics or synthesize organic products beyond the natural microbial metabolism. Anticipating the next generation of wastewater treatment plants driven by biological recovery technologies, this review is focused on the generation and re-synthesis of energetic resources and key resources to be recycled as raw materials in a cradle-to-cradle economy concept.

Qiao, L. X., Zhu, W. Y., Zhang, H. Y., and Wang, H. Effect of early administration of probiotics on gut microflora and feeding in pre-term infants: a randomized controlled trial. J.Matern.Fetal Neonatal Med. 2017; 30(1):13-16; PM: 26956782

ABSTRACT: BACKGROUND: This study aimed to evaluate the effect of early probiotic administration on gut microflora and influence on feeding in pre-term infants. *METHODS*: A double-blind, randomized, controlled clinical study was conducted to assess the effect of probiotics [live, combined lactobacillus and bifidobacterium (LCB)] supplementation in pre-term infants. Sixty hospitalized pre-term babies were randomly assigned to two groups: a probiotics-supplemented group and the control group. The primary endpoint was measurement of lactobacillus and bifidobacterium in the gut. The secondary outcome was the rate of feeding intolerance. *RESULTS*: In the first weekend, the quantity of gut lactobacillus and bifidobacterium was significantly higher in the probiotics-supplemented group than in the control group [7.84 +/- 0.35 versus 6.39 +/- 0.53 (log copy number/g wet fecal weight), p = 0.013; 8.52 +/- 0.23 versus 7.01 +/- 0.48, p = 0.024, respectively]. In the second weekend, the amount of gut lactobacillus and bifidobacterium in the probiotics-supplemented group remained significantly higher (8.62 +/- 0.28 versus 7.34 +/- 0.59, p = 0.036 and 9.45 +/- 0.64 versus 7.85 +/- 0.43, p = 0.007, respectively). Fewer patients in the probiotics-supplemented group developed a feeding intolerance (13.3% versus 46.7%, p = 0.013). *CONCLUSIONS*: Probiotic supplementation in

the hospitalized pre-term infants in the first 2 weeks of life resulted in higher amounts of lactobacillus and bifidobacterium in the gut and a concomitant lower rate of feeding intolerance.

Qiu, L., Yang, D., Tao, X., Yu, J., Xiong, H., and Wei, H. Enterobacter aerogenes ZDY01 attenuates choline-induced Trimethylamine N-oxide levels via remodeling gut microbiota in mice. J.Microbiol.Biotechnol. 5-17-2017; PM: 28511293

ABSTRACT: Trimethylamine N-oxide (TMAO), which is transformed from trimethylamine (TMA) through hepatic flavin-containing monooxygenases, can promote atherosclerosis. TMA is produced from dietary carnitine, phosphatidylcholine, and choline via the gut microbes. Previous works have shown that some small molecules, such as allicin, resveratrol, and 3,3-dimethyl-1-butanol, are used to reduce circulating TMAO levels. However, the use of bacteria as an effective therapy to reduce TMAO levels has not been reported. In the present study, 82 isolates were screened from healthy Chinese fecal samples on a basal salt medium supplemented with TMA as sole carbon source. The isolates belonged to the family Enterobacteriaceae, particularly to genera Klebsiella, Escherichia, Cronobacter, and Enterobacter. Serum TMAO and cecal TMA levels significantly decreased in choline-fed mice treated with Enterobacter aerogenes ZDY01 compared with those in choline-fed mice treated with phosphate-buffered saline. The proportions of Bacteroidales family S24-7 significantly increased, whereas the proportions of Helicobacteraceae and Prevotellaceae significantly decreased through the administration of E. aerogenes ZDY01. Results indicated that the use of probiotics to act directly on the TMA in the gut might be an alternative approach to reduce serum TMAO levels and to prevent the development of atherosclerosis and "fish odor syndrome" through the effect of TMA on the gut microbiota.

Rabah, H., Rosa do Carmo, F. L., and Jan, G. Dairy Propionibacteria: Versatile Probiotics. Microorganisms. 5-13-2017; 5(2); PM: 28505101

ABSTRACT: Dairy propionibacteria are used as cheese ripening starters, as biopreservative and as beneficial additives, in the food industry. The main species, Propionibacterium freudenreichii, is known as GRAS (Generally Recognized As Safe, USA, FDA). In addition to another dairy species, Propionibacterium acidipropionici, they are included in QPS (Qualified Presumption of Safety) list. Additional to their well-known technological application, dairy propionibacteria increasingly attract attention for their promising probiotic properties. The purpose of this review is to summarize the probiotic characteristics of dairy propionibacteria reported by the updated literature. Indeed, they meet the selection criteria for probiotic bacteria, such as the ability to endure digestive stressing conditions and to adhere to intestinal epithelial cells. This is a prerequisite to bacterial persistence within the gut. The reported beneficial effects are ranked according to property's type: microbiota modulation, immunomodulation, and cancer modulation. The proposed molecular mechanisms are discussed. Dairy propionibacteria are described as producers of nutraceuticals and beneficial metabolites that are responsible for their versatile probiotic attributes include short chain fatty acids (SCFAs), conjugated fatty acids, surface proteins, and 1,4-dihydroxy-2-naphtoic acid (DHNA). These metabolites possess beneficial properties and their production depends on the strain and on the growth medium. The choice of the fermented food matrix may thus determine the probiotic properties of the ingested

product. This review approaches dairy propionibacteria, with an interest in both technological abilities and probiotic attributes.

Radke, M., Picaud, J. C., Loui, A., Cambonie, G., Faas, D., Lafeber, H. N., de, Groot N., Pecquet, S. S., Steenhout, P. G., and Hascoet, J. M. Starter formula enriched in prebiotics and probiotics ensures normal growth of infants and promotes gut health: a randomized clinical trial. Pediatr.Res. 2017; 81(4):622-631; PM: 28002391

ABSTRACT: BACKGROUND: Prebiotics and probiotics exert beneficial effects by modulating gut microbiota and immune system. This study evaluates efficacy and safety of an infant formula containing bovine milk-derived oligosaccharides and Bifidobacterium animalis ssp lactis (B. lactis) (CNCM I-3446) on incidence of diarrhea and febrile infections during the first year of life (primary outcome). *METHODS*: Full-term infants receiving Test or Control (without bovine milk-derived oligosaccharide and B. lactis) formulae were enrolled in a multicenter, randomized, controlled, and double-blind trial with a reference breastfeeding group. *RESULTS*: 413 infants were assigned between Test (n = 206) and Control (n = 207) formula. There was no significant difference for diarrhea and febrile infections incidence between groups at 6 (odds ratio (95% confidence interval) = 0.56 (0.26-1.15), P = 0.096) and 12 mo (odds ratio = 0.66 (0.38-1.14), P = 0.119). Test formula was well tolerated, anthropometrics parameters were not significantly different between groups and aligned with WHO growth standards up to 12 mo. Data from test group showed that gut microbiota pattern, fecal IgA and stool pH were brought to be closer to those of breastfed infants. *CONCLUSION*: An infant formula enriched with bovine milk-derived oligosaccharide and B. lactis supports normal infant growth, is well tolerated and improves intestinal health markers. No differences in diarrhea and febrile infection incidence were found in the population studied.

Ramasethu, J. Prevention and treatment of neonatal nosocomial infections. Matern.Health Neonatol.Perinatol. 2017; 3:5; PM: 28228969

ABSTRACT: Nosocomial or hospital acquired infections threaten the survival and neurodevelopmental outcomes of infants admitted to the neonatal intensive care unit, and increase cost of care. Premature infants are particularly vulnerable since they often undergo invasive procedures and are dependent on central catheters to deliver nutrition and on ventilators for respiratory support. Prevention of nosocomial infection is a critical patient safety imperative, and invariably requires a multidisciplinary approach. There are no short cuts. Hand hygiene before and after patient contact is the most important measure, and yet, compliance with this simple measure can be unsatisfactory. Alcohol based hand sanitizer is effective against many microorganisms and is efficient, compared to plain or antiseptic containing soaps. The use of maternal breast milk is another inexpensive and simple measure to reduce infection rates. Efforts to replicate the anti-infectious properties of maternal breast milk by the use of probiotics, prebiotics, and synbiotics have met with variable success, and there are ongoing trials of lactoferrin, an iron binding whey protein present in large quantities in colostrum. Attempts to boost the immunoglobulin levels of preterm infants with exogenous immunoglobulins have not been shown to reduce nosocomial infections significantly. Over the last decade, improvements in the incidence of catheter-related infections have been achieved, with meticulous attention to every detail from insertion to maintenance, with some centers reporting zero rates for such infections. Other nosocomial infections like ventilator acquired pneumonia and staphylococcus aureus infection remain problematic, and outbreaks with multidrug resistant organisms continue to have disastrous consequences.

Management of infections is based on the profile of microorganisms in the neonatal unit and community and targeted therapy is required to control the disease without leading to the development of more resistant strains.

Ramirez, C. and Romero, J. Fine Flounder (Paralichthys adspersus) Microbiome Showed Important Differences between Wild and Reared Specimens. Front Microbiol. 2017; 8:271; PM: 28286497

ABSTRACT: The intestinal microbiota is involved in a wide range of biological processes that benefit the host, including providing nutrition and modulating the immune system. Fine flounder (Paralichthys adspersus) is a flatfish of commercial interest that is native to the Chilean coast. The high value of this flatfish has prompted the development of stock enhancement and aquaculture activities. Knowledge of microbiota may help to improve the cultivation of this species; however, few comparative studies have evaluated the intestinal microbiota composition in farmed versus wild fishes. Intestinal contents from wild and aquaculture fish were collected, and DNA was extracted. Subsequently, the V3-region of 16S rRNA was PCR amplified and sequenced using the Ion Torrent platform. The comparison between wild and aquaculture specimens revealed important differences in the composition of the microbiota. The most abundant phylum in wild flounder was Proteobacteria, with an average relative abundance of 68.1 +/- 15.4%; in contrast, in aquaculture flounder, this phylum had an average relative abundance of 30.8 +/- 24.1%. Reciprocally, the most abundant phylum in flounder aquaculture was Firmicutes, averaging 61.2 +/- 28.4%; in contrast, this phylum showed low abundance in wild flounder, in which it averaged 4.7 +/- 4%. The phylum Actinobacteria showed greater abundance in wild flounder, ranging from 21.7 +/- 18.8%, whereas, it averaged only 2.7 +/- 3.8% in aquaculture fish. Specific taxa that were differentially distributed between wild and aquaculture flounder were identified using a statistical approach. At the genus level, a total of four genera were differentially represented between the two conditions. Bacillus and Pseudomonas were more highly represented in aquaculture flounder, whereas Arthrobacter and Psychrobacter were observed in wild flounder. Furthermore, in both cases, predicted functions (metabolic pathways) indicated that those microbiota might provide beneficial effects for the host, but wild flounder showed more noteworthy pathways (EPA/DHA, SCFA, biotin). Our results highlight the differences in the microbiota composition between wild and reared fish. Knowing the composition of the intestinal microbiota of P. adspersus is the first step toward exploring the proper management of this species, as well as toward the development of probiotics and functional foods based on their requirements.

Ramos, M. A., Batista, S., Pires, M. A., Silva, A. P., Pereira, L. F., Saavedra, M. J., Ozorio, R. O., and Rema, P. Dietary probiotic supplementation improves growth and the intestinal morphology of Nile tilapia. Animal. 1-12-2017; 1-11; PM: 28077192

ABSTRACT: Probiotic administration can be a nutritional strategy to improve the immune response and growth performance of fish. The current study aimed to evaluate the effects of a probiotic blend (Bacillus sp., Pediococcus sp., Enterococcus sp., Lactobacillus sp.) as a dietary supplement on growth performance, feed utilization, innate immune and oxidative stress responses and intestinal morphology in juvenile Nile tilapia (Oreochromis niloticus). The probiotic was incorporated into a basal diet at three concentrations: 0 g/kg (A0: control), 3 g/kg (A1: 1.0x106 colony forming unit (CFU)/g) and 6 g/kg (A2: 2.3x106 CFU/g diet). After 8 weeks of probiotic feeding, weight and

specific growth rate where significantly higher in fish-fed A1 diet than in fish-fed A0. Alternative complement in plasma was significantly enhanced in fish-fed A2 when compared with A0. The hepatic antioxidant indicators were not affected by probiotic supplementation. Villi height and goblet cell counts increased significantly in the intestine of fish-fed A1 and A2 diets compared with A0. The dietary probiotic supplementation was maintained until 20 weeks of feeding. Then the selected immune parameters, digestive enzymes and apparent digestibility of diets were studied. No effect of probiotic feeding was observed after that longer period supplementation. The dietary supplementation of mixed species probiotic may constitute a valuable nutritional approach towards a sustainable tilapia aquaculture. The improvement of the immune responses and intestinal morphology play an important role in increasing growth performance, nutrient absorption and disease resistance in fish, important outcomes in such a competitive and developing aquaculture sector.

Ramos, O. L., Pereira, R. N., Martins, A., Rodrigues, R., Fucinos, C., Teixeira, J. A., Pastrana, L., Malcata, F. X., and Vicente, A. A. Design of whey protein nanostructures for incorporation and release of nutraceutical compounds in food. Crit Rev.Food Sci.Nutr. 5-3-2017; 57(7):1377-1393; PM: 26065435

ABSTRACT: Whey proteins are widely used as nutritional and functional ingredients in formulated foods because they are relatively inexpensive, generally recognized as safe (GRAS) ingredient, and possess important biological, physical, and chemical functionalities. Denaturation and aggregation behavior of these proteins is of particular relevance toward manufacture of novel nanostructures with a number of potential uses. When these processes are properly engineered and controlled, whey proteins may be formed into nanohydrogels, nanofibrils, or nanotubes and be used as carrier of bioactive compounds. This review intends to discuss the latest understandings of nanoscale phenomena of whey protein denaturation and aggregation that may contribute for the design of protein nanostructures. Whey protein aggregation and gelation pathways under different processing and environmental conditions such as microwave heating, high voltage, and moderate electrical fields, high pressure, temperature, pH, and ionic strength were critically assessed. Moreover, several potential applications of nanohydrogels, nanofibrils, and nanotubes for controlled release of nutraceutical compounds (e.g. probiotics, vitamins, antioxidants, and peptides) were also included. Controlling the size of protein networks at nanoscale through application of different processing and environmental conditions can open perspectives for development of nanostructures with new or improved functionalities for incorporation and release of nutraceuticals in food matrices.

Ramos, P. E., Cerqueira, M. A., Teixeira, J. A., and Vicente, A. A. Physiological Protection of Probiotic Microcapsules by Coatings. Crit Rev.Food Sci.Nutr. 3-31-2017; 0; PM: 28362165

ABSTRACT: Nowadays, food and nutrition have a greater impact in people's concerns, with the awareness that nutrition have a direct impact in health and wellbeing. Probiotics have an important role in this topic and consumers are starting to really understand their potential in health, leading to an increasing interest of the companies to their commercial use in foods. However, there are several limitations to the use of probiotics in foods and beverages, being one of them their efficiency (directly associated to their survival rate) upon ingestion. This work is focused in microencapsulation techniques that have been used to increase probiotics efficiency. More specifically, this work reviews the

most recent and relevant research about the production and coating techniques of probiotic-loaded microcapsules, providing an insight in the effect of these coatings in probiotics survival during the gastrointestinal phase. This review shows that coatings with the better performances in probiotics protection, against the harsh conditions of digestion, are chitosan, alginate, poly-L-lysine and whey protein. Chitosan presented an interesting performance in probiotics protection being able to maintain the initial concentration of viable probiotics during a digestive test. The analyses of different works also showed that the utilization of several coatings does not guarantee a better protection in comparison with monocoated microcapsules.

Rao, K. and Young, V. B. Probiotics for Prevention of Clostridium difficile Infection in Hospitalized Patients: Is the Jury Still Out? Gastroenterology. 4-28-2017; PM: 28461190

No Abstract Available.

Rao, S., Simmer, K., and Patole, S. Probiotic supplementation in neonates with major gastrointestinal surgical conditions: a systematic review. J.Matern.Fetal Neonatal Med. 4-25-2017; 1-7; PM: 28391755

ABSTRACT: *OBJECTIVES*: Neonates with major gastrointestinal surgical conditions frequently suffer from prolonged feed intolerance, infections, and need multiple courses of antibiotics. All these put them at risk of gut dysbiosis. Probiotic supplementation has the potential to minimise dysbiosis and improve clinical outcomes in such infants. Hence, we aimed to conduct a systematic review of probiotics in neonates with major surgical conditions of the gut. *METHODS*: Medline, Embase, the Cochrane Central Register of Controlled Trials (CENTRAL), and other databases were searched in September 2016. *RESULTS*: Two randomised controlled trials (RCTs) were included; the first was conducted in 24 neonates with gastroschisis, the second in eight neonates with various surgical conditions. In the first study, the overall microbial communities were not significantly different between groups, though analysis of the final specimens demonstrated higher Bifidobacteriaceae, lower Clostridiaceae, and trends toward lower Enterobacteriaceae, Enterococcaceae, Staphylococcaceae, and Streptococcaceae in the probiotic group. In the second study, there were significantly more Streptcoccaceae in the faecal samples in the probiotic group and significantly more Bifidobacteriaceae in the no probiotic group ($p < .05$). *CONCLUSIONS*: There is limited evidence regarding the role of probiotics in neonates with gastrointestinal surgical conditions. Adequately powered RCTs are needed to address this issue.

Rautava, S. Microbial Composition of the Initial Colonization of Newborns. Nestle.Nutr.Inst.Workshop Ser. 2017; 88:11-21; PM: 28346920

ABSTRACT: Early-life interaction with indigenous intestinal microbes is a prerequisite for healthy immune and metabolic maturation. Human infants acquire their gut microbiota predominantly from the mother. A considerable inoculum of microbes is received by the neonate during vaginal delivery. Recent observations suggest that human gut colonization may be initiated prenatally by microbes in amniotic fluid, but the significance of this phenomenon remains unknown. After birth, neonatal gut colonization is guided by human milk factors, which selectively promote the growth of specific

microbes, as well as by live microbes present in human milk. Aberrant gut colonization in early life has been associated with an increased risk of noncommunicable diseases in later life. Epidemiological and experimental studies suggest a causal relationship between early-life gut microbiota perturbations and disease risk. Perinatal antibiotic exposure, cesarean section delivery, postnatal antibiotic administration, and formula feeding, which may disrupt intestinal microecology, have been associated with disease development in later life. The modulation of gut microbiota in the perinatal period by pre- and probiotics, for example, may offer a means to reduce the risk of chronic diseases.

Redondo, N., Nova, E., Gheorghe, A., Diaz, L. E., Hernandez, A., and Marcos, A. Evaluation of Lactobacillus coryniformis CECT5711 strain as a coadjuvant in a vaccination process: a randomised clinical trial in healthy adults. Nutr.Metab (Lond). 2017; 14:2; PM: 28070204

ABSTRACT: BACKGROUND: Although the effects of probiotics on the immune system have been extensively evaluated under disease states, their role in healthy situations remains unclear, since changes are hardly expected under immunological homeostasis. EFSA indicates that vaccination protocols could be used to evaluate the potential role of probiotics to improve the immune response against antigen challenges. The aim of the study was to evaluate the effect of Lactobacillus coryniformis CECT5711 (Lc) on the specific immunity of healthy volunteers undergoing vaccination with Hepatitis A virus (HAV). *METHODS*: One hundred twenty-three healthy adults were randomised into three groups to follow a 6-week (wk) intervention and all received an intramuscular HAV vaccine 2 weeks after starting the intervention: 1) PRO1 received Lc for 2weeks (1 capsule/day; 3 x 109 CFU/capsule) and placebo capsules after vaccination; 2) PRO2 received a daily capsule of Lc (3 x 109 cfu/day) before and after the challenge; 3) Control group (C) received a daily placebo capsule before and after the vaccine. Blood samples were collected at the beginning (visit 1; V1) and after 2 (V2) and 6 weeks (V3) of the intervention. At each visit, lymphocyte subset counts and cytokine levels were analysed. Specific HAV antibodies were analysed at V1 and V3. To evaluate differences between groups, one-way ANOVA with Bonferroni post-hoc test were used regarding lymphocyte subset counts and specific HAV antibodies production, and Friedman test of related samples and Kendall concordance coefficient for cytokines production. Chi square test was used to analyse seroconversion rates. *RESULTS*: Specific HAV antibodies were significantly higher in PRO1 (50.54 +/- 29.57) compared to C (36.23 +/- 16.45) (P = 0.017) and showed an intermediate value in PRO2 (41.61 +/- 15.74). Seroconversion rates were similar in the three groups (97.3, 92.3 and 97.4% in C, PRO1 and PRO2 respectively). Memory T-helper lymphocytes increased in V3 vs. V1 (P = 0.032) in PRO2. No differences were found in cytokine concentrations. *CONCLUSION*: Mixed results have been found regarding the usefulness of Lc supplementation to increase the antigen-specific antibody response to an immune challenge. Clinical trial registration number: EudraCT Number 2016-000183-42. Registered 19 January 2016. Retrospectively registered.

Reid, G. Probiotic use in an infectious disease setting. Expert.Rev.Anti.Infect.Ther. 2017; 15(5):449-455; PM: 28276942

ABSTRACT: INTRODUCTION: The lethality of infectious diseases and deep concern over growing antimicrobial resistance make it essential that alternative or adjunct therapies be developed. *Areas covered*: Using papers published in PubMed, a case is presented to consider beneficial microbes as a means to improve management of infectious

diseases. Clinical evidence is mounting that certain probiotic microbes can contribute to this armamentarium. These could have an immediate effect against necrotizing enterocolitis, pre- and post-surgical procedures, antibiotic-associated infections, urogenital infections in women and for reducing the severity and duration of respiratory infections. While further studies will always be warranted irrespective of the intervention, and quality assurance and patient safety must remain a priority, the main barrier to implementation may well be unwarranted hesitation amongst physicians, healthcare administrators and regulators. Meanwhile, patients are already taking things into their own hands at a time when their knowledge of product selection is poor and clinical guidance is invariably missing. *Expert commentary*: Until vaccines and other alternatives emerge, it would be foolhardy to not use best practices to bring probiotics into mainstream infectious disease management. Our ability to manipulate microbial-host interactions offers hope before the last antibiotic stops being effective.

Reid, G. The development of probiotics for women's health. Can.J.Microbiol. 2017; 63(4):269-277; PM: 28177795

ABSTRACT: The idea you could use lactic acid bacteria to treat and prevent recurrence of vaginal infections was ridiculed in the early 1980s. Bacteria were the bad guys to be eradicated by current and emerging antibiotic classes. Thirty years later, probiotic administration of microbes is widespread worldwide, including for vaginal and bladder health in women, and the scientific basis and clinical efficacy data for this and multiple other applications prove the viability of this concept. The development of this approach, the creation of a definition for probiotics, and the expansion to other areas of women's health form the basis of this review.

Reimschuessel, R., Grabenstein, M., Guag, J., Nemser, S. M., Song, K., Qiu, J., Clothier, K. A., Byrne, B. A., Marks, S. L., Cadmus, K., Pabilonia, K., Sanchez, S., Rajeev, S., Ensley, S., Frana, T. S., Jergens, A. E., Chappell, K. H., Thakur, S., Byrum, B., Cui, J., Zhang, Y., Erdman, M. M., Rankin, S. C., Daly, R., Das, S., Ruesch, L., Lawhon, S. D., Zhang, S., Baszler, T., az-Campos, D., Hartmann, F., and Okwumabua, O. Multilaboratory Survey To Evaluate Salmonella Prevalence in Diarrheic and Nondiarrheic Dogs and Cats in the United States between 2012 and 2014. J.Clin.Microbiol. 2017; 55(5):1350-1368; PM: 28202802

ABSTRACT: Eleven laboratories collaborated to determine the periodic prevalence of Salmonella in a population of dogs and cats in the United States visiting veterinary clinics. Fecal samples (2,965) solicited from 11 geographically dispersed veterinary testing laboratories were collected in 36 states between January 2012 and April 2014 and tested using a harmonized method. The overall study prevalence of Salmonella in cats (3 of 542) was <1%. The prevalence in dogs (60 of 2,422) was 2.5%. Diarrhea was present in only 55% of positive dogs; however, 3.8% of the all diarrheic dogs were positive, compared with 1.8% of the nondiarrheic dogs. Salmonella-positive dogs were significantly more likely to have consumed raw food (P = 0.01), to have consumed probiotics (P = 0.002), or to have been given antibiotics (P = 0.01). Rural dogs were also more likely to be Salmonella positive than urban (P = 0.002) or suburban (P = 0.001) dogs. In the 67 isolates, 27 unique serovars were identified, with three dogs having two serovars present. Antimicrobial susceptibility testing of 66 isolates revealed that only four of the isolates were resistant to one or more antibiotics. Additional characterization of the 66 isolates was done using pulsed-field gel electrophoresis and whole-genome sequencing (WGS). Sequence data compared well to resistance phenotypic data and were submitted to the National Center for Biotechnology Information (NCBI). This study suggests an overall decline in

prevalence of Salmonella-positive dogs and cats over the last decades and identifies consumption of raw food as a major risk factor for Salmonella infection. Of note is that almost half of the Salmonella-positive animals were clinically nondiarrheic.

Reis, S. A., Conceicao, L. L., Rosa, D. D., Siqueira, N. P., and Peluzio, M. C. G. Mechanisms responsible for the hypocholesterolaemic effect of regular consumption of probiotics. Nutr.Res.Rev. 2017; 30(1):36-49; PM: 27995830

ABSTRACT: CVD affect a large proportion of the world's population, with dyslipidaemia as the major risk factor. The regular consumption of both probiotic bacteria and yeast has been associated with improvement in the serum lipid profile. Thus, the present review aims to describe and discuss the potential mechanisms responsible for the hypocholesterolaemic effect of regular consumption of probiotic bacteria and yeast. Regarding the hypocholesterolaemic effect of probiotic bacteria, the potential mechanisms responsible include: deconjugation of bile salts; modulation of lipid metabolism; and decreased absorption of intestinal cholesterol through co-precipitation of intestinal cholesterol with the deconjugated bile salts, incorporation and assimilation of cholesterol in the cell membrane of the probiotics, intestinal conversion of cholesterol in coprostanol, and inhibition of the expression of the intestinal cholesterol transporter Niemann-Pick C1 like 1 (NPC1L1) in the enterocytes. The potential mechanisms responsible for the hypocholesterolaemic effect of probiotic yeasts include: deconjugation of bile salts; co-precipitation of intestinal cholesterol with the deconjugated bile salts; incorporation and assimilation of cholesterol in the cell membrane; and inhibition of hepatic cholesterol synthesis. The regular consumption of probiotic bacteria and yeast, as a non-pharmaceutical approach to help manage cardiovascular risk, holds promise, according to the beneficial hypocholesterolaemic effects described herein. However, the hypocholesterolaemic effects vary according to the strains used, the physiological state of the host, and the type of diet to which the probiotics are added. Further studies are necessary to fill the gaps with regard to the knowledge related to this topic.

Ren, T., Zhu, J., Zhu, L., and Cheng, M. The Combination of Blueberry Juice and Probiotics Ameliorate Non-Alcoholic Steatohepatitis (NASH) by Affecting SREBP-1c/PNPLA-3 Pathway via PPAR-alpha. Nutrients. 2-27-2017; 9(3); PM: 28264426

ABSTRACT: Nonalcoholic steatohepatitis (NASH) is liver inflammation and a major threat to public health. Several pharmaceutical agents have been used for NASH therapy but their high-rate side effects limit the use. Blueberry juice and probiotics (BP) have anti-inflammation and antibacterial properties, and may be potential candidates for NASH therapy. To understand the molecular mechanism, Sprague Dawley rats were used to create NASH models and received different treatments. Liver tissues were examined using HE (hematoxylin and eosin) and ORO (Oil Red O) stain, and serum biochemical indices were measured. The levels of peroxisome proliferators-activated receptor (PPAR)-alpha, sterol regulatory element binding protein-1c (SREBP-1c), Patatin-like phospholipase domain-containing protein 3 (PNPLA-3), inflammatory cytokines and apoptosis biomarkers in liver tissues were measured by qRT-PCR and Western blot. HE and ORO analysis indicated that the hepatocytes were seriously damaged with more and larger lipid droplets in NASH models while BP reduced the number and size of lipid droplets ($p < 0.05$). Meanwhile, BP increased the levels of SOD (superoxide dismutase), GSH (reduced glutathione) and HDL-C (high-density lipoprotein cholesterol), and

reduced the levels of AST (aspartate aminotransferase), ALT (alanine aminotransferase), TG (triglycerides), LDL-C (low-density lipoprotein cholesterol) and MDA (malondialdehyde) in NASH models ($p < 0.05$). BP increased the level of PPAR-alpha (Peroxisome proliferator-activated receptor alpha), and reduced the levels of SREBP-1c (sterol regulatory element binding protein-1c) and PNPLA-3 (Patatin-like phospholipase domain-containing protein 3) ($p < 0.05$). BP reduced hepatic inflammation and apoptosis by affecting IL-6 (interleukin 6), TNF-alpha (Tumor necrosis factor alpha), caspase-3 and Bcl-2 in NASH models. Furthermore, PPAR-alpha inhibitor increased the level of SREBP-1c and PNPLA-3. Therefore, BP prevents NASH progression by affecting SREBP-1c/PNPLA-3 pathway via PPAR-alpha.

Rezapour, M., Ali, S., and Stollman, N. Diverticular Disease: An Update on Pathogenesis and Management. Gut Liver. 5-12-2017; PM: 28494576

ABSTRACT: Diverticular disease is one of the most common conditions in the Western world and one of the most common findings identified at colonoscopy. Recently, there has been a significant paradigm shift in our understanding of diverticular disease and its management. The pathogenesis of diverticular disease is thought to be multifactorial and include both environmental and genetic factors in addition to the historically accepted etiology of dietary fiber deficiency. Symptomatic uncomplicated diverticular disease (SUDD) is currently considered a type of chronic diverticulosis that is perhaps akin to irritable bowel syndrome. Mesalamine, rifaximin and probiotics may achieve symptomatic relief in some patients with SUDD, although their role(s) in preventing complications remain unclear. Antibiotic use for acute diverticulitis and elective prophylactic resection surgery are considered more individualized treatment modalities that take into account the clinical status, comorbidities and lifestyle of the patient. Our understanding of the pathogenesis of diverticular disease continues to evolve and is likely to be diverse and multifactorial. Paradigm shifts in several areas of the pathogenesis and management of diverticular disease are explored in this review.

Ribeiro, F. C., de Barros, P. P., Rossoni, R. D., Junqueira, J. C., and Jorge, A. O. Lactobacillus rhamnosus inhibits Candida albicans virulence factors in vitro and modulates immune system in Galleria mellonella. J.Appl.Microbiol. 2017; 122(1):201-211; PM: 27727499

ABSTRACT: AIM: The aim of this study was to evaluate the potential anti-Candida effects of Lactobacillus rhamnosus ATCC 9595 on Candida albicans ATCC 18804 using in vitro and in vivo models. *METHODS AND RESULTS*: The in vitro analysis evaluated the effects of L. rhamnosus on C. albicans's biofilm formation by CFU count and metabolic activity, filamentation capacity, and adhesion (ALS3 and HWP1) and transcriptional regulatory gene (BCR1 and CPH1) expression. The in vitro results showed that both the L. rhamnosus cells and supernatant reduced C. albicans biofilm formation, filamentation and gene expression. In the in vivo study, the treatment with L. rhamnosus supernatant increased 80% the survival of Galleria mellonella larvae infected with C. albicans. Furthermore, the supernatant of L. rhamnosus recruited haemocytes into the haemolymph (2.1-fold increase). *CONCLUSIONS*: Lactobacillus rhamnosus reduced the biofilm formation and filamentation of C. albicans in vitro by negatively regulating all studied C. albicans genes. Lactobacillus rhamnosus protected G. mellonella against experimental candidiasis in vivo. *SIGNIFICANCE AND IMPACT OF THE STUDY*: This study is the first study to report the anti-Candida properties of L. rhamnosus ATCC 9595. The supernatant of this

strain has immunomodulatory effects on the G. mellonella model and protects the larvae against pathogens.

Richards, G. P., Watson, M. A., Needleman, D. S., Uknalis, J., Boyd, E. F., and Fay, J. P. Mechanisms for Pseudoalteromonas piscicida-Induced Killing of Vibrios and Other Bacterial Pathogens. Appl.Environ.Microbiol. 6-1-2017; 83(11); PM: 28363962

ABSTRACT: Pseudoalteromonas piscicida is a Gram-negative gammaproteobacterium found in the marine environment. Three strains of pigmented P. piscicida were isolated from seawater and partially characterized by inhibition studies, electron microscopy, and analysis for proteolytic enzymes. Growth inhibition and death occurred around colonies of P. piscicida on lawns of the naturally occurring marine pathogens Vibrio vulnificus, Vibrio parahaemolyticus, Vibrio cholerae, Photobacterium damselae, and Shewanella algae Inhibition also occurred on lawns of Staphylococcus aureus but not on Escherichia coli O157:H7 or Salmonella enterica serovar Typhimurium. Inhibition was not pH associated, but it may have been related to the secretion of a cysteine protease with strong activity, as detected with a synthetic fluorogenic substrate. This diffusible enzyme was secreted from all three P. piscicida strains. Direct overlay of the Pseudoalteromonas colonies with synthetic fluorogenic substrates demonstrated the activity of two aminopeptidase Bs, a trypsin-like serine protease, and enzymes reactive against substrates for cathepsin G-like and caspase 1-like proteases. In seawater cultures, scanning electron microscopy revealed numerous vesicles tethered to the outer surface of P. piscicida and a novel mechanism of direct transfer of these vesicles to V. parahaemolyticus Vesicles digested holes in V. parahaemolyticus cells, while the P. piscicida congregated around the vibrios in a predatory fashion. This transfer of vesicles and vesicle-associated digestion of holes were not observed in other bacteria, suggesting that vesicle binding may be mediated by host-specific receptors. In conclusion, we show two mechanisms by which P. piscicida inhibits and/or kills competing bacteria, involving the secretion of antimicrobial substances and the direct transfer of digestive vesicles to competing bacteria.*IMPORTANCE*: Pseudoalteromonas species are widespread in nature and reduce competing microflora by the production of antimicrobial compounds. We isolated three strains of P. piscicida and characterized secreted and cell-associated proteolytic enzymes, which may have antimicrobial properties. We identified a second method by which P. piscicida kills V. parahaemolyticus It involves the direct transfer of apparently lytic vesicles from the surface of the Pseudoalteromonas strains to the surface of Vibrio cells, with subsequent digestion of holes in the Vibrio cell walls. Enzymes associated with these vesicles are likely responsible for the digestion of holes in the cell walls. Pseudoalteromonas piscicida has potential applications in aquaculture and food safety, in control of the formation of biofilms in the environment, and in food processing. These findings may facilitate the probiotic use of P. piscicida to inactivate pathogens and may lead to the isolation of enzymes and other antimicrobial compounds of pharmacological value.

Rishi, P., Arora, S., Kaur, U. J., Chopra, K., and Kaur, I. P. Better Management of Alcohol Liver Disease Using a 'Microstructured Synbox' System Comprising L. plantarum and EGCG. PLoS.One. 2017; 12(1):e0168459; PM: 28060832

ABSTRACT: Synergistic combination of probiotics with carbohydrate based prebiotics is widely employed for the treatment of various gut related disorders. However, such carbohydrate based prebiotics encourage the growth of pathogens and probiotics,

equally. Aim of the study was (i) to explore the possibility of using epigallocatechin gallate (EGCG) a phenolic compound, as a prebiotic for L.plantarum; (ii) to develop and evaluate a microstructured synbox (microencapsulating both probiotic and EGCG together) in rat model of alcohol liver disease (ALD); and, (iii) to confirm whether the combination can address issues of EGCG bioavailability and probiotic survivability in adverse gut conditions. Growth enhancing effect of EGCG on L. plantarum (12.8+/-0.5 log 10 units) was significantly (p</=0.05) better than inulin (11.4+/-0.38 log 10 units), a natural storage carbohydrate. The formulated synbox significantly modulated the levels of alcohol, endotoxin, hepatic enzymes and restored the hepatoarchitecture in comparison to simultaneous administration of free agents. Additionally, using a battery of techniques, levels of various cellular and molecular markers viz. NF-kB/p50, TNF-alpha, IL12/p40, and signalling molecules TLR4, CD14, MD2, MyD88 and COX-2 were observed to be suppressed. Developed microbead synbox, as a single delivery system for both the agents showed synergism and hence, holds promise as a therapeutic option for ALD management.

Ro, A. D. B., Simpson, M. R., Ro, T. B., Storro, O., Johnsen, R., Videm, V., and Oien, T. Reduced Th22 cell proportion and prevention of atopic dermatitis in infants following maternal probiotic supplementation. Clin.Exp.Allergy. 3-27-2017; PM: 28346719

ABSTRACT: BACKGROUND: In the randomized, controlled study Probiotics in the Prevention of Allergy among Children in Trondheim (ProPACT), maternal probiotic supplementation reduced the incidence of atopic dermatitis (AD) in the offspring. In the current study, we hypothesized that the effect was mediated by a shift in the T helper (Th) cells in the children. *OBJECTIVE*: To examine whether Th cell proportions were affected by maternal probiotic supplementation and thus could mediate the preventive effect of probiotics on AD. *METHODS*: A total of 415 pregnant women were randomized to ingest a combination of Lactobacillus rhamnosus GG (LGG), Bifidobacterium animalis subsp. lactis Bb-12 (Bb-12) and Lactobacillus acidophilus La-5 (La-5) or placebo, and their offspring were assessed for AD during the first 2 years of life. Peripheral blood collected at 3 months of age was analysed for regulatory T cells (n=140) and Th subsets (n=77) including Th1, Th2, Th9, Th17 and Th22. *RESULTS*: The proportion of Th22 cells was reduced in children in the probiotic group compared to the placebo group (median 0.038% vs 0.064%, P=.009). The difference between the probiotic and placebo groups was also observed in the children who did not develop AD during the 2-year follow-up. The proportion of Th22 cells was increased in children who developed AD compared to the children who did not develop AD (0.090% vs 0.044%, P<.001). Mediation analysis indicated that the preventive effect of probiotics was partially mediated through the reduction in Th22 cells. *CONCLUSION*: Perinatal maternal probiotic supplementation with a combination of LGG, Bb-12 and La-5 reduced the proportion of Th22 cells in 3-month-old children. This may partially explain the preventive effect of probiotics on AD.

Robles-Vera, I., Toral, M., Romero, M., Jimenez, R., Sanchez, M., Perez-Vizcaino, F., and Duarte, J. Antihypertensive Effects of Probiotics. Curr.Hypertens.Rep. 2017; 19(4):26; PM: 28315049

ABSTRACT: PURPOSE OF REVIEW: The present review focuses in the hypertension-associated changes in the microbiota and the current insights regarding the impact of probiotics on blood pressure in animal models and in human hypertensive patients. *RECENT FINDINGS*: Gut dysbiosis in hypertension is characterized by (i) the gut microbioma that is less diverse and less rich with an increased Firmicutes/Bacteroidetes

ratio and (ii) a decrease in acetate- and butyrate-producing bacteria and an increase in lactate-producing bacterial populations. The meta-analysis of the human studies supports that supplementation with probiotics reduces blood pressure. The mechanism of this antihypertensive effect of probiotics and its protective effect on endothelial function has not been fully elucidated. Further investigations are needed to clarify if the effects of probiotic bacteria result from the changes in the gut microbiota and its metabolic by-products; the restoration of the gut barrier function; and the effects on endotoxemia, inflammation, and renal sympathetic nerve activity.

Roca-Saavedra, P., Mendez-Vilabrille, V., Miranda, J. M., Nebot, C., Cardelle-Cobas, A., Franco, C. M., and Cepeda, A. Food additives, contaminants and other minor components: effects on human gut microbiota-a review. J.Physiol Biochem. 5-9-2017; PM: 28488210

ABSTRACT: Gut bacteria play an important role in several metabolic processes and human diseases, such as obesity and accompanying co-morbidities, such as fatty liver disease, insulin resistance/diabetes, and cardiovascular events. Among other factors, dietary patterns, probiotics, prebiotics, synbiotics, antibiotics, and non-dietary factors, such as stress, age, exercise, and climatic conditions, can dramatically impact the human gut microbiota equilibrium and diversity. However, the effect of minor food constituents, including food additives and trace contaminants, on human gut microbiota has received less attention. Consequently, the present review aimed to provide an objective perspective of the current knowledge regarding the impacts of minor food constituents on human gut microbiota and consequently, on human health.

Romijn, A. R., Rucklidge, J. J., Kuijer, R. G., and Frampton, C. A double-blind, randomized, placebo-controlled trial of Lactobacillus helveticus and Bifidobacterium longum for the symptoms of depression. Aust.N.Z.J.Psychiatry. 1-1-2017; 4867416686694; PM: 28068788

ABSTRACT: *OBJECTIVES*: This trial investigated whether probiotics improved mood, stress and anxiety in a sample selected for low mood. We also tested whether the presence or severity of irritable bowel syndrome symptoms, and levels of proinflammatory cytokines, brain-derived neurotrophic factor and other blood markers, would predict or impact treatment response. *METHOD*: Seventy-nine participants (10 dropouts) not currently taking psychotropic medications with at least moderate scores on self-report mood measures were randomly allocated to receive either a probiotic preparation (containing Lactobacillus helveticus and Bifidobacterium longum) or a matched placebo, in a double-blind trial for 8 weeks. Data were analysed as intent-to-treat. *RESULTS*: No significant difference was found between the probiotic and placebo groups on any psychological outcome measure (Cohen's d range = 0.07-0.16) or any blood-based biomarker. At end-point, 9 (23%) of those in the probiotic group showed a 60% change on the Montgomery-Asberg Depression Rating Scale (responders), compared to 10 (26%) of those in the placebo group ([Formula: see text], p = ns). Baseline vitamin D level was found to moderate treatment effect on several outcome measures. Dry mouth and sleep disruption were reported more frequently in the placebo group. *CONCLUSIONS*: This study found no evidence that the probiotic formulation is effective in treating low mood, or in moderating the levels of inflammatory and other biomarkers. The lack of observed effect on mood symptoms may be due to the severity, chronicity or treatment resistance of the sample; recruiting an antidepressant-naive sample experiencing mild, acute symptoms of low mood, may well yield a different result. Future studies taking a preventative approach or using probiotics as an adjuvant treatment may also be more

effective. Vitamin D levels should be monitored in future studies in the area. The results of this trial are preliminary; future studies in the area should not be discouraged.

Rosa, D. D., Dias, M. M. S., Grzeskowiak, L. M., Reis, S. A., Conceicao, L. L., and Peluzio, M. D. C. G. Milk kefir: nutritional, microbiological and health benefits. Nutr.Res.Rev. 2017; 30(1):82-96; PM: 28222814

ABSTRACT: Kefir is fermented milk produced from grains that comprise a specific and complex mixture of bacteria and yeasts that live in a symbiotic association. The nutritional composition of kefir varies according to the milk composition, the microbiological composition of the grains used, the time/temperature of fermentation and storage conditions. Kefir originates from the Caucasus and Tibet. Recently, kefir has raised interest in the scientific community due to its numerous beneficial effects on health. Currently, several scientific studies have supported the health benefits of kefir, as reported historically as a probiotic drink with great potential in health promotion, as well as being a safe and inexpensive food, easily produced at home. Regular consumption of kefir has been associated with improved digestion and tolerance to lactose, antibacterial effect, hypocholesterolaemic effect, control of plasma glucose, anti-hypertensive effect, anti-inflammatory effect, antioxidant activity, anti-carcinogenic activity, anti-allergenic activity and healing effects. A large proportion of the studies that support these findings were conducted in vitro or in animal models. However, there is a need for systematic clinical trials to better understand the effects of regular use of kefir as part of a diet, and for their effect on preventing diseases. Thus, the present review focuses on the nutritional and microbiological composition of kefir and presents relevant findings associated with the beneficial effects of kefir on human and animal health.

Rosenfeld, C. S. Homage to the 'H' in developmental origins of health and disease. J.Dev.Orig.Health Dis. 2017; 8(1):8-29; PM: 27577791

ABSTRACT: Abundant evidence exists linking maternal and paternal environments from pericopconception through the postnatal period to later risk to offspring diseases. This concept was first articulated by the late Sir David Barker and as such coined the Barker Hypothesis. The term was then mutated to Fetal Origins of Adult Disease and finally broadened to developmental origins of adult health and disease (DOHaD) in recognition that the perinatal environment can shape both health and disease in resulting offspring. Developmental exposure to various factors, including stress, obesity, caloric-rich diets and environmental chemicals can lead to detrimental offspring health outcomes. However, less attention has been paid to date on measures that parents can take to promote the long-term health of their offspring. In essence, have we neglected to consider the 'H' in DOHaD? It is the 'H' component that should be of primary concern to expecting mothers and fathers and those seeking to have children. While it may not be possible to eliminate exposure to all pernicious factors, prevention/remediation strategies may tip the scale to health rather than disease. By understanding disruptive DOHaD mechanisms, it may also illuminate behavioral modifications that parents can adapt before fertilization and throughout the neonatal period to promote the lifelong health of their male and female offspring. Three possibilities will be explored in the current review: parental exercise, probiotic supplementation and breastfeeding in the case of mothers. The 'H' paradigm should be the focus going forward as a healthy start can indeed last a lifetime.

Rossoni, R. D., Fuchs, B. B., de Barros, P. P., Velloso, M. D., Jorge, A. O., Junqueira, J. C., and Mylonakis, E. Lactobacillus paracasei modulates the immune system of Galleria mellonella and protects against Candida albicans infection. PLoS.One. 2017; 12(3):e0173332; PM: 28267809

ABSTRACT: Probiotics have been described as a potential strategy to control opportunistic infections due to their ability to stimulate the immune system. Using the non-vertebrate model host Galleria mellonella, we evaluated whether clinical isolates of Lactobacillus spp. are able to provide protection against Candida albicans infection. Among different strains of Lactobacillus paracasei, Lactobacillus rhamnosus and Lactobacillus fermentum, we verified that L. paracasei 28.4 strain had the greatest ability to prolong the survival of larvae infected with a lethal dose of C. albicans. We found that the injection of 107 cells/larvae of L. paracasei into G. mellonella larvae infected by C. albicans increased the survival of these insects compared to the control group (P = 0.0001). After that, we investigated the immune mechanisms involved in the protection against C. albicans infection, evaluating the number of hemocytes and the gene expression of antifungal peptides. We found that L. paracasei increased the hemocyte quantity (2.38 x 106 cells/mL) in relation to the control group (1.29 x 106 cells/mL), indicating that this strain is capable of raising the number of circulating hemocytes into the G. mellonella hemolymph. Further, we found that L. paracasei 28.4 upregulated genes that encode the antifungal peptides galiomicin and gallerymicin. In relation to the control group, L. paracasei 28.4 increased gene expression of galiomicin by 6.67-fold and 17.29-fold for gallerymicin. Finally, we verified that the prophylactic provision of probiotic led to a significant reduction of the number of fungal cells in G. mellonella hemolymph. In conclusion, L. paracasei 28.4 can modulate the immune system of G. mellonella and protect against candidiasis.

Rouelle, C., Arion, A., and Prevost, V. [Management and prevention of cow's milk protein allergy: Contribution of community pharmacists]. Ann.Pharm.Fr. 2017; 75(3):236-244; PM: 28187880

ABSTRACT: Cow's milk protein allergy (CMPA) is a public health issue in children whose quality of life is strongly affected. The objective of this article is to review the present state of knowledge on the CMPA, and highlight some emerging alternatives in its management and in its prevention. Good knowledge in the appropriate infant formula, exclusion diets, the handling of the emergency treatment thanks to the use of epinephrine auto-injector pens, the use of personalized care project and accessibility to allergic patients' association are factors that secure the management. Breastfeeding and appropriate dietary diversification are for their part major preventive measures. The use of probiotics and desensitization immunotherapy are interesting emerging tracks. The role of community pharmacists in all these steps is discussed. It is indeed a nearby health professional involved both in improving prevention and in the optimization of the management. Its educational posture is crucial in assisting patients to help them better understand the CMPA and its treatment; as part of its new tasks, he can be integrated into therapeutic education programs to help allergic children and their families in a multidisciplinary context to better manage their daily life.

Roussel, C., Sivignon, A., de Wiele, T. V., and Blanquet-Diot, S. Foodborne enterotoxigenic Escherichia coli: from gut pathogenesis to new preventive strategies involving probiotics. Future.Microbiol. 2017; 12:73-93; PM: 27983878

ABSTRACT: Enterotoxigenic Escherichia coli (ETEC) are a major cause of traveler's diarrhea and infant mortality in developing countries. Given the rise of antibiotic resistance worldwide, there is an urgent need for the development of new preventive strategies. Among them, a promising approach is the use of probiotics. Although many studies, mostly performed under piglet digestive conditions, have shown the beneficial effects of probiotics on ETEC by interfering with their survival, virulence or adhesion to mucosa, underlying mechanisms remain unclear. This review describes ETEC pathogenesis, its modulation by human gastrointestinal cues as well as novel preventive strategies with a particular emphasis on probiotics. The potential of in vitro models simulating human digestion in elucidating probiotic mode of action will be discussed.

Roy, U., Jessani, L. G., Rudramurthy, S. M., Gopalakrishnan, R., Dutta, S., Chakravarty, C., Jillwin, J., and Chakrabarti, A. Seven cases of Saccharomyces fungaemia related to use of probiotics. Mycoses. 2017; 60(6):375-380; PM: 28133894

ABSTRACT: Probiotics are increasingly used in critically ill patients without enough safety data. The aim of the present study was to determine the association of probiotics with Saccharomyces cerevisiae fungaemia. Seven patients with S. cerevisiae fungaemia were reported at two hospitals in India between July 2014 and September 2015. Detailed clinical history of patients was recorded. Besides the seven patient isolates, three probiotics sachets used in those patients and five unrelated clinical isolates were used for association study by Fluorescent amplified fragment length polymorphism (FAFLP). Antifungal susceptibility testing was performed by broth microdilution technique of CLSI (M27-A3) and interpreted according to CLSI (M27S4). Two patients were premature neonates and five were adults. They were admitted in intensive care unit and were on probiotics containing S. boulardii (except one adult patient). FAFLP analysis showed 96.4-99.7% similarity between blood and corresponding probiotic isolates. Of the three AFLP types (group I, II, II) identified, all the probiotic isolates clustered in group I (major cluster) including majority of the blood isolates. The isolates were susceptible to all antifungal agents tested. Five patients, who could be evaluated, responded promptly to echinocandins or voriconazole. As the prescription of probiotic containing S. boulardii in critically ill patient's leads to the fungaemia, we recommend avoiding this probiotic in those patients.

Russo, M., Giugliano, F. P., Quitadamo, P., Mancusi, V., Miele, E., and Staiano, A. Efficacy of a mixture of probiotic agents as complementary therapy for chronic functional constipation in childhood. Ital.J.Pediatr. 3-7-2017; 43(1):24; PM: 28270173

ABSTRACT: BACKGROUND: About 30% of constipated children continue to struggle with constipation beyond puberty. Growing interest has recently raised on the use of probiotics as complementary therapy for FC, in order to prevent the possible PEG-related intestinal dysbiosis. Our study aimed at evaluating the effect on childhood FC of a probiotic mixture (PM), including Bifidobacteria breve M-16 V(R), infantis M-63(R), and longum BB536(R). *METHODS*: Fifty-five consecutive children suffering from FC were randomly assigned into two groups: group A received a daily oral combination of PEG plus PM and group B received oral PEG only. Physical and clinical data were collected from each patient at week-1, week-2, week-4, and week-8. *RESULTS*: After 1 month,

children who experienced improvement in the PEG and in the PEG + PM group were 88 and 81.8%, respectively (p = 0.24). After 1 month from the end of the study treatment, a positive trend towards a higher rate of clinical remission was observed within children treated with PM compared to those who took only PEG (percentage of children off therapy: 64 vs 52, respectively; p = 0.28). *CONCLUSIONS*: PEG and PEG + PM are equally effective and safe in the treatment of children with chronic constipation. Nevertheless, further studies are needed to show if adding Bifidobacteria strains to conventional therapy may lead to a better long-term outcome.

Saber, A., Alipour, B., Faghfoori, Z., and Yari, Khosroushahi A. Cellular and molecular effects of yeast probiotics on cancer. Crit Rev.Microbiol. 2017; 43(1):96-115; PM: 27561003

ABSTRACT: The cancer is one of the main causes of human deaths worldwide. The exact mechanisms of initiation and progression of malignancies are not clear yet, but there is a common agreement about the role of colonic microbiota in the etiology of different cancers. Probiotics have been examined for their anti-cancer effects, and different mechanisms have been suggested about their antitumor functions. Nonpathogenic yeasts, as members of probiotics family, can be effective on gut microbiota dysbiosis. Generally safe yeasts have shown so many beneficial effects on human health. Probiotic yeasts influence physiology, metabolism, and immune homeostasis in the colon and contribute to cancer treatment due to possessing anti-inflammatory, anti-proliferative and anti-cancer properties. This study reviews some of the health-beneficial effects of probiotic yeasts and their biological substances like folic acid and beta-glucan on cancer and focuses on the possible cellular and molecular mechanisms of probiotic yeasts such as influencing pathogenic bacteria, inactivation of carcinogenic compounds, especially those derived from food, improvement of intestinal barrier function, modulation of immune responses, antitoxic function, apoptosis, and anti-proliferative effects.

Sadeghzadeh, J., Vakili, A., Sameni, H. R., Shadnoush, M., Bandegi, A. R., and Zahedi, Khorasani M. The Effect of Oral Consumption of Probiotics in Prevention of Heart Injury in a Rat Myocardial Infarction Model: a Histopathological, Hemodynamic and Biochemical Evaluation. Iran Biomed.J. 2017; 21(3):174-181; PM: 27874107

ABSTRACT: BACKGROUND: Despite the emerging evidence on beneficial effects of probiotics on the cardiovascular system, their impact on the management of ischemic heart diseases and its possible mechanism have not been elucidated. *METHODS*: Four viable probiotics bacterial strains, including Bifidobacterium breve, Lactobacillus casei, Lactobacillus bulgaricus and Lactobacillus acidophilus, at the concentrations of 2x106 colony-forming units/ml were orally administered to the rats daily for 14 days before the induction of infarct-like myocardial injury using isoproterenol. Subsequently, 24 h after myocardial injury, the right carotid artery and the left ventricle were catheterized for recording blood pressure and cardiac parameters. At the end of the experiment, the heart was removed for the evaluation of histopathological and biochemical parameters, as well as tumor necrosis factor-alpha (TNF-alpha) assay. *RESULTS*: The induction of acute myocardial injury resulted in significant (P</=0.01) left ventricular (LV) dysfunction, as shown by an increase in LV end-diastolic pressure and a decrease in LV dp/dt max, LV dp/dt min, LV systolic pressure, and blood pressure, as compared with normal rats. Pretreatment with viable probiotics significantly reduced lipid peroxidation and TNF-alpha level and improved cardiac function (P<0.01). *CONCLUSION*: This study shows that

viable probiotics have a cardioprotective effect on infarct-like myocardial injury through suppressing TNF-alpha and oxidative stress damage in a rat model. Probiotic supplements may be used as a new option for prophylaxis in patients at the risk of ischemic heart disease in future.

Safari, O., Paolucci, M., and Motlagh, H. A. Effects of synbiotics on immunity and disease resistance of narrow-clawed crayfish, Astacus leptodactylus leptodactylus (Eschscholtz, 1823). Fish.Shellfish.Immunol. 2017; 64:392-400; PM: 28363588

ABSTRACT: The aim of this study was to evaluate the effects of prebiotics (mannanoligosaccharide and xylooligosaccharide), probiotics (Enterococcus faecalis and Pediococcus acidilactici) and synbiotics for 126 days on the immune responses, hemolymph indices, antioxidant enzymes, and biological responses after a 48-hour Aeromonas hydrophila exposure of sub-adult crayfish (11.45 +/- 1.87 g). Most antibacterial activities were observed in the shell mucus of crayfish fed a diet containing xylooligosaccharide + E. faecalis and mannanoligosaccharide + Pediococcus acidilactici against Nocardia brasilience and Vibrio harveyi ($p < 0.05$). Feeding crayfish a xylooligosaccharide + E. faecalis diet increased protein levels and the activities of alkaline phosphatase and lysozyme in the shell mucus after the feeding trial and 48 h after the A. hydrophila-injection challenge ($p < 0.05$). The highest ratio of the lactobacillus count to the total viable count was observed in synbiotic diets ($p < 0.05$). Feeding crayfish a xylooligosaccharide + E. faecalis diet increased the growth rate and the resistance to the A. hydrophila-injection challenge ($p < 0.05$). These results revealed that feeding crayfish with synbiotic diets was more effective than a single administration with prebiotics and probiotics.

Salazar, N., Valdes-Varela, L., Gonzalez, S., Gueimonde, M., and de Los Reyes-Gavilan CG. Nutrition and the gut microbiome in the elderly. Gut Microbes. 3-4-2017; 8(2):82-97; PM: 27808595

ABSTRACT: The gut microbiota is the assembly of microorganisms living in our intestine and their genomes are known as the microbiome. The correct composition and functionality of this microbiome is essential for maintaining a "healthy status." Aging is related to changes in the gut microbiota which are frequently associated with physiological modifications of the gastrointestinal tract, as well as, to changes in dietary patterns, together with a concomitant decline in cognitive and immune function, all together contributing to frailty. Therefore, nutritional strategies directed at restoring the microbiota in the elderly have to be addressed from a global perspective, considering not only the microbiota but also other extra-intestinal targets of action. The present review aims at summarizing the current knowledge on intestinal microbiota alterations and other functions impaired in the elderly and to analyze tools for implementing nutritional strategies, through the use of probiotics, prebiotics or specific nutrients in order to counterbalance such alterations.

Saleem, A. M., Zanouny, A. I., and Singer, A. M. Growth performance, nutrients digestibility, and blood metabolites of lambs fed diets supplemented with probiotics during pre- and post-weaning period. Asian-Australas.J.Anim Sci. 2017; 30(4):523-530; PM: 28002935

ABSTRACT: OBJECTIVE: Two experiments were conducted to evaluate the effects on growth performance, digestibility, and blood metabolites of lambs during pre- and post-

weaning period of inclusion of a commercial probiotic (PRO) containing a mixture of two strains of Pediococcus, Pediococcus acidilactici (1x106 colony-forming unit [cfu]/g) and Pediococcus pentosaceus (1.3x106 cfu/g), with dextrose as the carrier compound compared to a diet based on concentrate mixture and wheat straw. *METHODS*: In exp. 1, 24 male lambs of about 15+/-2.6 d age and initial body weight (BW) of 5.52+/-0.6 kg were randomly allocated into three groups. One group received control diet without additives, and remainders received control diet supplemented with 0.5 or 1 g PRO/lamb/d. Daily feed intake and biweekly BW were recorded. In exp. 2, five lambs, (initial BW = 29.72+/-1.15 kg, age = 6.54+/-0.32 mo) were used as experimental animals in a digestion trial. They were fed the same diets as in Exp. 1. *RESULTS*: The supplementation of PRO did not result in any significant differences in milk intake, average daily gain (ADG), or total gain between treatments during the pre-weaning period. Total dry matter intake tended to be greater (p = 0.07) with addition of PRO in the post-weaning diets. During post-weaning phase, the final BW, ADG, total gain, and feed conversion ratio of the lambs receiving PRO treatments tended to be greater (p</=0.10) than the control group. Addition of PRO in post-weaning diet decreased (p</=0.01) blood urea and cholesterol concentrations. With the exception of ether extract digestibility, all nutrients digestibility were improved with inclusion PRO in the post-weaning diets. *CONCLUSION*: Lambs that received PRO in post-weaning diet appeared to show a better performance than lambs in pre-weaning period. Addition of the probiotic in the post-weaning diet trended towards improved dry matter intake, growth performance, feed conversion ratio, and nutrients digestibility.

Salehi-Abargouei, A., Ghiasvand, R., and Hariri, M. Prebiotics, Prosynbiotics and Synbiotics: Can They Reduce Plasma Oxidative Stress Parameters? A Systematic Review. Probiotics.Antimicrob.Proteins. 2017; 9(1):1-11; PM: 28044254

ABSTRACT: This study assessed the effectiveness of presybiotics, prosybiotics and synbiotics on reducing serum oxidative stress parameters. PubMed/Medline, Ovid, Google Scholar, ISI Web of Science and SCOPUS were searched up to September 2016. English language randomized clinical trials reporting the effect of presybiotics, prosybiotics or synbiotic interventions on serum oxidative stress parameters in human adults were included. Twenty-one randomized clinical trials met the inclusion criteria for systematic review. Two studies investigated prebiotics, four studies synbiotics and fifteen studies probiotics. According to our systematic review, prebiotic could decrease malondialdehyde and increase superoxidative dismutase, but evidence is not enough. In comparison with fructo-oligosaccharide, inulin is much more useful for oxidative stress reduction. Using probiotics with dairy products could reduce oxidative stress significantly, but probiotic in form of supplementation did not have any effect on oxidative stress. There is limited but supportive evidence that presybiotics, prosybiotics and synbiotics are effective for reducing oxidative stress parameters. Further randomized clinical trials with longer duration of intervention especially on population with increased oxidative stress are needed to provide more definitive results before any recommendation for clinical use of these interventions.

Salmeron, I. Fermented cereal beverages: from probiotic, prebiotic and synbiotic towards nanoscience designed healthy drinks. Lett.Appl.Microbiol. 4-4-2017; PM: 28378421

ABSTRACT: The consumption of fermented food by human kind goes a long way back in

history and there are as many types of fermented food as civilizations. Food science and technology has progressed from designing nutritional food towards food with health improvement characteristics such as functional foods. In this sense, the area of food with properties to improve gastrointestinal health like probiotics, prebiotics and synbiotics has been the most important segment within functional foods. Most of these products are dairy-based so the development of non-dairy gut improvement products has been of great interest for the food industry, resulting in the rise of cereal-based probiotic and synbiotic products. Finally, through nanoscience and the application of nanotechnology techniques in the food sector it has been possible to design fermented beverages with synbiotic properties, and the incorporation of nanoparticles with unique and specific bioactivity has opened a new horizon in this segment of food created to improve human health and well-being. This article is protected by copyright. All rights reserved.

Sanchez, B., Delgado, S., Blanco-Miguez, A., Lourenco, A., Gueimonde, M., and Margolles, A. Probiotics, gut microbiota, and their influence on host health and disease. Mol.Nutr.Food Res. 2017; 61(1); PM: 27500859

ABSTRACT: The gastrointestinal tract of mammals hosts a high and diverse number of different microorganisms, known as intestinal microbiota. Many probiotics were originally isolated from the gastrointestinal tract, and they were defined by the Food and Agriculture Organization of the United Nations (FAO)/WHO as "live microorganisms which when administered in adequate amounts confer a health benefit on the host." Probiotics exert their beneficial effects on the host through four main mechanisms: interference with potential pathogens, improvement of barrier function, immunomodulation and production of neurotransmitters, and their host targets vary from the resident microbiota to cellular components of the gut-brain axis. However, in spite of the wide array of beneficial mechanisms deployed by probiotic bacteria, relatively few effects have been supported by clinical data. In this regard, different probiotic strains have been effective in antibiotic-associated diarrhea or inflammatory bowel disease for instance. The aim of this review was to compile the molecular mechanisms underlying the beneficial effects of probiotics, mainly through their interaction with the intestinal microbiota and with the intestinal mucosa. The specific benefits discussed in this paper include among others those elicited directly through dietary modulation of the human gut microbiota.

Sanchez, E., Nieto, J. C., Vidal, S., Santiago, A., Martinez, X., Sancho, F. J., Sancho-Bru, P., Mirelis, B., Corominola, H., Juarez, C., Manichanh, C., Guarner, C., and Soriano, G. Fermented milk containing Lactobacillus paracasei subsp. paracasei CNCM I-1518 reduces bacterial translocation in rats treated with carbon tetrachloride. Sci.Rep. 4-3-2017; 7:45712; PM: 28368023

ABSTRACT: Probiotics can prevent pathological bacterial translocation by modulating intestinal microbiota and improving the gut barrier. The aim was to evaluate the effect of a fermented milk containing Lactobacillus paracasei subsp. paracasei CNCM I-1518 on bacterial translocation in rats with carbon tetrachloride (CCl4)-induced cirrhosis. Sprague-Dawley rats treated with CCl4 were randomized into a probiotic group that received fermented milk containing Lactobacillus paracasei subsp. paracasei CNCM I-1518 in drinking water or a water group that received water only. Laparotomy was performed one week after ascites development. We evaluated bacterial translocation, intestinal microbiota, the intestinal barrier and cytokines in mesenteric lymph nodes and serum. Bacterial translocation decreased and gut dysbiosis improved in the probiotic

group compared to the water group. The ileal beta-defensin-1 concentration was higher and ileal malondialdehyde levels were lower in the probiotic group than in water group. There were no differences between groups in serum cytokines but TNF-alpha levels in mesenteric lymph nodes were lower in the probiotic group than in the water group. Fermented milk containing Lactobacillus paracasei subsp. paracasei CNCM I-1518 decreases bacterial translocation, gut dysbiosis and ileal oxidative damage and increases ileal beta-defensin-1 expression in rats treated with CCl4, suggesting an improvement in the intestinal barrier integrity.

Sanchez, M., Darimont, C., Panahi, S., Drapeau, V., Marette, A., Taylor, V. H., Dore, J., and Tremblay, A. Effects of a Diet-Based Weight-Reducing Program with Probiotic Supplementation on Satiety Efficiency, Eating Behaviour Traits, and Psychosocial Behaviours in Obese Individuals. Nutrients. 3-15-2017; 9(3); PM: 28294985

ABSTRACT: This study evaluated the impact of probiotic supplementation (Lactobacillus rhamnosus CGMCC1.3724 (LPR)) on appetite sensations and eating behaviors in the context of a weight-reducing program. Obese men (n = 45) and women (n = 60) participated in a double-blind, randomized, placebo-controlled trial that included a 12-week weight loss period (Phase 1) based on moderate energy restriction, followed by 12 weeks of weight maintenance (Phase 2). During the two phases of the program, each subject consumed two capsules per day of either a placebo or a LPR formulation (10 mg of LPR equivalent to 1.6 108 CFU/capsule, 210 mg of oligofructose, and 90 mg of inulin). The LPR supplementation increased weight loss in women that was associated with a greater increase in the fasting desire to eat (p = 0.03). On the other hand, satiety efficiency (satiety quotient for desire to eat) at lunch increased (p = 0.02), whereas disinhibition (p = 0.05) and hunger (p = 0.02) scores decreased more in the LPR-treated women, when compared with the female control group. Additionally, the LPR female group displayed a more pronounced decrease in food craving (p = 0.05), and a decrease in the Beck Depression Inventory score (p = 0.05) that was significantly different from the change noted in the placebo group (p = 0.02), as well as a higher score in the Body Esteem Scale questionnaire (p = 0.06). In men, significant benefits of LPR on fasting fullness and cognitive restraint were also observed. Taken together, these observations lend support to the hypothesis that the gut-brain axis may impact appetite control and related behaviors in obesity management.

Santanna, A. F., Filete, P. F., Lima, E. M., Porto, M. L., Meyrelles, S. S., Vasquez, E. C., Endringer, D. C., Lenz, D., Abdalla, D. S., Pereira, T. M., and Andrade, T. U. Chronic administration of the soluble, nonbacterial fraction of kefir attenuates lipid deposition in LDLr-/- mice. Nutrition. 2017; 35:100-105; PM: 28241975

ABSTRACT: OBJECTIVES: Kefir is obtained by the action of acidic bacteria and yeasts that exist in symbiotic association in kefir grains. Recently, this fermented milk drink has been recommended for the treatment of several clinical conditions, such as inflammatory, gastrointestinal, or cardiovascular-related diseases, or a combination of these diseases. However, its effects on atherosclerosis are not yet clear. The aim of this study was to prove that chronic treatment with a soluble, nonbacterial fraction of kefir could reduce the progression of atherosclerosis in low-density lipoprotein receptor-deficient (LDLr-/-) mice. *METHODS*: LDLr-/- mice were divided into four groups as follows: *RESULTS*: The soluble, nonbacterial fraction of kefir reduced lipid deposition (P < 0.05) independent of hypercholesterolemia. Moreover, kefir was capable of diminishing the circulating

proinflammatory intereukin (IL)-6 level and the ratio of tumor necrosis factor-alpha to IL-10 (50% and 42%, P < 0.05, respectively) and augmenting the antiinflammatory IL-10 level by approximately 74% (P < 0.05). *CONCLUSIONS*: Chronic treatment with a soluble nonbacterial fraction of kefir was able to decrease the lipid deposition in LDLr-/- hypercholesteremic mice, at least in part through modifying the circulating cytokine profile. The beneficial effects of kefir provide new perspectives for its use as an adjuvant in the prevention of atherosclerosis.

Santisteban, M. M., Qi, Y., Zubcevic, J., Kim, S., Yang, T., Shenoy, V., Cole-Jeffrey, C. T., Lobaton, G. O., Stewart, D. C., Rubiano, A., Simmons, C. S., Garcia-Pereira, F., Johnson, R. D., Pepine, C. J., and Raizada, M. K. Hypertension-Linked Pathophysiological Alterations in the Gut. Circ.Res. 1-20-2017; 120(2):312-323; PM: 27799253

ABSTRACT: RATIONALE: Sympathetic nervous system control of inflammation plays a central role in hypertension. The gut receives significant sympathetic innervation, is densely populated with a diverse microbial ecosystem, and contains immune cells that greatly impact overall inflammatory homeostasis. Despite this uniqueness, little is known about the involvement of the gut in hypertension. *OBJECTIVE*: Test the hypothesis that increased sympathetic drive to the gut is associated with increased gut wall permeability, increased inflammatory status, and microbial dysbiosis and that these gut pathological changes are linked to hypertension. *METHODS AND RESULTS*: Gut epithelial integrity and wall pathology were examined in spontaneously hypertensive rat and chronic angiotensin II infusion rat models. The increase in blood pressure in spontaneously hypertensive rat was associated with gut pathology that included increased intestinal permeability and decreased tight junction proteins. These changes in gut pathology in hypertension were associated with alterations in microbial communities relevant in blood pressure control. We also observed enhanced gut-neuronal communication in hypertension originating from paraventricular nucleus of the hypothalamus and presenting as increased sympathetic drive to the gut. Finally, angiotensin-converting enzyme inhibition (captopril) normalized blood pressure and was associated with reversal of gut pathology. *CONCLUSIONS*: A dysfunctional sympathetic-gut communication is associated with gut pathology, dysbiosis, and inflammation and plays a key role in hypertension. Thus, targeting of gut microbiota by innovative probiotics, antibiotics, and fecal transplant, in combination with the current pharmacotherapy, may be a novel strategy for hypertension treatment.

Sarao, L. K. and Arora, M. Probiotics, prebiotics, and microencapsulation: A review. Crit Rev.Food Sci.Nutr. 1-22-2017; 57(2):344-371; PM: 25848935

ABSTRACT: The development of a suitable technology for the production of probiotics is a key research for industrial production, which should take into account the viability and the stability of the organisms involved. Microbial criteria, stress tolerance during processing, and storage of the product constitute the basis for the production of probiotics. Generally, the bacteria belonging to the genera Lactobacillus and Bifidobacterium have been used as probiotics. Based on their positive qualities, probiotic bacteria are widely used in the production of food. Interest in the incorporation of the probiotic bacteria into other products apart from dairy products has been increasing and represents a great challenge. The recognition of dose delivery systems for probiotic bacteria has also resulted in research efforts aimed at developing probiotic food outside the dairy sector. Producing probiotic juices has been considered more in the recent

years, due to an increased concern in personal health of consumers. This review focuses on probiotics, prebiotics, and the microencapsulation of living cells.

Sardecka, I., Krogulska, A., and Toporowska-Kowalska, E. The influence of dietary immunomodulatory factors on development of food allergy in children. Postepy Dermatol.Alergol. 2017; 34(2):89-96; PM: 28507485

ABSTRACT: In the last few years many studies have been conducted on the role of dietary and environmental factors in the prevention of allergic diseases among children. Many studies have shown that the diet of pregnant women and children in their early postnatal life, rich in antioxidants, vitamin D, and fatty acids is beneficial as it reduces the risk of allergy in their future life. Moreover, there are many reports about the main role of gut microbiota and probiotics in the allergy prevention, what can indicate new ways of procedures in allergic diseases.

Sarjapuram, N., Mekala, N., Singh, M., and Tatu, U. The Potential of Lactobacillus casei and Entercoccus faecium Combination as a Preventive Probiotic Against Entamoeba. Probiotics.Antimicrob.Proteins. 2017; 9(2):142-149; PM: 27709564

ABSTRACT: Travellers' diarrhoea caused by enteric protozoa like Entamoeba histolytica is among the most common protozoan diseases in developing countries. In developing countries, amoebiasis is the second most prevalent protozoan disease. This protozoan parasite is often known to coexist as a part of the normal gut microbiota. It is estimated that around 50-60 % of population in developing countries might be harbouring Entamoeba in an asymptomatic manner. Due to physiological perturbation or upon immuno-compromise, it can become virulent and then cause diarrhoea, bloody stools and may invade other organs if left untreated. Nitroimidazole drugs, namely metronidazole and tinidazole, are widely used to treat protozoan infections. These drugs often show dose-dependent side effects. With emerging antibiotic resistance, novel therapeutics to prevent parasitic infections is required. This study aims to study effect of probiotics on prevention of Amoebiasis. In this study, we have investigated the effect of selected probiotics on the growth of Entamoeba. From the list of probiotics being currently used, five bacterial strains were selected for testing. These probiotic strains were co-cultured with Entamoeba, and their effect on Entamoeba proliferation was checked. Of the five probiotics chosen, individual treatments of Lactobacillus casei and Enterococcus faecium showed a significant reduction of up to 71 % in parasite survival only at higher CFUs. When the two probiotics were used in combination, the percentage of survival reduced gradually further to 80 % at a total CFU of 109 cells/ml of bacteria. The study lays the foundation for providing cost-effective prophylactic treatment for amoebiasis without the overuse of antibiotics.

Satish Kumar, C. S., Kondal, Reddy K., Boobalan, G., Gopala, Reddy A., Sudha Rani Chowdhary, C. H., Vinoth, A., Jayakanth, K., and Srinivasa, Rao G. Immunomodulatory effects of Bifidobacterium bifidum 231 on trinitrobenzenesulfonic acid-induced ulcerative colitis in rats. Res.Vet.Sci. 2017; 110:40-46; PM: 28159236

ABSTRACT: AIM: Ulcerative colitis and Crohn's disease are two important chronic Inflammatory bowel diseases (IBD) characterized by prominent intestinal inflammation.

Probiotics are the bacteria that promote the host health by its immunomodulatory activity. The present study investigated the correlation between in vitro adhesion and immunomodulatory properties, and to assess the therapeutic potential of Bifidobacterium bifidum 231 (BIF 231), a new strain of probiotic in ulcerative colitis in rats. *METHODS*: In vitro adhesion assays and immunomodulatory effect of BIF 231 on interleukins (IL-1beta and IL-10) in IEC-6 cell lines were quantified by gram staining, scanning electron microscopy and q-PCR respectively. Colitis was induced by intra-rectal instillation of trinitrobenzenesulfonic acid. Colitis was evaluated by alterations in colon gross morphology, histologically and biochemically. Colonic interleukin-1beta (IL-1beta) and interleukin-10 (IL-10) mRNA and protein expression were assessed by q-PCR, ELISA and western blot. *RESULTS*: BIF 231 showed better adhesion and immunomodulation by up-regulating IL-10 levels in IEC-6 cell lines. In vivo studies with treatment of BIF 231 (1.4x1011 CFU/rat/day) revealed anti-inflammatory effects both macroscopically and histologically. BIF 231 lowered TBARS, nitric oxide and augmented GSH levels. BIF 231 treatment to colitic rats down regulated IL-1beta levels with concurrent increase in IL-10 levels. *CONCLUSIONS*: BIF 231 exerted beneficial in vitro adhesion and immunomodulatory properties which facilitated the recovery of the damaged tissue in TNBS-induced colitis.

Satish, L., Gallo, P. H., Johnson, S., Yates, C. C., and Kathju, S. Local Probiotic Therapy with Lactobacillus plantarum Mitigates Scar Formation in Rabbits after Burn Injury and Infection. Surg.Infect.(Larchmt.). 2017; 18(2):119-127; PM: 27788042

ABSTRACT: BACKGROUND: Infection is the most common complication in burn-injured patients and is believed to contribute to the hypertrophic scarring frequently observed in such injury. Pseudomonas aeruginosa is a common pathogen in burn wound infection. We examined the effect of local probiotic therapy with Lactobacillus plantarum on the severity of the scarring following burn wounding and infection with P. aeruginosa in a rabbit model. *METHODS*: Full-thickness burn wounds were inoculated with control vehicle or L. plantarum; wounds were then challenged with bioluminescent P. aeruginosa. The time course of the ensuing infection was monitored by quantification of the emitted light. After allowing wounds to contract to near completion, they were harvested and analyzed for markers of scar formation. *RESULTS*: Application of L. plantarum curtailed both the severity and the length of the pseudomonal infection. Probiotic therapy significantly reduced both Type I collagen mRNA concentrations and total collagen protein accumulation in infected wounds, consistent with reduced scarring. Surprisingly, the probiotic showed a nearly equivalent effect in uninfected wounds. Masson's trichrome staining confirmed these findings histologically. *CONCLUSIONS*: Lactobacillus plantarum shows exciting potential as a therapeutic agent to both counteract burn wound infection and to alleviate scarring even in the absence of infection.

Sayon-Orea, C., Martinez-Gonzalez, M. A., Ruiz-Canela, M., and Bes-Rastrollo, M. Associations between Yogurt Consumption and Weight Gain and Risk of Obesity and Metabolic Syndrome: A Systematic Review. Adv.Nutr. 2017; 8(1):146S-154S; PM: 28096138

ABSTRACT: The role of yogurt consumption in the risk of developing overweight, obesity, or metabolic syndrome has been the subject of epidemiologic studies over the last 10 y. A comprehensive literature search on MEDLINE and ISI Web of Knowledge from 1966 through June 2016 was conducted to examine the relation between yogurt consumption and weight gain, as well as the risk of overweight, obesity, or metabolic syndrome, in

prospective cohort studies. Ten articles met all the inclusion criteria and were included in our systematic review. Of the 10 cohort studies, 3 analyzed the relation between yogurt consumption and the risk of overweight or obesity, 8 analyzed changes in waist circumference or weight changes, 3 studied the association with the risk of developing metabolic syndrome, and 1 studied the probability of abdominal obesity reversion. Although an inverse association between yogurt consumption and the risk of developing overweight or obesity was not fully consistent or always statistically significant, all studies but one showed in their point estimates inverse associations between yogurt consumption and changes in waist circumference, changes in weight, risk of overweight or obesity, and risk of metabolic syndrome during follow-up, although not all estimates were statistically significant (2 studies). Prospective cohort studies consistently suggested that yogurt consumption may contribute to a reduction in adiposity indexes and the risk of metabolic syndrome. Therefore, there is a need for more prospective studies and high-quality randomized clinical trials to confirm this apparent inverse association.

Scalabrin, D., Harris, C., Johnston, W. H., and Berseth, C. L. Long-term safety assessment in children who received hydrolyzed protein formulas with Lactobacillus rhamnosus GG: a 5-year follow-up. Eur.J.Pediatr. 2017; 176(2):217-224; PM: 27975116

ABSTRACT: Extensively hydrolyzed (EH) formula with Lactobacillus rhamnosus GG (LGG) was demonstrated to alleviate cow's milk allergy (CMA) symptoms and promote faster acquisition of tolerance to cow's milk protein. We previously demonstrated that partially hydrolyzed (PH) and EH formulas with LGG supported normal growth in healthy-term infants through 120 days of age. The objective of the current study was to evaluate growth, development, and specific adverse events through 5 years of age in participants from that cohort who continued receiving study formula. Infants who completed a double-blind, randomized growth and tolerance study were eligible to continue receiving the assigned study formula through 1 year of age (control: EH casein formula, EHF, or one of two investigational formulas: EH casein formula with LGG (EHF-LGG) or a PH formula with LGG (PHF-LGG)) and participate in follow-up through 5 years of age. Anthropometric measures, behavior development, and specific adverse events were recorded. No significant differences in achieved weight and height or behavioral development outcomes at 3 or 5 years of age were observed among study groups. Few statistically significant differences in the incidence of specific infection-related events through years 3 or 5 were observed among study groups, none of which were considered clinically relevant. *CONCLUSION*: Extensively and partially hydrolyzed formulas with LGG were associated with normal growth and development and long-term safety through 5 years of age. What is Known: * Infants with cow's milk allergy often experience allergic manifestations that can lead to poor nutrition status and poor growth. * Providing partially hydrolyzed (PH) and EH formulas with or without LGG in infants can support normal growth in healthy-term infants. What is New: * This study provides long-term safety data for the first 5 years of life on the use of extensively and partially hydrolyzed formulas with LGG when fed through 1 year of age. * Extensively and partially hydrolyzed formulas with LGG are associated with normal growth, development, and long-term safety through 5 years of age.

Scalfaro, C., Iacobino, A., Nardis, C., and Franciosa, G. Galleria mellonella as an in vivo model for assessing the protective activity of probiotics against gastrointestinal bacterial pathogens. FEMS Microbiol.Lett. 4-1-2017; 364(7); PM: 28369512

ABSTRACT: The antagonistic activity against gastrointestinal bacterial pathogens is an important property of probiotic bacteria and a desirable feature for pre-selection of novel strains with probiotic potential. Pre-screening of candidate probiotics for antibacterial activity should be based on in vitro and in vivo tests. This study investigated whether the protective activity of probiotic bacteria against gastrointestinal bacterial pathogens can be evaluated using Galleria mellonella larvae as an in vivo model. Larvae were pre-inoculated with either of two widely used probiotic bacteria, Lactobacillus rhamnosus GG or Clostridium butyricum Miyairi 588, and then challenged with Salmonella enterica Typhimurium, enteropathogenic Escherichia coli or Listeria monocytogenes. Survival rates increased in the probiotic pretreated larvae compared with control larvae inoculated with pathogens only. The hemocyte density increased as well in the probiotic pretreated larvae, indicating that both probiotics induce an immune response in the larvae. The antibacterial activity of probiotics against the pathogens was also assayed by an in vitro agar spot test: results were partially consistent with those obtained by the G. mellonella protection assay. The results obtained, as a whole, suggest that G. mellonella larvae are a potentially useful in vivo model that can complement in vitro assays for pre-screening of candidate probiotics.

Schaeck, M., Reyes-Lopez, F. E., Vallejos-Vidal, E., Van, Cleemput J., Duchateau, L., Van den, Broeck W., Tort, L., and Decostere, A. Cellular and transcriptomic response to treatment with the probiotic candidate Vibrio lentus in gnotobiotic sea bass (Dicentrarchus labrax) larvae. Fish.Shellfish.Immunol. 2017; 63:147-156; PM: 28119147

ABSTRACT: The present study aimed at evaluating the cellular and transcriptomic responses induced by the probiotic candidate Vibrio lentus with gnotobiotic European sea bass (Dicentrarchus labrax, Linnaeus 1785) larvae. For this, a histomorphological analysis was performed using the terminal deoxynucleotidyltransferase-mediated dUTP nick end labeling (TUNEL) and the anti-proliferating cell nuclear antigen (PCNA) assay. In addition, a global transcriptomic approach was adopted to study the whole body mRNA changes upon administration of V. lentus by microarrays with the custom Agilent sea bass oligonucleotide-microarray v2.0 (4 x 44 K). Following V. lentus administration, the apoptotic and cell proliferative indexes did not show significant differences between treatments for hindgut nor for midgut. However, V. lentus treatment did significantly modify the gene expression related not only to cell proliferation and cell death, but also to cell adhesion, reactive oxygen species metabolism, iron transport, and immune response. Our data represent the first global analysis of the effects of the probiotic candidate V. lentus on the gene expression profile in gnotobiotic European sea bass, and as such, provides a first delineation of the mechanisms by which this agent interacts with its host and exerts its beneficial effects.

Schreck, Bird A., Gregory, P. J., Jalloh, M. A., Risoldi, Cochrane Z., and Hein, D. J. Probiotics for the Treatment of Infantile Colic: A Systematic Review. J.Pharm.Pract. 2017; 30(3):366-374; PM: 26940647

ABSTRACT: OBJECTIVE: To evaluate whether clinical data support the safety and efficacy of probiotics for the management of infantile colic. *BACKGROUND*: Probiotics have been suggested as a potential strategy for infantile colic, and the specific species that have been studied in healthy infants are considered to be safe. *METHODOLOGY*: A systematic review was conducted to identify randomized controlled trials (RCTs) evaluating the use

of probiotic supplementation in infants with colic. RCTs with a primary end point assessing crying or fussing time were selected. A meta-analysis comparing "responders" to "nonresponders" in infants receiving probiotic versus control was conducted. The quality of trials selected was assessed. *RESULTS*: Five RCTs assessing 2 different strains of the probiotic Lactobacillus reuteri in mostly breastfed infants were identified. Analysis of response rates showed that infants receiving probiotics had a 2.3-fold greater chance of having a 50% or greater decrease in crying/fussing time compared to controls (P = .01). Probiotic supplementation was not associated with any adverse events. *CONCLUSION*: Supplementation with the probiotic L. reuteri in breastfed infants appears to be safe and effective for the management of infantile colic. Further research is needed to determine the role of probiotics in infants who are formula-fed.

Schwendicke, F., Korte, F., Dorfer, C. E., Kneist, S., Fawzy El-Sayed, K., and Paris, S. Inhibition of Streptococcus mutans Growth and Biofilm Formation by Probiotics in vitro. Caries Res. 2017; 51(2):87-95; PM: 28118640

ABSTRACT: To exert anticaries effects, probiotics are described to inhibit growth and biofilm formation of cariogenic bacteria such as Streptococcus mutans (SM). We screened 8 probiotics and assessed how SM growth or biofilm formation inhibition affects cariogenicity of probiotic-SM mixed-species biofilms in vitro. Growth inhibition was assessed by cocultivating probiotics and 2 SM strains (ATCC 20532/25175) on agar. Probiotics were either precultured before SM cultivation (exclusion), or SM precultured prior to probiotic cultivation (displacement). Inhibition of SM culture growth was assessed visually. Inhibition of SM biofilm formation on bovine enamel was assessed using a continuous-flow short-term biofilm model, again in exclusion or displacement mode. The cariogenicity of mixed-species biofilms of SM with the most promising growth and biofilm formation inhibiting probiotic strains was assessed using an artificial mouth model, and enamel mineral loss (DeltaZ) was measured microradiographically. We found limited differences in SM growth inhibition in exclusion versus displacement mode, and in inhibition of SM 20532 versus 25175. Results were therefore pooled. Lactobacillus acidophilus LA-5 inhibited significantly more SM culture growth than most other probiotics. L. casei LC-11 inhibited SM biofilm formation similarly to other alternatives but showed the highest retention of probiotics in the biofilms ($p < 0.05$). Mineral loss from SM monospecies biofilms (DeltaZ = 9,772, 25th/75th percentiles: 6,277/13,558 vol% x microm) was significantly lower than from mixed-species SM x LA-5 biofilms (DeltaZ = 24,578, 25th/75th percentiles: 19,081/28,768 vol% x microm; $p < 0.01$) but significantly higher than from SM x LC-11 biofilms (DeltaZ = 4,835, 25th/75th percentiles: 263/7,865 vol% x microm; $p < 0.05$). Probiotics inhibiting SM culture growth do not necessarily reduce the cariogenicity of SM-probiotic biofilms. Nevertheless, SM biofilm formation inhibition may be relevant in the reduction of cariogenicity.

Schwingshackl, L., Boeing, H., Stelmach-Mardas, M., Gottschald, M., Dietrich, S., Hoffmann, G., and Chaimani, A. Dietary Supplements and Risk of Cause-Specific Death, Cardiovascular Disease, and Cancer: A Systematic Review and Meta-Analysis of Primary Prevention Trials. Adv.Nutr. 2017; 8(1):27-39; PM: 28096125

ABSTRACT: Our aim was to assess the efficacy of dietary supplements in the primary prevention of cause-specific death, cardiovascular disease (CVD), and cancer by using meta-analytical approaches. Electronic and hand searches were performed until August 2016. Inclusion criteria were as follows: 1) minimum intervention period of 12 mo; 2)

primary prevention trials; 3) mean age >/=18 y; 4) interventions included vitamins, fatty acids, minerals, supplements containing combinations of vitamins and minerals, protein, fiber, prebiotics, and probiotics; and 5) primary outcome of all-cause mortality and secondary outcomes of mortality or incidence from CVD or cancer. Pooled effects across studies were estimated by using random-effects meta-analysis. Overall, 49 trials (69 reports) including 287,304 participants met the inclusion criteria. Thirty-two trials were judged as low risk-, 15 trials as moderate risk-, and 2 trials as high risk-of-bias studies. Supplements containing vitamin E (RR: 0.88; 95% CI: 0.80, 0.96) significantly reduced cardiovascular mortality risk, whereas supplements with folic acid reduced the risk of CVD (RR: 0.81; 95% CI: 0.70, 0.94). Vitamins D, C, and K; selenium; zinc; magnesium; and eicosapentaenoic acid showed no significant risk reduction for any of the outcomes. On the contrary, vitamin A was linked to an increased cancer risk (RR: 1.16; 95% CI: 1.00, 1.35). Supplements with beta-carotene showed no significant effect; however, in the subgroup with beta-carotene given singly, an increased risk of all-cause mortality by 6% (RR: 1.06; 95% CI: 1.02, 1.10) was observed. Taken together, we found insufficient evidence to support the use of dietary supplements in the primary prevention of cause-specific death, incidence of CVD, and incidence of cancer. The application of some supplements generated small beneficial effects; however, the heterogeneous types and doses of supplements limit the generalizability to the overall population.

Scourboutakos, M. J., Franco-Arellano, B., Murphy, S. A., Norsen, S., Comelli, E. M., and L'Abbe, M. R. Mismatch between Probiotic Benefits in Trials versus Food Products. Nutrients. 4-19-2017; 9(4); PM: 28422059

ABSTRACT: Probiotic food products contain a variety of different bacterial strains and may offer different health effects. The objective was to document the prevalence and dosage of probiotic strains in the Canadian food supply and to review the literature investigating these strains in order to understand what health benefits these products may offer. The Food Label Information Program was used to identify probiotic-containing products in the food supply. PubMed, Web of Science, and Embase were searched for randomized controlled trials that tested the health effects of these strains in humans. There were six probiotic strains/strain combinations identified in the food supply. Thirty-one studies investigated these strains and found that they are associated with decreased diarrhea and constipation, improved digestive symptoms, glycemic control, antioxidant status, blood lipids, oral health, and infant breastfeeding outcomes, as well as enhanced immunity and support for Helicobacter pylori eradication. There were a limited number of studies investigating these strains. Many studies were funded by the food industry and tested dosages that were up to twenty-five times the dosage found in most food products. Probiotic food products could have health benefits not currently reported on their labels. However, many dosages are too low to provide the benefits demonstrated in clinical trials. Further research is needed to enable more effective use of these functional foods.

Sebastian Domingo, J. J. Review of the role of probiotics in gastrointestinal diseases in adults. Gastroenterol.Hepatol. 2-6-2017; PM: 28185664

ABSTRACT: BACKGROUND: Probiotics may act as biological agents that modify the intestinal microbiota and certain cytokine profiles, which can lead to an improvement in certain gastrointestinal diseases. *OBJECTIVES*: To conduct a review of the evidence of the role of probiotics in certain gastrointestinal diseases in adults. SEARCH METHODS: Review conducted using appropriate descriptors, filters and limits in the PubMed database

(MEDLINE). *SELECTION CRITERIA*: The MeSH terms used were Probiotics [in the title] AND Gastrointestinal Diseases, with the following limits or filters: Types of study: Systematic Reviews, Meta-Analysis, Guideline, Practice Guideline, Consensus Development Conference (and Consensus Development Conference NIH), Randomized Controlled Trial, Controlled Clinical Trial and Clinical Trial; age: adults (19 or older); language: English and Spanish; in humans, and with at least one abstract. *DATA COLLECTION AND ANALYSIS*: Full texts of all the Systematic Reviews and meta-analyses directly related to the review's objective were obtained, as well as the Randomised Controlled Trials of the studies that were considered relevant and of sufficient quality for this review. *MAIN RESULTS*: Certain probiotics, different for each process, have proven to be effective and beneficial in cases of acute infectious diarrhoea, antibiotic-associated diarrhoea, Clostridium difficile-associated diarrhoea, pouchitis and Helicobacter pylori infection eradication. *AUTHORS' CONCLUSIONS*: Although some probiotics have not demonstrated any benefit, there are certain gastrointestinal diseases in which the use of probiotics, true biological agents, can be recommended.

Seganfredo, F. B., Blume, C. A., Moehlecke, M., Giongo, A., Casagrande, D. S., Spolidoro, J. V. N., Padoin, A. V., Schaan, B. D., and Mottin, C. C. Weight-loss interventions and gut microbiota changes in overweight and obese patients: a systematic review. Obes.Rev. 5-19-2017; PM: 28524627

ABSTRACT: Imbalances in the gut microbiota, the bacteria that inhabit the intestines, are central to the pathogenesis of obesity. This systematic review assesses the association between the gut microbiota and weight loss in overweight/obese adults and its potential manipulation as a target for treating obesity. This review identified 43 studies using the keywords 'overweight' or 'obesity' and 'microbiota' and related terms; among these studies, 17 used dietary interventions, 11 used bariatric surgery and 15 used microbiota manipulation. The studies differed in their methodologies as well as their intervention lengths. Restrictive diets decreased the microbiota abundance, correlated with nutrient deficiency rather than weight loss and generally reduced the butyrate producers Firmicutes, Lactobacillus sp. and Bifidobacterium sp. The impact of surgical intervention depended on the given technique and showed a similar effect on butyrate producers, in addition to increasing the presence of the Proteobacteria phylum, which is related to changes in the intestinal absorptive surface, pH and digestion time. Probiotics differed in strain and duration with diverse effects on the microbiota, and they tended to reduce body fat. Prebiotics had a bifidogenic effect and increased butyrate producers, likely due to cross-feeding interactions, contributing to the gut barrier and improving metabolic outcomes. All of the interventions under consideration had impacts on the gut microbiota, although they did not always correlate with weight loss. These results show that restrictive diets and bariatric surgery reduce microbial abundance and promote changes in microbial composition that could have long-term detrimental effects on the colon. In contrast, prebiotics might restore a healthy microbiome and reduce body fat.

Seidavi, A., Dadashbeiki, M., imohammadi-Saraei, M. H., van den, Hoven R., Payan-Carreira, R., Laudadio, V., and Tufarelli, V. Effects of dietary inclusion level of a mixture of probiotic cultures and enzymes on broiler chickens immunity response. Environ.Sci.Pollut.Res.Int. 2017; 24(5):4637-4644; PM: 27966084

ABSTRACT: The current study was conducted to analyse the effect of a mixture of probiotic cultures and enzymes (Probio Enzyme, XVET GmbH, Germany) on the immune

response and weight of central lymphoid organs and liver in broilers. A total of 270 male chickens were randomly divided into nine groups, with three replicates of 10 birds each. Treatment groups were fed for either 22 or 42 days with different levels of Probio Enzyme 250, 500, 750 and 1000 g/ton, whereas the control group fed a basal diet without Probio Enzyme. To analyse the effects of dietary supplementation on broilers humoral immune response, the antibodies titres for avian influenza (AI) and Newcastle disease virus (NDV) and to the sheep red blood cells (SRBC) challenge were assayed in birds from each experimental unit, along with the assessment of the weight of the main lymphoid organs and liver. The addition of the Probio Enzyme mixture did not significantly affect the titres of the antibodies against AI and NDV at day 42, despite the wide individual variation observed specially on the antibody titres at day 33. Treatments affected the production of IgG after the second challenge with SRBC ($P = 0.003$), which was transposed to the correspondent total Ig titres ($P = 0.044$). Conversely, a lower birds' body weight (BW) was found in the majority of treated groups compared to control ($P = 0.031$). The spleen was the only lymphoid organ showing differences in the absolute and relative weight ($P = 0.003$ and $P = 0.001$, respectively). No differences were found in thymus and Bursa of Fabricius weights. In conclusion, broilers treated with Probio Enzyme showed a satisfactory immune response compared with control, despite the wide variation found after the first vaccine challenge against AI. Moreover, the probiotic mixture dose and duration modulated differently the immune response and the spleen weight, unaffecting the central lymphoid organs weight.

Seifi, K., Karimi Torshizi, M. A., Rahimi, S., and Kazemifard, M. Efficiency of early, single-dose probiotic administration methods on performance, small intestinal morphology, blood biochemistry, and immune response of Japanese quail. Poult.Sci. 5-17-2017; PM: 28521051

ABSTRACT: The aim of the present study was to investigate the efficacy of early probiotics (single dose) administered in different ways, on quails' performance, small intestine morphology, blood biochemistry, and immune response. In total, 192 day-old chicks were used in one of the following experimental groups before being transferred to a raising room: 1) Control (no probiotic administered), 2) oral gavage, 3) spray, and 4) vent lip. Four replicates of 12 chicks per cage were considered for each treatment and birds were raised up to 35 d in the same conditions. Probiotic treated birds had higher d 1 to 35 feed intake than the control group ($P < 0.05$). In addition, oral-gavaged birds had a higher body weight gain as compared to the control ($P < 0.05$). The values of duodenum length and villus height of the oral group and ileum length and villus height of the vent lip group were greater than that of the control ($P < 0.01$). Regardless of the method of administration, probiotics resulted in deeper crypts and in a higher number of goblet cells in the duodenum and ileum as compared to the control ($P < 0.01$). The administration of probiotics resulted in increased plasma uric acid ($P < 0.05$), glucose, and total protein ($P < 0.01$). The concentration of hemoglobin was slightly higher in probiotic-supplemented groups. While a decreased concentration of triglyceride was observed in vent-lip probiotic-administered birds compared to control ($P < 0.05$), the concentration of cholesterol was not significantly affected by treatments ($P > 0.01$). None of the immune-related parameters were affected by the probiotic ($P > 0.05$). Single dose usage of probiotics exerts its beneficial effects on quails' body weight gain, feed intake and mortality in 1 to 35 d period, regardless of the route of administration. This work generally supports the efficacy of single-dose usage of probiotics and suggests the spray of probiotics as an early, single-dose administration method.

Seme, H., Bogovic, Matijasic B., Svigelj, K., Langerholc, T., Fujs, S., Horvat, J., Zlatic, E., Gjuracic, K., Petkovic, H., Stempelj, M., Kos, B., Suskovic, J., and Kosec, G. Generation of Lactobacillus plantarum strains with improved potential to target gastrointestinal disorders related to sugar malabsorption. Food Res.Int. 2017; 94:45-53; PM: 28290366

ABSTRACT: Malabsorption of dietary sugars is a common cause of gastrointestinal discomfort, affecting up to one in three people with debilitating symptoms, such as abdominal pain, osmotic diarrhoea, bloating and flatulence. Besides dietary interventions, it has been suggested that ingestion of lactobacilli may alleviate these symptoms. The objectives of this study were to generate strains with improved potential to ameliorate sugar malabsorption related gastrointestinal disorders. Initial selection was made from 183 natural isolates of lactic acid bacteria, on the basis of broad sugar fermentation ability, absence of gas production, gastrointestinal survival and susceptibility to important medical antimicrobials. Two strains of L. plantarum (KR6 and M5) exhibited favourable characteristics for all criteria, and were further optimised through random mutagenesis and selection approaches. Ultraviolet light (UV) exposure resulted in mutants characterized by better survival (for 1.9 log and 1.4 log) in gastrointestinal conditions. Subsequent exposure to ethyl methanesulfonate (EMS) provided mutants with greater tolerance to glucose induced catabolic repression. UV and UV-EMS mutants of L. plantarum M5 showed improved adhesion ability. As a result of this optimisation, L. plantarum MP2026 and L. plantarum MP2420 have been identified as promising candidates for probiotics, intended for alleviation of gastrointestinal discomfort originating from sugar malabsorption.

Seminario-Amez, M., Lopez-Lopez, J., Estrugo-Devesa, A., yuso-Montero, R., and Jane-Salas, E. Probiotics and oral health: A systematic review. Med.Oral Patol.Oral Cir.Bucal. 5-1-2017; 22(3):e282-e288; PM: 28390121

ABSTRACT: BACKGROUND: Probiotics are microorganisms, mainly bacteria, which benefit the host's health. Many studies support the role of probiotics as a contributor to gastrointestinal health, and nowadays many authors are trying to prove its influence in oral health maintenance. *OBJECTIVES*: To review the published literature with the purpose of knowing the importance of using probiotics as a preventive and therapeutic method for oral infectious diseases management. *MATERIAL AND METHODS*: An electronic search in PubMed database with the keywords "oral health AND probiotics AND dentistry" was conducted. The inclusion criteria were: randomized clinical trials (RCTs) that assess the action of any probiotic strain in the treatment and / or prevention of an infectious oral disease, RCTs that assess the action of any probiotic strain on counting colony forming units (CFU) of oral pathogens, systematic reviews and meta-analysis. The Jadad scale was used to assess the high quality of RCTs. *RESULTS*: Fifteen articles were considered for this review. Of which, 12 were RCTs of good / high quality (Jadad scale), two meta-analysis and one systematic review. *CONCLUSIONS*: The literature reviewed suggests probiotics usage could be beneficial for the maintenance of oral health, due to its ability to decrease the colony forming units (CFU) counts of the oral pathogens. However, randomized clinical trials with long-term follow-up periods are needed to confirm their efficacy in reducing the prevalence/incidence of oral infectious diseases. Furthermore, the recognition of specific strains with probiotic activity for each infectious oral disease is required, in order to determine exact dose, treatment time and ideal vehicles.

Severance, E. G., Gressitt, K. L., Stallings, C. R., Katsafanas, E., Schweinfurth, L. A., Savage, C. L., Adamos, M. B., Sweeney, K. M., Origoni, A. E., Khushalani, S., Dickerson, F. B., and Yolken, R. H. Probiotic normalization of Candida albicans in schizophrenia: A randomized, placebo-controlled, longitudinal pilot study. Brain Behav.Immun. 2017; 62:41-45; PM: 27871802

ABSTRACT: The molecules and pathways of the gut-brain axis represent new targets for developing methods to diagnose and treat psychiatric disorders. Manipulation of the gut microbiome with probiotics may be a therapeutic strategy with the potential to relieve gastrointestinal (GI) comorbidities and improve psychiatric symptoms. Candida albicans and Saccharomyces cerevisiae, commensal yeast species, can be imbalanced in the unhealthy human microbiome, and these fungal exposures were previously found elevated in schizophrenia. In a longitudinal, double-blind, placebo-controlled, pilot investigation of 56 outpatients with schizophrenia, we examined the impact of probiotic treatment on yeast antibody levels, and the relationship between treatment and antibody levels on bowel discomfort and psychiatric symptoms. We found that probiotic treatment significantly reduced C. albicans antibodies over the 14-week study period in males, but not in females. Antibody levels of S. cerevisiae were not altered in either treatment group. The highest levels of bowel discomfort over time occurred in C. albicans-seropositive males receiving the placebo. We observed trends towards improvement in positive psychiatric symptoms in males treated with probiotics who were seronegative for C. albicans. Results from this pilot study hint at an association of C. albicans seropositivity with worse positive psychiatric symptoms, which was confirmed in a larger cohort of 384 males with schizophrenia. In conclusion, the administration of probiotics may help normalize C. albicans antibody levels and C. albicans-associated gut discomfort in many male individuals. Studies with larger sample sizes are warranted to address the role of probiotics in correcting C. albicans-associated psychiatric symptoms.

Sgibnev, A. and Kremleva, E. Influence of Hydrogen Peroxide, Lactic Acid, and Surfactants from Vaginal Lactobacilli on the Antibiotic Sensitivity of Opportunistic Bacteria. Probiotics.Antimicrob.Proteins. 2017; 9(2):131-141; PM: 27832440

ABSTRACT: We studied as hydrogen peroxide, lactic acid, or surfactants from clinical isolates of vaginal lactobacilli and cell-free supernatants from probiotic strain LCR35 can influence on the sensitivity of opportunistic bacteria to antibiotics. We found that the most effective in increasing sensitivity to antibiotics were hydrogen peroxide and surfactants or their combination but no lactic acid. In some cases, the effect of the composition of hydrogen peroxide and surfactants was clearly higher than the sum of effects of these substances alone. With using of the supernatant of LCR35 was shown that the combination of surfactant and lactate has greater effect compared with surfactants alone. In concluding, metabolites of vaginal lactobacilli are suitable for the role of "antibiotic assistants" and it can help solve the problems the antibiotic resistance.

Shao, D., Yao, L., Riaz, M. S., Zhu, J., Shi, J., Jin, M., Huang, Q., and Yang, H. Simulated microgravity affects some biological characteristics of Lactobacillus acidophilus. Appl.Microbiol.Biotechnol. 2017; 101(8):3439-3449; PM: 28013406

ABSTRACT: The effects of weightlessness on enteric microorganisms have been extensively studied, but have mainly been focused on pathogens. As a major component of the microbiome of the human intestinal tract, probiotics are important to keep the host healthy. Accordingly, understanding their changes under weightlessness

conditions has substantial value. This study was carried out to investigate the characteristics of Lactobacillus acidophilus, a typical probiotic for humans, under simulated microgravity (SMG) conditions. The results revealed that SMG had no significant impact on the morphology of L. acidophilus, but markedly shortened its lag phase, enhanced its growth rate, acid tolerance ability up to pH < 2.5, and the bile resistance at the bile concentration of <0.05%. SMG also decreased the sensitivity of L. acidophilus to cefalexin, sulfur gentamicin, and sodium penicillin. No obvious effect of SMG was observed on the adhesion ability of L. acidophilus to Caco-2 cells. Moreover, after SMG treatment, both the culture of L. acidophilus and its liquid phase exhibited higher antibacterial activity against S. typhimurium and S. aureus in a time-dependent manner. The SMG treatment also increased the in vitro cholesterol-lowering ability of L. acidophilus by regulating the expression of the key cholesterol metabolism genes CYP7A1, ABCB11, LDLR, and HMGCR in the HepG2 cell line. Thus, the SMG treatment did have considerable influence on some biological activities and characteristics of L. acidophilus related to human health. These findings provided valuable information for understanding the influence of probiotics on human health under simulated microgravity conditions, at least.

Sharif, A., Kashani, H. H., Nasri, E., Soleimani, Z., and Sharif, M. R. The Role of Probiotics in the Treatment of Dysentery: a Randomized Double-Blind Clinical Trial. Probiotics.Antimicrob.Proteins. 3-21-2017; PM: 28321826

ABSTRACT: Diarrhea is considered as an important cause of morbidity and mortality, even though one of the main reasons of death following diarrhea is initiated by dysentery. In recent years, the consumption of probiotics has been proposed for the treatment of infectious diarrhea. Despite most of the studies on probiotics have focused on acute watery diarrhea, few studies in the field of dysentery have found beneficial effects of probiotics. This study is a randomized double-blind clinical trial. The patients were randomly placed into control and case groups. In the intervention group, the patients received probiotics in the form of Kidilact(R) sachet, which contained high amounts of 7-strain friendly bacteria strains of Lactobacillus casei, Lactobacillus acidophilus, Lactobacillus rhamnosus, Lactobacillus bulgaricus, Bifidobacterium infantis, Bifidobacterium breve, and Streptococcus thermophiles. On the other hand, the patients in the control group received placebo sachets on a daily basis for 5 days. It is notable that the treatment protocol of acute dysentery was done on both groups. The results of this study showed significant differences in the duration of blood in diarrhea between probiotic consumers (2.62 days) and the control group (3.16 days) (P value = 0.05). Additionally, significant differences in the average length of hospitalization in probiotic consumers (3.16 days) and control (3.66 days), (P value = 0.02) could be claimed that the consumption of probiotics is effective in reducing the duration of dysentery and diarrhea. The results of this study suggest that the use of probiotics can be effective in reducing the duration of blood in diarrhea. This study was also recorded in the Iran center of clinical trials registration database (IRCT2014060617985N1).

Sharma, C., Gulati, S., Thakur, N., Singh, B. P., Gupta, S., Kaur, S., Mishra, S. K., Puniya, A. K., Gill, J. P. S., and Panwar, H. Antibiotic sensitivity pattern of indigenous lactobacilli isolated from curd and human milk samples. 3 Biotech. 2017; 7(1):53; PM: 28444600

ABSTRACT: The gut microbiota plays a vital role in host well-being and lactic acid bacteria (LAB) have gained an overwhelming attention as health promoter. This

perception has evolved from traditional dairy products to a money-spinning market of probiotics. The safety of probiotics is coupled to their intended use and LAB may act as pool of antimicrobial resistance genes that could be transferred to pathogens, either in food matrix or in gastrointestinal tract, which could be detrimental to host. This study evaluated the antibiotic susceptibility patterns of LAB isolated from curd (20) and human milk (11) samples. Antibiotic susceptibility was determined against 26 common antibiotics, following reference disc diffusion assay. A varied response in terms of susceptibility and resistance towards antibiotics was recorded. Among curd isolates, D7 (Lactobacillus plantarum) was the most resistant followed by D4, D8, D10 and D25. Among human milk isolates, HM-1 (L. casei) showed the highest resistance profile. All LAB isolates displayed high susceptibility pattern towards imipenem and meropenem. In general, high resistivity was exhibited by human milk isolates. The present study showed that antibiotic resistance is widespread among different lactobacilli, which may pose a food safety concern. Therefore, antibiotic sensitivity should be considered as a vital tool for safety assessment of probiotics.

Sharma, C., Singh, B. P., Thakur, N., Gulati, S., Gupta, S., Mishra, S. K., and Panwar, H. Antibacterial effects of Lactobacillus isolates of curd and human milk origin against food-borne and human pathogens. 3 Biotech. 2017; 7(1):31; PM: 28401466

ABSTRACT: This study was undertaken to assess the antibacterial efficacy of lactobacilli isolated from curd and human milk samples. Identities of thirty-one different lactobacilli (20 from curd and 11 from human milk) were confirmed by genus-specific PCR and 16S rRNA-based sequencing. These strains belonged to five species, Lactobacillus casei, L. delbrueckii, L. fermentum, L. plantarum, and L. pentosus. Antibacterial activities of cell-free supernatants (CFSs) of all the Lactobacillus isolates were estimated through standard agar-well diffusion assay, against commonly occurring food-borne and clinically important human pathogens. None of the lactobacilli cell-free supernatant (CFS) exhibited inhibitory activity against four pathogens, namely Staphylococcus aureus, Listeria monocytogenes, Escherichia coli, and Klebsiella pneumoniae. Bacillus cereus, Salmonella enterica serovar Typhi, and Shigella flexneri were moderately inhibited by majority of CFSs, whereas, weak activity was observed against Pseudomonas aeruginosa and Proteus mirabilis. CFS of some of the curd isolates displayed antagonistic activity against Streptococcus mutans; however, human milk lactobacilli did not displayed any inhibitory activity against them. As expected, Nisin (Nisaplin(R)) showed inhibitory activity against Gram-positive, S. aureus, B. cereus, and L. monocytogenes. Interestingly, few of the examined CFSs exhibited inhibitory activities against both Gram-positive and Gram-negative pathogens. Findings from this study support the possibility to explore the tested lactobacilli and their CFSs as natural bio-preservatives, alone or in combination with approved bacteriocins in food and pharma formulations after validating their safety.

Sharma, K., Mahajan, R., Attri, S., and Goel, G. Selection of indigenous Lactobacillus paracasei CD4 and Lactobacillus gastricus BTM 7 as probiotic: assessment of traits combined with principal component analysis. J.Appl.Microbiol. 2017; 122(5):1310-1320; PM: 28236643

ABSTRACT: AIMS: The population of the Himalayan region is known to consume a variety of fermented and nonfermented foods and as a result they have been benefited in terms of overall health, because of the associated beneficial microbes. Therefore, the focus of the present study was to identify new strains of lactic acid bacteria (LAB) from dairy products such as milk (cow, goat, buffalo) and fermented products (curd and

buttermilk) with properties suitable for use as probiotic cultures. *METHODS AND RESULTS*: A total of 75 isolates tentatively identified as LAB from 100 samples were initially screened for production of beta-haemolysin as indicators of virulence which resulted in 38 isolates with no haemolytic activity. Further subtractive screening based on resistance to gastrointestinal tract barriers (acid and bile salts) resulted in the selection of the eight most promising strains. All these eight strains were resistant to pH 2.0, 1% bile concentration and pancreatin (1 mg l-1). Among the eight isolates, three isolates were identified as Brevibacillus thermoruber and the others as Brevibacillus aydinogluensis, Lactobacillus gastricus, L. paracasei, Enterococcus sp. Weisella confusa based on 16S rDNA region. Among these isolates, L. paracasei CD4 and L. gastricus BTM7 indicated maximum tolerance to simulated gastric environment. Both the isolates possessed highest score for cell surface hydrophobicity, cell autoaggregation, adherence to Caco-2 cell lines and antimicrobial activity against clinical isolates of Escherichia coli and Shigella sp. comparable to standard strain of Lactobacillus rhamnosus GG. Further principal component analysis and clustering analysis based on Euclidean Similarity index of probiotic characters revealed that L. paracasei strain CD4 and L. gastricus strain BTM7 were placed closest to reference strain L. rhamnosus GG and were therefore identified as most promising probiotic candidate cultures. *CONCLUSIONS*: These characteristics suggest that these strains could be excellent candidates for probiotics. *SIGNIFICANCE AND IMPACT OF THE STUDY*: Milk-based products serve as reservoir for bacterial species with probiotic attributes.

Shashidhar, A., Suman Rao, P. N., Nesargi, S., Bhat, S., and Chandrakala, B. S. Probiotics for Feed Tolerance in Very Low Birth Weight Neonates - A Randomized Controlled Trial. Indian Pediatr. 3-29-2017; PM: 28368269

ABSTRACT: *OBJECTIVE*: To measure the efficacy of a probiotic formulation on time to reach full enteral feeds in VLBW (very low birth weight) newborns. *DESIGN*: A blinded randomized control trial. SETTING: A tertiary care neonatal intensive care unit (NICU) in Southern India between August 2012 to November 2013. *PARTICIPANTS*: 104 newborns with a birth weight of 750-1499 g on enteral feeds. *INTERVENTION*: Probiotic group (n=52) received a multicomponent probiotic formulation of Lactobacillus acidophilus, Lactobacillus rhamnosus, Bifidobacterium longum and Saccharomyces boulardii once a day at a dose of 1.25x109 CFU from the time of initiation of enteral feeds till discharge and the control group (n=52) received only breast milk. *OUTCOME MEASURES*: Time to reach full enteral feeds (150 mL/kg/day). *RESULTS*: The mean (SD) time to reach full enteral feeding was 11.2 (8.3) days in probiotic vs. 12.7 (8.9)in no probiotic group; (P=0.4), and was not significantly different between the two study groups. There was a trend towards lower necrotizing enterocolitis in the probiotic group (4% vs. 12%). *CONCLUSION*: Probiotic supplementation does not seem to result in significant improvement of feed tolerance in VLBW newborns.

Shehata, A. A., Tarabees, R., Basiouni, S., Gamil, M., Kamal, A. S., and Kruger, M. Phenotypic and Genotypic Characterization of Bacteriocinogenic Enterococci Against Clostridium botulinum. Probiotics.Antimicrob.Proteins. 2017; 9(2):182-188; PM: 27914002

ABSTRACT: The present study aimed to characterize Enterococcus faecalis (n = -6) and Enterococcus faecium (n = 1) isolated from healthy chickens to find a novel perspective probiotic candidate that antagonize Clostridium botulinum types A, B, D, and E. The isolated enterococci were characterized based on phenotypic properties, PCR, and

matrix-assisted laser desorption/ionization time of flight (MALDI-TOF). The virulence determinants including hemolytic activity on blood agar, gelatinase activity, sensitivity to vancomycin, and presence of gelatinase (gelE) and enterococcal surface protein (esp) virulence genes were investigated. Also, the presence of enterocin structural genes enterocin A, enterocin B, enterocin P, enterocin L50A/B, bacteriocin 31, enterocin AS48, enterocin 1071A/1071B, and enterocin 96 were assessed using PCR. Lastly, the antagonistic effect of the selected Enterococcus spp. on the growth of C. botulinum types A, B, D, and E was studied. The obtained results showed that four out of six E. faecalis and one E. faecium proved to be free from the tested virulence markers. All tested enterococci strains exhibited more than one of the tested enterocin. Interestingly, E. faecalis and E. faecium significantly restrained the growth of C. botulinum types A, B, D, and E. In conclusion, although, the data presented showed that bacteriocinogenic Enterococcus strains lacking of virulence determinants could be potentially used as a probiotic candidate against C. botulinum in vitro; however, further investigations are still urgently required to verify the beneficial effects of the tested Enterococcus spp. in vivo.

Shen, N. T., Maw, A., Tmanova, L. L., Pino, A., Ancy, K., Crawford, C. V., Simon, M. S., and Evans, A. T. Timely Use of Probiotics in Hospitalized Adults Prevents Clostridium difficile Infection: A Systematic Review With Meta-Regression Analysis. Gastroenterology. 2-10-2017; PM: 28192108

ABSTRACT: BACKGROUND & AIMS: Systematic reviews have provided evidence for the efficacy of probiotics in preventing Clostridium difficile infection (CDI), but guidelines do not recommend probiotic use for prevention of CDI. We performed an updated systematic review to help guide clinical practice. *METHODS*: We searched MEDLINE, EMBASE, International Journal of Probiotics and Prebiotics, and The Cochrane Library databases for randomized controlled trials evaluating use of probiotics and CDI in hospitalized adults taking antibiotics. Two reviewers independently extracted data and assessed risk of bias and overall quality of the evidence. Primary and secondary outcomes were incidence of CDI and adverse events, respectively. Secondary analyses examined the effects of probiotic species, dose, timing, formulation, duration, and study quality. *RESULTS*: We analyzed data from 19 published studies, comprising 6261 subjects. The incidence of CDI in the probiotic cohort, 1.6% (54 of 3277), was lower than of controls, 3.9% (115 or 2984) ($P < .001$). The pooled relative risk of CDI in probiotic users was 0.42 (95% confidence interval, 0.30-0.57; $I2 = 0.0\%$). Meta-regression analysis demonstrated that probiotics were significantly more effective if given closer to the first antibiotic dose, with a decrement in efficacy for every day of delay in starting probiotics ($P = .04$); probiotics given within 2 days of antibiotic initiation produced a greater reduction of risk for CDI (relative risk, 0.32; 95% confidence interval, 0.22-0.48; $I2 = 0\%$) than later administration (relative risk, 0.70; 95% confidence interval, 0.40-1.23; $I2 = 0\%$) ($P = .02$). There was no increased risk for adverse events among patients given probiotics. The overall quality of the evidence was high. *CONCLUSIONS*: In a systematic review with meta-regression analysis, we found evidence that administration of probiotics closer to the first dose of antibiotic reduces the risk of CDI by >50% in hospitalized adults. Future research should focus on optimal probiotic dose, species, and formulation. Systematic Review Registration: PROSPERO CRD42015016395.

Shi, Y., Zhai, Q., Li, D., Mao, B., Liu, X., Zhao, J., Zhang, H., and Chen, W. Restoration of cefixime-induced gut microbiota changes by Lactobacillus cocktails and fructooligosaccharides in a mouse model. Microbiol.Res. 2017; 200:14-24; PM: 28527760

ABSTRACT: Probiotics have been used to rebuild the antibiotic-induced dysfunction in gut microbiota, but whether the different strains of probiotics result in similar or reverse effects remains unclear. In this study, the different recovery effects of two cocktails (each contains four strains) of Lactobacillus and fructooligosaccharide against cefixime-induced change of gut microbiota were evaluated in C57BL/6J mice. The results show that the use of cefixime caused a reduction in the diversities of the microbial community and led to significantly decreasing to one preponderant Firmicutes phylum, which was difficult to restore naturally in the short term. The gut microbiota compositions of the groups treated with the probiotic cocktails were much more diverse than those of the natural recovery group. The effects of Lactobacillus cocktails against the cefixime-induced gut microbiota change may mainly be due to the beneficial SCFAs production in vivo and also be related to the good cell adhesion properties performed in vitro. Meanwhile, the restoration of the cefixime-induced gut microbiota was significantly different between two Lactobacillus groups since the Lactobacillus strains with high levels of fructooligosaccharide use and better cell adhesion properties performed considerably better than the Lactobacillus strains with high survival rates in the gastrointestinal tract. The contents of short-chain fatty acids in ceca were increased to 26.483+/-1.925 and 25.609+/-2.782mumol/g in the two probiotic cocktail groups respectively compared to 15.791+/-0.833mumol/g (P<0.05) in control group. Moreover, intestinal inflammation was alleviated by administration of the Lactobacillus cocktails. However, fructooligasaccharide administration showed certain effects on gut microbiota restoration (such as an increase of Akkermansia), although its effect on the entire microbiome structure is not so obvious.

Shida, K., Sato, T., Iizuka, R., Hoshi, R., Watanabe, O., Igarashi, T., Miyazaki, K., Nanno, M., and Ishikawa, F. Daily intake of fermented milk with Lactobacillus casei strain Shirota reduces the incidence and duration of upper respiratory tract infections in healthy middle-aged office workers. Eur.J.Nutr. 2017; 56(1):45-53; PM: 26419583

ABSTRACT: PURPOSE: Although several studies have demonstrated the efficacy of probiotics for preventing upper respiratory tract infections (URTIs) in at-risk populations, including children and the elderly, few studies have investigated the efficacy of probiotics in healthy adults living normal, everyday lives. Thus, we tried to evaluate the effects of Lactobacillus casei strain Shirota-fermented milk (LcS-FM) on the incidence of URTIs in healthy middle-aged office workers. *METHODS*: In a randomized controlled trial, 96 eligible male workers aged 30-49 years consumed LcS-FM containing 1.0 x 1011 viable LcS cells or control milk (CM) once daily for 12 weeks during the winter season. URTI episodes were evaluated by a physician via a questionnaire of URTI symptoms. *RESULTS*: The incidence of URTIs during the intervention period was significantly lower in the LcS-FM group than in the CM group (22.4 vs. 53.2 %, P = 0.002). The time-to-event analysis showed that the LcS-FM group had a significantly higher URTI-free rate than the CM group over the test period (log-rank test: chi 2 11.25, P = 0.0008). The cumulative number of URTI episodes and cumulative days with URTI symptoms per person was lower in the LcS-FM group, and the duration per episode was shorter. Inhibition of both reductions in NK cell activity in peripheral blood mononuclear cells and increases in salivary cortisol levels was observed in the LcS-FM group. *CONCLUSION*: The results suggest that the daily intake of fermented milk with LcS may reduce the risk of URTIs in healthy middle-aged office workers, probably through modulation of the immune system.

Shigemori, S. and Shimosato, T. Applications of Genetically Modified Immunobiotics with High Immunoregulatory Capacity for Treatment of Inflammatory Bowel Diseases. Front Immunol. 2017; 8:22; PM: 28179904

ABSTRACT: Inflammatory bowel diseases (IBDs), including ulcerative colitis and Crohn's disease, are chronic inflammatory diseases characterized by dysregulated immune responses of the gastrointestinal tract. In recent years, the incidence of IBDs has increased in developed nations, but their prophylaxis/treatment is not yet established. Site-directed delivery of molecules showing anti-inflammatory properties using genetically modified (gm)-probiotics shows promise as a new strategy for the prevention and treatment of IBD. Advantages of gm-probiotics include (1) the ability to use bacteria as a delivery vehicle, enabling safe and long-term use by humans, (2) decreased risks of side effects, and (3) reduced costs. The intestinal delivery of anti-inflammatory proteins such as cytokines and enzymes using Lactococcus lactis has been shown to regulate host intestinal homeostasis depending on the delivered protein-specific machinery. Additionally, clinical experience using interleukin 10-secreting Lc. lactis has been shown to be safe and to facilitate biological containment in IBD therapy. On the other hand, some preclinical studies have demonstrated that gm-strains of immunobiotics (probiotic strains able to beneficially regulate the mucosal immunity) provide beneficial effects on intestinal inflammation as a result of the synergy between the immunoregulatory effects of the bacterium itself and the anti-inflammatory effects of the delivered recombinant proteins. In this review, we discuss the rapid progression in the development of strategies for the prophylaxis and treatment of IBD using gm-probiotics that exhibit immune regulation effects (gm-immunobiotics). In particular, we discuss the type of strains used as delivery agents.

Shokri, D., Khorasgani, M. R., Mohkam, M., Fatemi, S. M., Ghasemi, Y., and Taheri-Kafrani, A. The Inhibition Effect of Lactobacilli Against Growth and Biofilm Formation of Pseudomonas aeruginosa. Probiotics.Antimicrob.Proteins. 3-14-2017; PM: 28293865

ABSTRACT: The emergence of antibiotic-resistant and food-spoilage microorganisms has renewed efforts to identify safe and natural alternative agents of antibiotics such as probiotics. The aim of this study was the isolation of lactobacilli as potential probiotics from local dairy products with broad antibacterial and anti-biofilm activities against antibiotic-resistant strains of Pseudomonas aeruginosa and determination of their inhibition mechanism. Antibiotic susceptibility and classification of acquired resistance profiles of 80 P. aeruginosa strains were determined based on Centers for Disease Control and Prevention (CDC) new definition as multidrug-resistant (MDR), extensively drug-resistant (XDR), and pan-drug-resistant (PDR) followed by antibacterial assessment of lactobacilli against them by different methods. Among the 80 P. aeruginosa strains, 1 (1.3%), 50 (62.5%), and 78 (97.5%) were PDR, XDR, and MDR, respectively, and effective antibiotics against them were fosfomycin and polymyxins. Among 57 isolated lactobacillus strains, two strains which were identified as Lactobacillus fermentum using biochemical and 16*S* rDNA methods showed broad inhibition/killing and anti-biofilm effects against all P. aeruginosa strains. They formed strong biofilms and had bile salts and low pH tolerance. Although investigation of inhibition mechanism of these strains showed no bacteriocin production, results obtained by high-performance liquid chromatography (HPLC) analysis indicated that their inhibitory effect was the result of production of three main organic acids including lactic acid, acetic acid, and formic acid. Considering the broad activity of these two L. fermentum strains, they can potentially be used in bio-control of drug-resistant strains of P. aeruginosa.

Shokryazdan, P., Faseleh, Jahromi M., Navidshad, B., and Liang, J. B. Effects of prebiotics on immune system and cytokine expression. Med.Microbiol.Immunol. 2017; 206(1):1-9; PM: 27704207

ABSTRACT: Nowadays, use of prebiotics as feed and food additives has received increasing interest because of the beneficial effects of prebiotics on the health of animals and humans. One of the beneficial effects of prebiotics is stimulation of immune system, which can be direct or indirect through increasing population of beneficial microbes or probiotics, especially lactic acid bacteria and bifidobacteria, in the gut. An important mechanism of action of probiotics and prebiotics, by which they can affect the immune system, is changing the expression of cytokines. The present review tried to summarize the findings of studies that investigated the effects of prebiotics on immune system with focusing on their effects on cytokine expression. Generally, most of reviewed studies indicated beneficial effects for prebiotics in terms of improving immune system, by increasing the expression of anti-inflammatory cytokines, while reducing the expressions of proinflammatory cytokines. However, most of studies mainly considered the indirect effects of prebiotics on the immune system (through changing the composition and population of gut microbiota), and their direct effects still need to be further studied using prebiotics with different degree of polymerization in different hosts.

Shokryazdan, P., Faseleh, Jahromi M., Liang, J. B., Ramasamy, K., Sieo, C. C., and Ho, Y. W. Effects of a Lactobacillus salivarius mixture on performance, intestinal health and serum lipids of broiler chickens. PLoS.One. 2017; 12(5):e0175959; PM: 28459856

ABSTRACT: The ban or severe restriction on the use of antibiotics in poultry feeds to promote growth has led to considerable interest to find alternative approaches. Probiotics have been considered as such alternatives. In the present study, the effects of a Lactobacillus mixture composed from three previously isolated Lactobacillus salivarius strains (CI1, CI2 and CI3) from chicken intestines on performance, intestinal health status and serum lipids of broiler chickens has been evaluated. Supplementation of the mixture at a concentration of 0.5 or 1 g kg-1 of diet to broilers for 42 days improved body weight, body weight gain and FCR, reduced total cholesterol, LDL-cholesterol and triglycerides, increased populations of beneficial bacteria such as lactobacilli and bifidobacteria, decreased harmful bacteria such as E. coli and total aerobes, reduced harmful cecal bacterial enzymes such as beta-glucosidase and beta-glucuronidase, and improved intestinal histomorphology of broilers. Because of its remarkable efficacy on broiler chickens, the L. salivarius mixture could be considered as a good potential probiotic for chickens, and its benefits should be further evaluated on a commercial scale.

Sidhu, M. and van der, Poorten D. The gut microbiome. Aust.Fam.Physician. 2017; 46(4):206-211; PM: 28376573

ABSTRACT: *BACKGROUND*: More than a trillion, mostly good, microbes live within our gastrointestinal tract and are responsible for vital metabolic, immune and nutritional functions. Dysbiosis, meaning a maladaptive imbalance of the microbiome, is associated with many common diseases and is a target for therapy. *OBJECTIVE*: This article provides an overview of the gut microbiome in health and disease, highlighting conditions such as Clostridium difficile infection, inflammatory bowel disease, irritable bowel syndrome, obesity and non-alcoholic fatty liver disease, with which dysbiosis is associated.

Information about treatments that affect the gut microbiome, including probiotics and faecal microbiota transplant, are discussed. *DISCUSSION*: As our knowledge of the microbiome increases, we are likely to better understand the complex interactions that cause disease, and develop new and more effective treatments for many common conditions.

Silva, B. C., Sandes, S. H., Alvim, L. B., Bomfim, M. R., Nicoli, J. R., Neumann, E., and Nunes, A. C. Selection of a candidate probiotic strain of Pediococcus pentosaceus from the faecal microbiota of horses by in vitro testing and health claims in a mouse model of Salmonella infection. J.Appl.Microbiol. 2017; 122(1):225-238; PM: 27813217

ABSTRACT: *AIMS*: The aim of this study was to verify the suitable use of candidate 'probiotics' selected by in vitro tests and the importance of in vivo assays to nominate micro-organisms as probiotics and alternative prophylactic treatments for Salmonella Typhimurium infection. *METHODS AND RESULTS*: Thirty-three lactic acid bacteria (LAB) isolated from foal's faeces were assessed based on the main desirable functional in vitro criteria. Based on these results, Pediococcus pentosaceus strain 40 was chosen to evaluate its putative probiotic features in a mouse model of Salmonella infection. Daily intragastric doses of Ped. pentosaceus 40 for 10 days before and 10 days after Salmonella challenge (106 CFU of Salm. Typhimurium per mouse) led to a significant aggravation in mouse health by increasing weight loss, worsening clinical symptoms and anticipating the time and the number of deaths by Salmonella. Pediococcus pentosaceus modulated cell-mediated immune responses by up-regulation of the gene expression of the proinflammatory cytokines IFN-gamma and TNF-alpha in the small intestine. *CONCLUSION*: The usual criteria were used for in vitro screening of a large number of LAB for desirable probiotic functional properties. However, the best candidate probiotic strain identified, Ped. pentosaceus #40, aggravated the experimental disease in mice. *SIGNIFICANCE AND IMPACT OF THE STUDY*: These findings emphasize the need for prophylactic or therapeutic effectiveness to be demonstrated in in vivo models to make precise health claims.

Silverman, M. A., Konnikova, L., and Gerber, J. S. Impact of Antibiotics on Necrotizing Enterocolitis and Antibiotic-Associated Diarrhea. Gastroenterol.Clin.North Am. 2017; 46(1):61-76; PM: 28164853

ABSTRACT: Antibiotic treatment alters the composition and metabolic function of the intestinal microbiota. These alterations may contribute to the pathogenesis of necrotizing enterocolitis (NEC) and antibiotic-associated diarrhea (AAD). Recent studies are beginning to unravel the contribution of specific groups of microbes and their metabolic pathways to these diseases. Probiotics or other microbiota-targeted therapies may provide effect strategies to prevent and treat NEC and AAD.

Singh, B., Singh, J. P., Shevkani, K., Singh, N., and Kaur, A. Bioactive constituents in pulses and their health benefits. J.Food Sci.Technol. 2017; 54(4):858-870; PM: 28303037

ABSTRACT: Pulses are good sources of bioactive compounds such as polyphenols, phytosterols and non-digestible carbohydrates that play important physiological as well as metabolic roles. These compounds vary in concentration amongst different pulse species and varieties. Pulse seed coats are rich in water-insoluble fibres and polyphenols

(having high antioxidant activities), while cotyledons contain higher soluble fibres, oligosaccharides, slowly digestible and resistant starch content. Ferulic acid is the most abundant phenolic acid present in pulses, while flavonol glycosides, anthocyanins and tannins are responsible for the seed coat colour. Sitosterol (most abundant), stigmasterol, and campesterol are the major phytosterols present in pulses. Pulse fibres, resistant starch and oligosaccharides function as probiotics and possess several other health benefits such as anti-inflammatory, anti-tumour, and reduce glucose as well as lipid levels. Beans and peas contain higher amounts of oligosaccharides than other pulses. Processing methods affect resistant starch, polyphenol composition and generally increase antioxidant activities of different pulses. In this review, the current information on pulse polyphenols, phytosterols, resistant starch, dietary fibre, oligosaccharides, antioxidant and associated health benefits are discussed.

Singh, B., Mal, G., and Marotta, F. Designer Probiotics: Paving the Way to Living Therapeutics. Trends Biotechnol. 5-5-2017; PM: 28483159

ABSTRACT: Enhancing the functional repertoire of probiotics is a promising approach to cope with the inexorable rise of antibiotic-resistant pathogens and the rather slow development of new antibiotics. Probiotics that deliver novel therapeutics efficiently and with site specificity are emerging living therapeutics that may transform existing paradigms of disease diagnosis and prevention.

Singh, S., Sharma, R. K., Malhotra, S., Pothuraju, R., and Shandilya, U. K. Lactobacillus rhamnosus NCDC17 ameliorates type-2 diabetes by improving gut function, oxidative stress and inflammation in high-fat-diet fed and streptozotocintreated rats. Benef.Microbes. 4-26-2017; 8(2):243-255; PM: 28008783

ABSTRACT: Restoration of dysbiosed gut microbiota through probiotic may have profound effect on type 2 diabetes. In the present study, rats were fed high fat diet (HFD) for 3 weeks and injected with low dose streptozotocin to induce type 2 diabetes. Diabetic rats were then fed Lactobacillus rhamnosus NCDC 17 and L. rhamnosus GG with HFD for six weeks. L. rhamnosus NCDC 17 improved oral glucose tolerance test, biochemical parameters (fasting blood glucose, plasma insulin, glycosylated haemoglobin, free fatty acids, triglycerides, total cholesterol, low-density lipoprotein cholesterol and high-density lipoprotein cholesterol), oxidative stress (thiobarbituric acid reactive substance and activities of catalase, superoxide dismutase and glutathione peroxidase in blood and liver), bifidobacteria and lactobacilli in cecum, expression of glucagon like peptide-1 producing genes in cecum, and adiponection in epididymal fat, while decreased propionate proportions (%) in caecum, and expression of tumour necrosis factor-alpha and interlukin-6 in epididymal fat of diabetic rats as compared to diabetes control group. These findings offered a base for the use of L. rhamnosus NCDC 17 for the improvement and early treatment of type 2 diabetes.

Singh, T. P., Kaur, G., Kapila, S., and Malik, R. K. Antagonistic Activity of Lactobacillus reuteri Strains on the Adhesion Characteristics of Selected Pathogens. Front Microbiol. 2017; 8:486; PM: 28377765

ABSTRACT: Adhesion ability of probiotics is the key factor that decides their colonization in the gastrointestinal tract and potential to inhibit pathogens. Therefore, adhesion ability

can be considered as a key determinant for probiotic efficacy. Presents study documents the antagonistic activity of viable/untreated, Lithium chloride (LiCl) treated or heat-killed forms of eight probiotic Lactobacillus reuteri strains on the adhesion characteristics of selected pathogens. All strains investigated were able to adhere to Caco-2 cells. L. reuteri strains tested were able to inhibit and displace ($P < 0.05$) the adhesion of Escherichia coli ATCC25922, Salmonella typhi NCDC113, Listeria monocytogenes ATCC53135, and Enterococcus faecalis NCDC115. The probiotic strain L. reuteri LR6 showed the strongest adhesion and pathogen inhibition ability among the eight L. reuteri strains tested. In addition, the abilities to inhibit and to displace adhered pathogens depended on both the probiotic and the pathogen strains tested suggesting the involvement of various mechanisms. The adhesion and antagonistic potential of the probiotic strains were significantly decreased upon exposure to 5 M LiCl, showing that surface molecules, proteinaceous in nature, are involved. The heat-killed forms of the probiotic L. reuteri strains also inhibited the attachment of selected pathogens to Caco-2 cells. In conclusion, in vitro assays showed that L. reuteri strains, as viable or heat-killed forms, are adherent to Caco-2 cells and are highly antagonistic to pathogens tested in which surface associated proteins play an important role.

Sirichokchatchawan, W., Temeeyasen, G., Nilubol, D., and Prapasarakul, N. Protective Effects of Cell-Free Supernatant and Live Lactic Acid Bacteria Isolated from Thai Pigs Against a Pandemic Strain of Porcine Epidemic Diarrhea Virus. Probiotics.Antimicrob.Proteins. 4-22-2017; PM: 28434154

ABSTRACT: Porcine epidemic diarrhea virus (PEDV) is a coronavirus which causes severe diarrhea and fatal dehydration in piglets. In general, probiotic supplements could enhance recovery and protect piglets against enteric pathogens. Seven local lactic acid bacteria (LAB), (Ent. faecium 79N and 40N, Lact. plantarum 22F, 25F and 31F, Ped. acidilactici 72N and Ped. pentosaceus 77F) from pig feces were well-characterized as high potential probiotics. Cell-free supernatants (CFS) and live LAB were evaluated for antiviral activities by co-incubation on Vero cells and challenged with a pandemic strain of PEDV isolated from pigs in Thailand. Cell survival and viral inhibition were determined by cytopathic effect (CPE) reduction assay and confirmed by immunofluorescence. At 1:16, CFS dilution (pH 6.3-6.8) showed no cytotoxicity in Vero cells and was therefore used as the dilution for antiviral assays. The diluted CFS of all Lact. plantarum showed the antiviral effect against PEDV; however, the same antiviral effect could not be observed in Ent. faecium and Pediococcus strains. In competitive experiment, only live Lact. plantarum 25F and Ped. pentosaceus 77F showed CPE reduction in the viral infected cells to <50% observed field area. This study concluded that the CFS of all tested lactobacilli, and live Lact. plantarum (22F and 25F) and Pediococcus strains 72N and 77F could reduce infectivity of the pandemic strain of PEDV from pigs in Thailand on the target Vero cells.

Sisa, C., Turroni, S., Amici, R., Brigidi, P., Candela, M., and Cerri, M. Potential role of the gut microbiota in synthetic torpor and therapeutic hypothermia. World J.Gastroenterol. 1-21-2017; 23(3):406-413; PM: 28210076

ABSTRACT: Therapeutic hypothermia is today used in several clinical settings, among them the gut related diseases that are influenced by ischemia/reperfusion injury. This perspective paved the way to the study of hibernation physiology, in natural hibernators, highlighting an unexpected importance of the gut microbial ecosystem in hibernation

and torpor. In natural hibernators, intestinal microbes adaptively reorganize their structural configuration during torpor, and maintain a mutualistic configuration regardless of long periods of fasting and cold temperatures. This allows the gut microbiome to provide the host with metabolites, which are essential to keep the host immunological and metabolic homeostasis during hibernation. The emerging role of the gut microbiota in the hibernation process suggests the importance of maintaining a mutualistic gut microbiota configuration in the application of therapeutic hypothermia as well as in the development of new strategy such as the use of synthetic torpor in humans. The possible utilization of tailored probiotics to mold the gut ecosystem during therapeutic hypothermia can also be taken into consideration as new therapeutic strategy.

Slomka, V., Hernandez-Sanabria, E., Herrero, E. R., Zaidel, L., Bernaerts, K., Boon, N., Quirynen, M., and Teughels, W. Nutritional stimulation of commensal oral bacteria suppresses pathogens: the prebiotic concept. J.Clin.Periodontol. 2017; 44(4):344-352; PM: 28128467

ABSTRACT: AIM: To identify potential oral prebiotics that selectively stimulate commensal, albeit beneficial bacteria of the resident oral microbial community while suppressing the growth of pathogenic bacteria. *MATERIAL AND METHODS*: Using Phenotype MicroArrays as a high-throughput method, the change in respiratory activity of 16 oral bacteria in response to 742 nutritional compounds was screened. Most promising prebiotic compounds were selected and applied in single species growth and biofilm formation assays, as well as dual species (beneficial-pathogen) competition assays. *RESULTS*: Increased respiratory activity could not always be related to an increase in growth or biofilm formation. Six compounds were used in dual species competition assays to directly monitor if selective nutritional stimulation of the beneficial bacterium results in the suppression of the pathogenic bacterium. Two compounds, beta-methyl-d-galactoside and N-acetyl-d-mannosamine, could be identified as potential oral prebiotic compounds, triggering selectively beneficial oral bacteria throughout the experiments and shifting dual species biofilm communities towards a beneficial dominating composition at in vitro level. *CONCLUSION*: Our observations support the hypothesis that nutritional stimulation of beneficial bacteria by prebiotics could be used to restore the microbial balance in the oral cavity and by this promote oral health.

So, S. S., Wan, M. L., and El-Nezami, H. Probiotics-mediated suppression of cancer. Curr.Opin.Oncol. 2017; 29(1):62-72; PM: 27792053

ABSTRACT: PURPOSE OF REVIEW: Probiotics can be used as an adjuvant for cancer prevention or/and treatment through their abilities to modulate intestinal microbiota and host immune response. Although most of the recent reviews have focused on the potential role of probiotics against colon cancer, only few of them include the probiotic effect on extraintestinal cancers. The present review covers the most important findings from the literature published during the past 20 months (from January 2015 to August 2016) regarding the probiotics-mediated suppression of both gastrointestinal and extraintestinal cancers and the underlying mechanisms. *RECENT FINDINGS*: A comprehensive literature search in Pubmed, Science direct and Google scholar databases was conducted to locate all relevant articles that investigated the effect of probiotics on prevention/treatment of both gastrointestinal and extraintestinal cancers. Different mechanisms for the beneficial effects of probiotics against cancer were also discussed, mainly via modulation of gut microbiota which thereby influences host metabolism and immunity. *SUMMARY*: Despite laboratory-based studies having

demonstrated encouraging outcomes that probiotics possess antitumor effects, the benefits should not be exaggerated before we get more results from human clinical trials. These are very important before the medical community can accept the use of probiotics as an alternative therapy for cancer control.

Sola-Oladokun, B., Culligan, E. P., and Sleator, R. D. Engineered Probiotics: Applications and Biological Containment. Annu.Rev.Food Sci.Technol. 2-28-2017; 8:353-370; PM: 28125354

ABSTRACT: Bioengineered probiotics represent the next generation of whole cell-mediated biotherapeutics. Advances in synthetic biology, genome engineering, and DNA sequencing and synthesis have enabled scientists to design and develop probiotics with increased stress tolerance and the ability to target specific pathogens and their associated toxins, as well as to mediate targeted delivery of vaccines, drugs, and immunomodulators directly to host cells. Herein, we review the most significant advances in the development of this field. We discuss the critical issue of biological containment and consider the role of synthetic biology in the design and construction of the probiotics of the future.

Soleimani, A., Zarrati, Mojarrad M., Bahmani, F., Taghizadeh, M., Ramezani, M., Tajabadi-Ebrahimi, M., Jafari, P., Esmaillzadeh, A., and Asemi, Z. Probiotic supplementation in diabetic hemodialysis patients has beneficial metabolic effects. Kidney Int. 2017; 91(2):435-442; PM: 27927601

ABSTRACT: This study determined the effects of probiotic supplementation on glycemic control, lipid concentrations, biomarkers of inflammation and oxidative stress in 60 diabetic patients on hemodialysis in a parallel randomized double-blind placebo-controlled clinical trial. Participants were initially matched based on sex, duration of dialysis and diabetes, body mass index and age. Subsequently, they were randomly divided into two groups to take either a capsule containing the probiotics Lactobacillus acidophilus, Lactobacillus casei and Bifidobacterium bifidum or placebo for 12 weeks. Based on three-day dietary records throughout the trial, there was no significant change in dietary macro- and micro-nutrients or total dietary fiber to confound results. After the 12 weeks, analysis of patients who received probiotic supplements compared with the placebo showed they had significantly decreased fasting plasma glucose (-22.0 vs. +6.6 mg/dl), serum insulin (-6.4 vs. +2.3 mulU/ml), homeostasis model of assessment-estimated insulin resistance (-2.9 vs. +2.5), homeostasis model of assessment-estimated beta-cell function (-14.1 vs. +6.1) and HbA1c (-0.4 vs. -0.1%,), and improved quantitative insulin sensitivity check index (+0.03 vs. -0.02). Additionally, compared with the placebo, probiotic supplementation resulted in significant reductions in serum high-sensitivity C-reactive protein (-1933 vs. +252 ng/ml), plasma malondialdehyde (-0.3 vs. +1.0 mumol/l), subjective global assessment scores (-0.7 vs. +0.7) and total iron binding capacity (-230 vs. +33 mug/dl), and a significant increase in plasma total antioxidant capacity (+15 vs. -88 mmol/l). Thus, probiotic supplementation for 12 weeks among diabetic hemodialysis patients had beneficial effects on parameters of glucose homeostasis, and some biomarkers of inflammation and oxidative stress.

Soltan Dallal, M. M., Davoodabadi, A., Abdi, M., Hajiabdolbaghi, M., Sharifi Yazdi, M. K., Douraghi, M., and Tabatabaei Bafghi, S. M. Inhibitory effect of Lactobacillus plantarum

and Lb. fermentum isolated from the faeces of healthy infants against nonfermentative bacteria causing nosocomial infections. New Microbes.New Infect. 2017; 15:9-13; PM: 27830081

ABSTRACT: Nosocomial infection constitutes a major public health problem worldwide. Increasing antibiotic resistance of pathogens associated with nosocomial infections has also become a major therapeutic challenge for physicians. Thus, development of alternative treatment protocols, such as the use of probiotics, matters. The aim of this research was to determine the antagonistic properties of Lactobacillus plantarum and Lb. fermentum isolated from the faeces of healthy infants against nonfermentative bacteria causing nosocomial infections. One hundred five samples of nosocomial infections were collected and processed for bacterial isolation and antimicrobial susceptibility testing following standard bacteriologic techniques. The antibiotic susceptibility test was performed by the disk diffusion method, and antagonistic effect of Lactobacillus strains was investigated by well diffusion method. Of 105 samples, a total of 29 bacterial strains were identified as nonfermentative bacteria, including 17 Acinetobacter baumannii and 12 Pseudomonas aeruginosa. A. baumannii showed high resistance to tested antibiotics except ampicillin/sulbactam, and P. aeruginosa showed resistance to ampicillin/sulbactam and gentamicin and sensitive to amikacin and meropenem. Lb. plantarum had antagonistic properties against both A. baumannii and P. aeruginosa strains. Lb. plantarum had considerable effects on preventing the growth of A. baumannii and P. aeruginosa strains. However, further research is needed to better understanding of these effects on P. aeruginosa.

Song, Y. G. and Lee, S. H. Inhibitory effects of Lactobacillus rhamnosus and Lactobacillus casei on Candida biofilm of denture surface. Arch.Oral Biol. 2017; 76:1-6 PM: 28063305

ABSTRACT: OBJECTIVE: Candida albicans biofilm is associated with denture-related stomatitis and oral candidiasis of elderly. Probiotics are beneficial bacteria and have antibacterial activity against pathogenic bacteria. The purpose of this study was to investigate the antifungal activity of various probiotics against C. albicans and the inhibitory effects of probiotics on Candida biofilm on the denture surface. *DESIGN*: The spent culture media of various probiotics were investigated the antifungal efficacy against C. albicans. Candida biofilm was formed on a denture base resin and was then treated with Lactobacillus rhamnosus and Lactobacillus casei. Also, the biofilms of L. rhamnosus and L. casei were formed and were sequentially treated with C. albicans. Colony-forming units of C. albicans on the denture surface were counted after spreading on agar plate. The denture base resin was treated with the spent culture media for 30days, after which the denture surface roughness was analyzed with an atomic force microscope. *RESULTS*: L. rhamnosus and L. casei exhibited stronger antifungal activity than other probiotics. The spent culture medium of L. rhamnosus and L. casei exhibited the antifungal activity against blastoconidia and biofilm of C. albicans. L. rhamnosus and L. casei showed the antifungal activity against Candida biofilm, and the biofilm of L. rhamnosus and L. casei inhibited formation of Candida biofilm on denture surface. Neither of the probiotics affected the surface roughness of the denture base resin. *CONCLUSIONS*: L. rhamnosus and L. casei may be the ideal probiotics for the prevention and treatment of denture-related stomatitis.

Souza, R. F., Jardin, J., Cauty, C., Rault, L., Bouchard, D. S., Bermudez-Humaran, L. G., Langella, P., Monedero, V., Seyffert, N., Azevedo, V., Le, Loir Y., and Even, S. Contribution of sortase

SrtA2 to Lactobacillus casei BL23 inhibition of Staphylococcus aureus internalization into bovine mammary epithelial cells. PLoS.One. 2017; 12(3):e0174060; PM: 28323870

ABSTRACT: Probiotics have been considered as a promising strategy to prevent various diseases in both humans and animals. This approach has gained interest in recent years as a potential means to control bovine mastitis. In a previous study, we found that several L. casei strains, including BL23, were able to inhibit the internalization of S. aureus, a major etiologic agent of mastitis, into bovine mammary epithelial cells (bMEC). This antagonism required a direct contact between L. casei and bMEC or S. aureus, suggesting the inhibition relied on interactions between L. casei cell surface components and bMEC. In this study, we have investigated the impact of some candidates which likely influence bacteria host cell interactions. We have shown that L. casei BL23 fbpA retained its inhibitory potential, indicating that L. casei BL23 antagonism did not rely (solely) on competition between S. aureus and L. casei fibronectin-binding proteins for adhesion to bMEC. We have then investigated the impact of four sortase mutants, srtA1, srtA2, srtC1 and srtC2, and a double mutant (srtA1-srtA2) on L. casei BL23 inhibitory potential. Sortases are responsible for the anchoring on the bacterial cell wall of LPXTG-proteins, which reportedly play an important role in bacteria-host cell interaction. All the srt mutants tested presented a reduced inhibition capacity, the most pronounced effect being observed with the srtA2 mutant. A lower internalization capacity of L. casei srtA2 into bMEC was also observed. This was associated with several changes at the surface of L. casei BL23 srtA2 compared to the wild type (wt) strain, including altered abundance of some L.

Speranza, B., Petruzzi, L., Bevilacqua, A., Gallo, M., Campaniello, D., Sinigaglia, M., and Corbo, M. R. Encapsulation of Active Compounds in Fruit and Vegetable Juice Processing: Current State and Perspectives. J.Food Sci. 5-9-2017; PM: 28485539

ABSTRACT: The production of value-added and/or functional juices has increased significantly in recent years, following an increased consumer demand to promote health and/or prevent disease through diet and nutrition. Micro and nano-encapsulation are promising technologies to protect and deliver sensitive compounds, allowing a controlled release in the target sites. This paper offers an overview of current applications, limits and challenges of encapsulation technologies in the production of fruit and vegetable juices, with a particular emphasis on products derived from different botanical sources.

Sprenger, N., Odenwald, H., Kukkonen, A. K., Kuitunen, M., Savilahti, E., and Kunz, C. FUT2-dependent breast milk oligosaccharides and allergy at 2 and 5 years of age in infants with high hereditary allergy risk. Eur.J.Nutr. 2017; 56(3):1293-1301; PM: 26907090

ABSTRACT: PURPOSE: Manifestation of allergic disease depends on genetic predisposition, diet and commensal microbiota. Genetic polymorphism of mothers determines their breast milk glycan composition. One major determinant is the fucosyltransferase 2 (FUT2, secretor gene) that was shown to be linked to commensal microbiota establishment. We studied whether FUT2-dependent breast milk oligosaccharides are associated with allergic disease in breast-fed infants later in life. *METHODS*: We analyzed FUT2-dependent oligosaccharides in breast milk samples of mothers (n = 266) from the placebo group of a randomized placebo-controlled trial of prebiotics and probiotics as preventive against allergic disease in infants with high allergy

risk (trial registry number: NCT00298337). Using logistic regression models, we studied associations between FUT2-dependent breast milk oligosaccharides and incidence of allergic disease at 2 and 5 years of age. *RESULTS*: At 2 years, but not at 5 years of age, we observed a presumed lower incidence ($p < 0.1$) for IgE-associated eczema manifestation in C-section-born infants who were fed breast milk containing FUT2-dependent oligosaccharides. By logistic regression, we observed a similar relation ($p < 0.1$) between presence of FUT2-dependent breast milk oligosaccharides and IgE-associated disease and IgE-associated eczema in C-section-born infants only. When testing with the levels of breast milk oligosaccharide 2'-fucosyllactose as proxy for FUT2 activity, we observed significant ($p < 0.05$) associations in the C-section-born infants with 'any allergic disease,' IgE-associated disease, eczema and IgE-associated eczema. *CONCLUSION*: The data indicate that infants born by C-section and having a high hereditary risk for allergies might have a lower risk to manifest IgE-associated eczema at 2 years, but not 5 years of age, when fed breast milk with FUT2-dependent milk oligosaccharides. Further studies with larger cohorts and especially randomized controlled intervention trials are required to build on these preliminary observations.

Srinivas, B., Rani, G. S., Kumar, B. K., Chandrasekhar, B., Krishna, K. V., Devi, T. A., and Bhima, B. Evaluating the probiotic and therapeutic potentials of Saccharomyces cerevisiae strain (OBS2) isolated from fermented nectar of toddy palm. AMB.Express. 2017; 7(1):2; PM: 28050843

ABSTRACT: The purpose of this study is to evaluate the probiotic characteristics of 15 yeast strains isolated from nectar of toddy palm. Initially, the collected samples were inoculated on yeast extract peptone dextrose agar plates and the colonies so obtained were culturally and morphologically characterized. Commercial probiotic yeast, Saccharomyces boulardii served as the control in these experiments. Of the 15 yeast strains, the isolates that were resistant to antibiotics and worked synergistically with other cultures were considered for further evaluation. Selected isolates were evaluated in vitro for tolerance to simulated gastrointestinal conditions such as temperature, pH, bile and gastric juice. Further the yeast isolates were evaluated for their pathogenicity and adherence to intestinal epithelial cells. The 2 yeast isolates with efficient probiotic properties were finally characterized by sequencing their 5.8 S rRNA and partial sequences of internal transcribed spacer 1 and 2. The sequences were BLAST searched in the National Center for Biotechnology Information, nucleic acid database for sequence similarity of organisms and phylogenetic evolutionary analysis was carried out. Based on maximum similarity of basic local alignment search tool results, organisms were characterized as Pichia kudriavzevii OBS1 (100%) and Saccharomyces cerevisiae OBS2 (96%) and sequences were finally deposited in the GenBank data library. Among these two isolates, S. cerevisiae OBS2 displayed slight/moderate antioxidant and anticancer property. Hence, strain OBS2 can be utilized and explored as a potential probiotic for therapeutic applications.

Stadermann, K. B., Blom, J., Borgmeier, C., Sciberras, N., Herbold, S., Kipker, M., Meurer, G., Molck, S., Petri, D., Pelzer, S., and Schneider, J. First complete genome sequence of Bacillus glycinifermentans B-27. J.Biotechnol. 4-21-2017; PM: 28438580

ABSTRACT: The first complete genome sequence of Bacillus glycinifermentans B-27 was determined by SMRT sequencing generating a genome sequence with a total length of 4,607,442 bases. Based on this sequence 4738 protein-coding sequences were predicted and used to identify gene clusters that are related to the production of secondary

metabolites such as Lichenysin, Bacillibactin and Bacitracin. This genomic potential combined with the ability of B. glycinifermentans B-27 to grown in bile containing media might contribute to a future application of this strain as probiotic in productive livestock potentially inhibiting competing and pathogenic organisms.

Stange, E. F. Improvement of a 'Leaky' Intestinal Barrier. Dig.Dis. 2017; 35(1-2):21-24; PM: 28147355

ABSTRACT: In Crohn's disease, the mucus layer appears to be defective in terms of low defensin levels and lack of antibacterial activity. These deficiencies actually explain the Montreal phenotypes and the stable localization of disease in the terminal ileum with low alpha-defensins from Paneth cells and/or low beta-defensins in colonic disease, respectively. Conversely, in ulcerative colitis (UC) the defensin production is normal or even induced, but the mucus layer is thinner and patchy, more in the liquid form and also chemically altered so that antibacterial peptides are not retained and lost into the luminal bacterial bulk. Therefore, both barrier problems allow slow bacterial attachment and invasion, ultimately triggering the massive response of adaptive immunity and tissue destruction. Therefore, leakiness should refer to the antibacterial barrier and not to the general barrier against small molecules, such as mannitol or lactulose, which are not antigenic. The most promising approach in UC seems to be the use of probiotics or the natural compound lecithin as a stabilizer of mucus structure to enhance the barrier. While a phase II study has yielded positive results, the results of the ongoing phase III study are eagerly awaited. It is quite possible that the protective effect of smoking in UC is related to mucus production in the colon also, but this is not an option. Another alternative would be to shift cell differentiation in the colon towards goblet cell; the relevant differentiation factors are known. In Crohn's disease, the direct oral application of defensins might be effective if release and binding to the mucus are achieved. In the experimental colitis model, this works quite well. In conclusion, in a situation where enthusiasm about so-called biologics is declining due to loss of response over time, searching for the primary defects in inflammatory bowel disease and treating them may well be worthwhile, although it is unlikely to provide rapid relief.

Stavrou, G. and Kotzampassi, K. Gut microbiome, surgical complications and probiotics. Ann.Gastroenterol. 2017; 30(1):45-53; PM: 28042237

ABSTRACT: The trigger for infectious complications in patients following major abdominal operations is classically attributed to endogenous enteral bacterial translocation, due to the critical condition of the gut. Today, extensive gut microbiome analysis has enabled us to understand that almost all "evidence-based" surgical or medical intervention (antibiotics, bowel preparation, opioids, deprivation of nutrition), in addition to stress-released hormones, could affect the relative abundance and diversity of the enteral microbiome, allowing harmful bacteria to proliferate in the place of depressed beneficial species. Furthermore, these bacteria, after tight sensing of host stress and its consequent humoral alterations, can and do switch their virulence accordingly, towards invasion of the host. Probiotics are the exogenously given, beneficial clusters of live bacteria that, upon digestion, seem to succeed in partially restoring the distorted microbial diversity, thus reducing the infectious complications occurring in surgical and critically ill patients. This review presents the latest data on the interrelationship between the gut microbiome and the occurrence of complications after colon surgery, and the efficacy of probiotics as therapeutic instruments for changing the bacterial imbalance.

Stout, E., Klaenhammer, T., and Barrangou, R. CRISPR-Cas Technologies and Applications in Food Bacteria. Annu.Rev.Food Sci.Technol. 2-28-2017; 8:413-437; PM: 28245154

ABSTRACT: Clustered regularly interspaced short palindromic repeats (CRISPRs) and CRISPR-associated (Cas) proteins form adaptive immune systems that occur in many bacteria and most archaea. In addition to protecting bacteria from phages and other invasive mobile genetic elements, CRISPR-Cas molecular machines can be repurposed as tool kits for applications relevant to the food industry. A primary concern of the food industry has long been the proper management of food-related bacteria, with a focus on both enhancing the outcomes of beneficial microorganisms such as starter cultures and probiotics and limiting the presence of detrimental organisms such as pathogens and spoilage microorganisms. This review introduces CRISPR-Cas as a novel set of technologies to manage food bacteria and offers insights into CRISPR-Cas biology. It primarily focuses on the applications of CRISPR-Cas systems and tools in starter cultures and probiotics, encompassing strain-typing, phage resistance, plasmid vaccination, genome editing, and antimicrobial activity.

Strunk, T., Hibbert, J., Doherty, D., Granland, C., Trend, S., Simmer, K., Burgner, D., Patole, S., and Currie, A. Probiotics and antimicrobial protein and peptide levels in preterm infants. Acta Paediatr. 3-12-2017; PM: 28294428

ABSTRACT: *AIM*: To characterise the secreted and inducible antimicrobial protein and peptide (APP) levels in a prospective cohort of preterm infants (<30 weeks gestational age) with or without Bifidobacterium breve M16V supplementation during the first month of life. *METHODS*: We analysed serial biosamples of infants who did (n = 13) or did not receive (n = 62) B. breve (3 x 109 cfu/day). Peripheral blood was obtained on days 1, 14 and 28, and infant stool prior to commencement of probiotic supplementation and on day 21. Levels of APP (bactericidal/permeability inducing protein (BPI), beta defensins 1 and 2, lactoferrin, human cathelicidin, secretory phospholipase A2) in plasma and stool were determined. Further, we characterised induced APP levels in whole blood cultured with live S. epidermidis or with agonists of Toll-like receptors 2/6 and 4. *RESULTS*: Stool, plasma and stimulated blood APP levels changed significantly during the first month of life. Supplementation with B. breve did not affect basal or stimulated APP levels except for a transient increase in inducible BPI. *CONCLUSION*: Supplementation with B. breve does not appear to act via modulation of systemic or enteric APP expression in preterm infants although small effects cannot be excluded. Further work with other probiotic preparations is warranted.

Sugahara, H., Yao, R., Odamaki, T., and Xiao, J. Z. Differences between live and heat-killed bifidobacteria in the regulation of immune function and the intestinal environment. Benef.Microbes. 4-26-2017; 1-10; PM: 28441886

ABSTRACT: Probiotics are live microorganisms that confer a health benefit on the host, such as improvement of the intestinal environment, modulation of immune function and energy metabolism. Heat-killed probiotic strains have also been known to exhibit some physiological functions; however, the differences between live and heat-killed probiotics have not been well elucidated. In this study, we investigated the differences between live and heat-killed Bifidobacterium breve M-16V, a probiotic strain, in the regulation of immune function, intestinal metabolism and intestinal gene expression of the host using

gnotobiotic mouse model and omics approaches. Both live and heat-killed cells of B. breve M-16V showed immune-modulating effects that suppressed pro-inflammatory cytokine production in spleen cells and affected intestinal metabolism; however, live cells exhibited a more remarkable effect in the regulation of intestinal metabolism and intestinal gene expression involved in nutrient metabolism. Our findings are valuable for considering the health benefits of live and heat-killed bacteria and the usefulness of different forms of probiotics.

Sugiharto, S., Yudiarti, T., Isroli, I., Widiastuti, E., and Putra, F. D. Intestinal microbial ecology and hematological parameters of broiler fed cassava waste pulp fermented with Acremonium charticola. Vet.World. 2017; 10(3):324-330; PM: 28435195

ABSTRACT: AIM: The aim of this study was to evaluate the effect of feeding Acremonium charticola-fermented cassava pulp (AC-FCP) on the intestinal microbial ecology and hematological indices of broiler chickens. *MATERIALS AND METHODS*: A total of 240 male Lohman day-old-chicks were randomly allotted to one of the four experimental diets including control diet, control diet + antimicrobials (neomycin; 300 mg/kg diet), diet containing AC-FCP (16 g/100 g diet) or diet containing AC-FCP + antimicrobials. At day 28, the birds from each pen were blood sampled, sacrificed and immediately the internal organs were removed and weighed. Digesta were obtained from the ileum and cecum. *RESULTS*: Birds fed AC-FCP had lower ($p<0.05$) coliform bacteria count in the ileal digesta than birds fed control diet or control diet + antimicrobials. Butiric acid was higher ($p<0.05$) in the cecal content of birds fed AC-FCP than in other birds. Propionic acid was also higher in AC-FCP fed birds than in other birds although statistically not significant. The percentages of lymphocytes and heterophils were higher ($p<0.05$) and tended ($p=0.07$) to be lower, respectively, in broilers fed control diet than in other birds. The birds provided control diet had lower ($p<0.05$) heterophils to lymphocytes ratio compared to those receiving AC-FCP or AC-FCP + antimicrobials. Serum total protein and globulin were higher ($p<0.01$) in birds fed control diet or control diet + antimicrobials compared to AC-FCP or AC-FCP + antimicrobials fed birds. Serum albumin was lower ($p<0.01$) in AC-FCP birds than that in other birds. There was a tendency ($p=0.09$) that birds fed AC-FCP diet had lower total serum cholesterol than other birds. *CONCLUSION*: Feeding AC-FCP has potential to improve the intestinal health and protect the birds from acute infections.

Sun, X., Qiu, H., and Jin, Y. Highly efficient treatment of aerobic vaginitis with simple acidic buffered gels: The importance of pH and buffers on the microenvironment of vaginas. Int.J.Pharm. 6-15-2017; 525(1):175-182; PM: 28414136

ABSTRACT: Aerobic vaginitis (AV) leads to uterus deep infection or preterm birth. Antibacterial agents are not optimal therapeutics of AV. Here, we report a series of temperature-sensitive in situ forming acidic buffered gels for topical treatment of AV, involving lactate, acetate, and citrate gels at pH 3.5, 5.0, and 6.5. AV rat models were prepared following vaginal infection with Staphylococcus aureus and Escherichia coli. In vitro/in vivo studies of the buffered gels were performed compared with ofloxacin gels and blank gels. All the buffered gels showed the lower in vitro antibacterial activities than ofloxacin gels but the better in vivo anti-S. aureus effects and similar anti-E. coli effects. The buffered gels improved Lactobacillus growth in the vaginas. Both the healthy rat vaginal pH and the pH of rat vaginas treated with the buffered gels were about 6.5 though the AV rat models or ones treated with ofloxacin gels still remained at the high pH more than 7.0. After treatments with the buffered gels, the vaginal smears changed to a

clean state nearly without aerobic bacteria, the vaginal tissues were refreshed, and the immunoreactions were downregulated. The acidic buffered gels bring rapid decrease of local vaginal pH, high antibacterial activities, improvement of probiotics, and alleviation of inflammation. They are simple, highly efficient, and safe anti-AV formulations.

Surendran, Nair M., Amalaradjou, M. A., and Venkitanarayanan, K. Antivirulence Properties of Probiotics in Combating Microbial Pathogenesis. Adv.Appl.Microbiol. 2017; 98:1-29; PM: 28189153

ABSTRACT: Probiotics are nonpathogenic microorganisms that confer a health benefit on the host when administered in adequate amounts. Ample evidence is documented to support the potential application of probiotics for the prevention and treatment of infections. Health benefits of probiotics include prevention of diarrhea, including antibiotic-associated diarrhea and traveler's diarrhea, atopic eczema, dental carries, colorectal cancers, and treatment of inflammatory bowel disease. The cumulative body of scientific evidence that demonstrates the beneficial effects of probiotics on health and disease prevention has made probiotics increasingly important as a part of human nutrition and led to a surge in the demand for probiotics in clinical applications and as functional foods. The ability of probiotics to promote health is attributed to the various beneficial effects exerted by these microorganisms on the host. These include lactose metabolism and food digestion, production of antimicrobial peptides and control of enteric infections, anticarcinogenic properties, immunologic enhancement, enhancement of short-chain fatty acid production, antiatherogenic and cholesterol-lowering attributes, regulatory role in allergy, protection against vaginal or urinary tract infections, increased nutritional value, maintenance of epithelial integrity and barrier, stimulation of repair mechanism in cells, and maintenance and reestablishment of well-balanced indigenous intestinal and respiratory microbial communities. Most of these attributes primarily focus on the effect of probiotic supplementation on the host. Hence, in most cases, it can be concluded that the ability of a probiotic to protect the host from infection is an indirect result of promoting overall health and well-being. However, probiotics also exert a direct effect on invading microorganisms. The direct modes of action resulting in the elimination of pathogens include inhibition of pathogen replication by producing antimicrobial substances like bacteriocins, competition for limiting resources in the host, antitoxin effect, inhibition of virulence, antiadhesive and antiinvasive effects, and competitive exclusion by competition for binding sites or stimulation of epithelial barrier function. Although much has been documented about the ability of probiotics to promote host health, there is limited discussion on the above mentioned effects of probiotics on pathogens. Being in an era of antibiotic resistance, a better understanding of this complex probiotic-pathogen interaction is critical for development of effective strategies to control infections. Therefore, this chapter will focus on the ability of probiotics to directly modulate the infectious nature of pathogens and the underlying mechanisms that mediate these effects.

Suryavanshi, M. V., Paul, D., Doijad, S. P., Bhute, S. S., Hingamire, T. B., Gune, R. P., and Shouche, Y. S. Draft genome sequence of Lactobacillus plantarum strains E2C2 and E2C5 isolated from human stool culture. Stand.Genomic.Sci. 2017; 12:15; PM: 28163824

ABSTRACT: Probiotic Lactobacillus species offer various health benefits, thus have been employed in treatment and prevention of various diseases. Due to the differences in the isolation source and the site of action, most of the lactobacilli tested in-vitro for probiotics

properties fail to extend similar effects in-vivo. Consequently, the search of autochthonous, efficacious and probably population specific probiotics is a high priority in the probiotics research. In this regards, whole genome sequencing of as many Lactobacillus as possible will help to deepen our understanding of biology and their health effects. Here, we provide the genomic insights of two coherent oxalic acid tolerant Lactobacillus species (E2C2 and E2C5) isolated from two different healthy human gut flora. These two isolates were found to have higher tolerance towards oxalic acid (300 mM sodium oxalate). The draft genome of strain E2C2 consists of 3,603,563 bp with 3289 protein-coding genes, 94 RNA genes, and 43.99% GC content, while E2C5 contained 3,615,168 bp, 3293 coding genes (93.4% of the total genes), 95 RNA genes and 43.97% GC content. Based on 16S rRNA gene sequence analysis followed by in silico DNA-DNA hybridization studies, both the strains were identified as Lactobacillus plantarum belonging to family Lactobacillaceae within the phylum Firmicutes. Both the strains were genomically identical, sharing 99.99% CDS that showed 112 SNPs. Both the strains also exhibited deconjugation activity for the bile salts while genome analysis revealed that the L. plantarum strains E2C2 and E2C5 also have the ability to produce vitamins, biotin, alpha- and beta- glucosidase suggesting potential probiotic activities of the isolates. The description presented here is based on the draft genomes of strains E2C2 and E2C5 which are submitted to GenBank under the accession numbers LSST00000000.1 and LTCD00000000.1, respectively.

Suzuki, T., Masui, A., Nakamura, J., Shiozawa, H., Aoki, J., Nakae, H., Tsuda, S., Imai, J., Hideki, O., Matsushima, M., Mine, T., Tamura, A., Ohtsu, T., Asami, Y., and Takagi, A. Yogurt Containing Lactobacillus gasseri Mitigates Aspirin-Induced Small Bowel Injuries: A Prospective, Randomized, Double-Blind, Placebo-Controlled Trial. Digestion. 2017; 95(1):49-54; PM: 28052291

ABSTRACT: BACKGROUND: Although there is evidence about the beneficial effects of probiotics, their effects on aspirin-induced small bowel injuries have not been well examined. We evaluated the effects of the probiotic Lactobacillus gasseri OLL2716 (LG) on aspirin-induced small intestinal lesions, such as ulcers, erosions, reddened lesions, and bleeding. *SUMMARY*: This study enrolled 64 patients who received aspirin for more than 1 month and provided written informed consent to be part of the study. The patients received 112 ml of yogurt containing LG or placebo twice daily for 6 weeks. Small bowel injuries were evaluated by capsule endoscopy before and after consuming the yogurt. The effect of LG on patient symptoms was also assessed using the Frequency Scale for the Symptoms of Gastroesophageal Reflux Disease (FSSG) and Gastrointestinal Symptom Rating Scale (GSRS) questionnaires before and after 6 weeks of treatment. There was no significant difference in any baseline characteristics and the number of small bowel mucosal breaks between the 2 groups. In contrast with the placebo group, the LG group had significantly fewer small bowel mucosal breaks and reddened lesions after 6 weeks ($p < 0.01$). The FSSG and GSRS scores were also significantly improved in the LG group but not in the placebo group. *Key Messages*: This double-blind, placebo-controlled study found that LG may be useful in reducing aspirin-induced small bowel injuries and in mitigating gastrointestinal symptoms.

Tachedjian, G., Aldunate, M., Bradshaw, C. S., and Cone, R. A. The role of lactic acid production by probiotic Lactobacillus species in vaginal health. Res.Microbiol. 4-20-2017; PM: 28435139

ABSTRACT: Vaginal eubiosis is characterised by beneficial lactobacillus-dominated microbiota. In contrast, vaginal dysbiosis (e.g. bacterial vaginosis, BV), characterised by an overgrowth of multiple anaerobes, is associated with an increased risk of adverse urogenital and reproductive health outcomes. A major distinguishing feature between the vaginal environment in states of eubiosis and dysbiosis is a high concentration of lactic acid, produced by lactobacilli, that acidifies the vagina in eubiosis versus a sharp drop in lactic acid and an increase in pH in dysbiosis. Here we review the antimicrobial, antiviral and immunomodulatory properties of lactic acid and the use of lactic acid and lactobacilli probiotics in preventing or treating BV.

Tagliabue, A., Ferraris, C., Uggeri, F., Trentani, C., Bertoli, S., de, Giorgis, V, Veggiotti, P., and Elli, M. Short-term impact of a classical ketogenic diet on gut microbiota in GLUT1 Deficiency Syndrome: A 3-month prospective observational study. Clin.Nutr.ESPEN. 2017; 17:33-37; PM: 28361745

ABSTRACT: BACKGROUND&AIMS: The classical ketogenic diet (KD) is a high-fat, very low-carbohydrate normocaloric diet used for drug-resistant epilepsy and Glucose Transporter 1 Deficiency Syndrome (GLUT1 DS). In animal models, high fat diet induces large alterations in microbiota producing deleterious effects on gut health. We carried out a pilot study on patients treated with KD comparing their microbiota composition before and after three months on the diet. *METHODS*: Six patients affected by GLUT1 DS were asked to collect fecal samples before and after three months on the diet. RT - PCR analysis was performed in order to quantify Firmicutes, Bacteroidetes, Bifidobacterium spp., Lactobacillus spp., Clostridium perfringens, Enterobacteriaceae, Clostridium cluster XIV, Desulfovibrio spp. and Faecalibacterium prausnitzii. *RESULTS*: Compared with baseline, there were no statistically significant differences at 3 months in Firmicutes and Bacteroidetes. However fecal microbial profiles revealed a statistically significant increase in Desulfovibrio spp. ($p = 0.025$), a bacterial group supposed to be involved in the exacerbation of the inflammatory condition of the gut mucosa associated to the consumption of fats of animal origin. *CONCLUSIONS*: A future prospective study on the changes in gut microbiota of all children with epilepsy started on a KD is warranted. In patients with dysbiosis demonstrated by fecal samples, it my be reasonable to consider an empiric trial of pre or probiotics to potentially restore the <<ecological balance>> of intestinal microbiota.

Takada, M., Nishida, K., Gondo, Y., Kikuchi-Hayakawa, H., Ishikawa, H., Suda, K., Kawai, M., Hoshi, R., Kuwano, Y., Miyazaki, K., and Rokutan, K. Beneficial effects of Lactobacillus casei strain Shirota on academic stress-induced sleep disturbance in healthy adults: a double-blind, randomised, placebo-controlled trial. Benef.Microbes. 4-26-2017; 8(2):153-162; PM: 28443383

ABSTRACT: The present study examined whether Lactobacillus casei strain Shirota (LcS) improves sleep quality under psychological stress. A double-blind, placebo-controlled trial was conducted in healthy 4th year medical students exposed to academic examination stress. The trial was repeated over two consecutive years in different groups of students, and the data were pooled. For 8 weeks prior to and 3 weeks after a national standardised examination, a total of 48 and 46 subjects received a daily dose of 100 ml of LcS-fermented milk or non-fermented placebo milk, respectively. Study measures included subjective anxiety, overnight single-channel electroencephalography (EEG)

recordings, and the Oguri-Shirakawa-Azumi (OSA) sleep inventory scores of subjective sleep quality. Total OSA scores were significantly lower than baseline on the day before the exam and recovered after the exam, indicating a stress-induced decline in sleep quality. There was a significant positive effect of LcS treatment on OSA factors for sleepiness on rising and sleep length. Sleep latency measured by EEG lengthened as the exam approached in the placebo group but was significantly suppressed in the LcS group. The percentage of stage 3 non-REM (N3) sleep decreased in the placebo group as the exam approached, whereas it was maintained in the LcS group throughout the trial. Delta power during the first sleep cycle, measured as an index of sleep intensity, increased as the exam approached in the LcS group and was significantly higher than in the placebo group. These findings suggest that daily consumption of LcS may help to maintain sleep quality during a period of increasing stress. The observed retention of N3 sleep and increased delta power in the LcS group may have contributed to higher perceived sleep satisfaction.

Takeda, S., Igoshi, K., Tsend-Ayush, C., Oyunsuren, T., Sakata, R., Koga, Y., Arima, Y., and Takeshita, M. Lactobacillus paracasei strain 06TCa19 suppresses inflammatory chemokine induced by Helicobacter pylori in human gastric epithelial cells. Hum.Cell. 4-22-2017; PM: 28434172

ABSTRACT: Helicobacter (H.) pylori infection is an important risk factor for gastric cancer that causes gastric inflammation. Inflammatory chemokines such as interleukin (IL)-8 and regulated on activation normal T cell expressed and secreted (RANTES) are elevated in the gastric mucosa by H. pylori. This study aimed to investigate the effects of Lactobacillus paracasei strain 06TCa19, a probiotic strain, on IL-8 and RANTES expression and production induced by H. pylori using human gastric epithelial cell lines. Strain 06TCa19 was shown to suppress H. pylori-mediated elevation of gene expression related to these chemokines in MKN45 cells. The strain also suppressed the increase in IL-8 and RANTES products induced by H. pylori in AGS cells as well as in MKN45 cells. In MKN45 cells inoculated with H. pylori, strain 06TCa19 was shown to downregulate the activation of NF-kappaB and p38 MAPK signaling pathways. Additionally, the level of the CagA virulence protein of H. pylori in the MKN45 cells and the number of viable H. pylori adhering to MKN45 cells decreased with the addition of strain 06TCa19. Moreover, the strain 06TCa19 notably increased lactic acid in the supernatant of MKN45 cells. Thus, lactic acid released from strain 06TCa19 might have inhibited the adhesion of H. pylori to MKN45 cells and prevented the insertion of H. pylori CagA into the cells, and elevation of IL-8 and RANTES genes and proteins might be suppressed by downregulating the NF-kappaB and p38 MAPK pathways. Therefore, use of strain 06TCa19 may prevent H. pylori-associated gastric inflammation.

Talebi Bezmin, Abadi A. Helicobacter pylori treatment: New perspectives using current experience. J.Glob.Antimicrob.Resist. 2017; 8:123-130; PM: 28131855

ABSTRACT: Infection with Helicobacter pylori plays an essential role in the development of duodenal and gastric ulcers as well as in the pathobiology of gastric adenocarcinoma. Thus, successful elimination of the bacterium can reduce the risk of development of these diseases. Currently, most guidelines recommend standard triple therapy (amoxicillin+clarithromycin+proton pump inhibitor), although its efficacy is rapidly falling. Notably, traditional first-line therapy fails in almost 32% of H. pylori-carrying cases, suggesting the importance of choosing the best formulation for first-line therapy.

Hence, due to the decreasing effectiveness of first-line treatment, we should be prepared to confront increasing H. pylori therapeutic defeat. Owing to increasing reports of antibiotic resistance worldwide, newer approaches and directions are necessary for managing this problematic infection. Developing and providing better anti-H. pylori strategies (probiotics, antibiotic therapy and non-traditional medicine) without using current clinical experience in treating the infection is impossible. Furthermore, development and examination of new preventive vaccines may also be a new therapeutic direction. Taken together, with regard to current experience, clinicians are highly recommended to consider all alternatives to eradicate H. pylori until a universal vaccine becomes practically available. This article aims to give an overview regarding the current status of H. pylori treatment, accordingly designing an actual overview to gain optimal strategies against this infection.

Tamanai-Shacoori, Z., Smida, I., Bousarghin, L., Loreal, O., Meuric, V., Fong, S. B., Bonnaure-Mallet, M., and Jolivet-Gougeon, A. Roseburia spp.: a marker of health? Future.Microbiol. 2017; 12:157-170; PM: 28139139

ABSTRACT: The genus Roseburia consists of obligate Gram-positive anaerobic bacteria that are slightly curved, rod-shaped and motile by means of multiple subterminal flagella. It includes five species: Roseburia intestinalis, R. hominis, R. inulinivorans, R. faecis and R. cecicola. Gut Roseburia spp. metabolize dietary components that stimulate their proliferation and metabolic activities. They are part of commensal bacteria producing short-chain fatty acids, especially butyrate, affecting colonic motility, immunity maintenance and anti-inflammatory properties. Modification in Roseburia spp. representation may affect various metabolic pathways and is associated with several diseases (including irritable bowel syndrome, obesity, Type 2 diabetes, nervous system conditions and allergies). Roseburia spp. could also serve as biomarkers for symptomatic pathologies (e.g., gallstone formation) or as probiotics for restoration of beneficial flora.

Tan, H., Fu, Y., Yang, C., and Ma, J. Effects of metronidazole combined probiotics over metronidazole alone for the treatment of bacterial vaginosis: a meta-analysis of randomized clinical trials. Arch.Gynecol.Obstet. 2017; 295(6):1331-1339; PM: 28386675

ABSTRACT: OBJECT: To evaluate the curative effect of metronidazole combined probiotics over metronidazole alone in the treatment of BV. *METHODS*: We are searching randomized controlled trials on major online databases including PubMed, Science Direct, and Cochrane Database between 1990 and 2015. The primary outcome measure was the cure rate of BV. Cochran's Chi-square test (Q test) was used to test for heterogeneity among trials, and the I 2 index. We used mixed-effects modeling for parameters of the summary hazard ratios (HRs), odds ratios (ORs), and their 95% confidence intervals (CIs). *RESULTS*: Analysis suggests the cure rate of BV [RR = 1.12, 95% CI (0.94-1.32), p = 0.20], and the I 2 index was 83%. The value of I 2 index decreased to 16% after removing the study of Anukam et al., and Amsel 1.04 (95% CI 0.96-1.13) (p = 0.35), Nugent 1.02 (95% CI 0.94-1.11), short-term 1.01 (95% CI 0.93-1.10) (p = 0.79), long-term 1.06 (95% CI 0.98-1.14) (p = 0.13), Europe 1.06 (95% CI 0.95-1.19) (p = 0.32), Non-Europe 0.99 (95% CI 0.94-1.05) (p = 0.83). When the two same groups data were combined, respectively, the RRs for all studies were the same as 1.03 (95% CI 0.96-1.09) (p = 0.42) showing that there is not statistically significant in relevant stratums. *CONCLUSION*: The result has showed an overall little significance for the efficacy of metronidazole combined probiotics over metronidazole alone for the treatment of BV. We need more

further studies to provide enough evidence to confirm the benefits of probiotics in the treatment of BV.

Tan, J. S., Yeo, C. R., and Popovich, D. G. Fermentation of protopanaxadiol type ginsenosides (PD) with probiotic Bifidobacterium lactis and Lactobacillus rhamnosus. Appl.Microbiol.Biotechnol. 5-6-2017; PM: 28478490

ABSTRACT: Ginsenosides are believed to be the principal components behind the pharmacological actions of ginseng, and their bioactive properties are closely related to the type, position, and number of sugar moieties attached to the aglycone; thus, modification of the sugar chains may markedly change their biological activities. In this study, major protopanaxadiol type ginsenosides (PD) Rb1, Rc, and Rb2 were isolated from Panax ginseng and were transformed using two probiotic strains namely Bifidobacterium lactis Bi-07 and Lactobacillus rhamnosus HN001 to obtain specific deglycosylated ginsenosides. It was demonstrated that B. lactis transformed ginsenosides Rb1, Rc, and Rb2 to Rd within 1 h of fermentation and rare ginsenoside F2 by the conversion of Rd after 12-h fermentation. The maximum Rd concentration was 147.52 +/- 1.45 mug/mL after 48-h fermentation as compared to 45.85 +/- 0.71 mug/mL before fermentation. In contrast, L. rhamnosus transformed Rb1, Rc, and Rb2 into Rd as the final metabolite after 72-h fermentation. B. lactis displayed significantly ($p < 0.05$) higher beta-glucosidase activity against p-nitrophenyl-beta-glucopyranoside than L. rhamnosus and higher bioconversion efficiency during fermentation. The present study suggests that the fermentation of major PD type ginsenosides with B. lactis Bi-07 may serve as an effective means to afford bioactive deglycosylated ginsenosides and to create novel ginsenoside extracts.

Tan, T. P., Ba, Z., Sanders, M. E., D'Amico, F. J., Roberts, R. F., Smith, K. H., and Merenstein, D. J. Safety of Bifidobacterium animalis Subsp. Lactis (B. lactis) Strain BB-12-Supplemented Yogurt in Healthy Children. J.Pediatr.Gastroenterol.Nutr. 2017; 64(2):302-309; PM: 28114246

ABSTRACT: OBJECTIVES: Probiotics are live microorganisms that may provide health benefits to the individual when consumed in sufficient quantities. For studies conducted on health or disease endpoints on probiotics in the United States, the Food and Administration has required those studies to be conducted as investigational new drugs. This phase I, double-blinded, randomized, controlled safety study represents the first requirement of this pathway. The purpose of the study was to determine the safety of Bifidobacterium animalis subsp. lactis (B lactis) strain BB-12 (BB-12)-supplemented yogurt when consumed by a generally healthy group of children. The secondary aim was to assess the effect of BB-12-supplemented yogurt on the gut microbiota of the children. *METHODS*: Sixty children ages 1 to 5 years were randomly assigned to consume 4 ounces of either BB-12-supplemented yogurt or nonsupplemented control yogurt daily for 10 days. The primary outcome was to assess safety and tolerability, as determined by the number of reported adverse events. *RESULTS*: A total of 186 nonserious adverse events were reported, with no significant differences between the control and BB-12 groups. No significant changes due to probiotic treatment were observed in the gut microbiota of the study cohort. *CONCLUSIONS*: BB-12-supplemented yogurt is safe and well-tolerated when consumed by healthy children. The present study will form the basis for future randomized clinical trials investigating the potential effects of BB-12-supplemented yogurt in different disease states.

Tanaka, K., Tsukahara, T., Yanagi, T., Nakahara, S., Furukawa, O., Tsutsui, H., and Koshida, S. Bifidobacterium bifidum OLB6378 Simultaneously Enhances Systemic and Mucosal Humoral Immunity in Low Birth Weight Infants: A Non-Randomized Study. Nutrients. 2-26-2017; 9(3); PM: 28245626

ABSTRACT: Probiotic supplementation has been part of the discussion on methods to enhance humoral immunity. Administration of Bifidobacterium bifidum OLB6378 (OLB6378) reduced the incidence of late-onset sepsis in infants. In this non-randomized study, we aimed to determine the effect of administration of live OLB6378 on infants' humoral immunity. Secondly, we tried to elucidate whether similar effects would be observed with administration of non-live OLB6378. Low birth weight (LBW) infants weighing 1500-2500 g were divided into three groups: Group N (no intervention), Group L (administered live OLB6378 concentrate), and Group H (administered non-live OLB6378 concentrate). The interventions were started within 48 h after birth and continued until six months of age. Serum immunoglobulin G (IgG) levels (IgG at one month/IgG at birth) were significantly higher in Group L than in Group N ($p < 0.01$). Group H exhibited significantly higher serum IgG levels ($p < 0.01$) at one month of age and significantly higher intestinal secretory immunoglobulin A (SIgA) levels ($p < 0.05$) at one and two months of age than Group N. No difference was observed in the mortality or morbidity between groups. Thus, OLB6378 administration in LBW infants enhanced humoral immunity, and non-live OLB6378, which is more useful as a food ingredient, showed a more marked effect than the viable bacteria.

Tang, Y., Wu, Y., Huang, Z., Dong, W., Deng, Y., Wang, F., Li, M., and Yuan, J. Administration of probiotic mixture DM#1 ameliorated 5-fluorouracil-induced intestinal mucositis and dysbiosis in rats. Nutrition. 2017; 33:96-104; PM: 27427511

ABSTRACT: OBJECTIVE: The use of probiotics to alleviate chemotherapy-induced intestinal mucositis is supported by clinical consensus. However, no studies to date, to our knowledge, have systematically analyzed the effects of a probiotic mixture on chemotherapy-induced mucositis or assessed changes in the intestinal microbiota after probiotic treatment. The aim of this study was to report the effects of a probiotic mixture, DM#1, on intestinal mucositis and dysbiosis of rats treated with 5-fluorouracil (5-FU). *METHODS*: Twenty-eight male Sprague Dawley rats weighing 180 to 220 g were randomly divided into four groups: control, 5-FU, probiotic high (PH), and probiotic low (PL). Except for the control group, all other groups received intraperitoneal injections of 5-FU for 5 d, and the PH and PL groups received DM#1 intragastrically (1 x 109 or 1 x 108 colony-forming units/kg, respectively) for 8 d. One day after the last administration, rats were sacrificed and the ilea were removed for histopathologic assessment and evaluation of permeability, myeloperoxidase activity, levels of cytokines (interleukin [IL]-4, IL-6, tumor necrosis factor [TNF]-alpha), and mRNA of toll-like receptors (TLR; TLR2, TLR4, and TLR9). Additionally, intestinal microbiota profiles were analyzed by polymerase chain reaction (PCR)-denaturing gradient gel electrophoresis and quantitative real-time PCR. *RESULTS*: Treatment with DM#1 ameliorated 5-FU-induced intestinal mucosal injury in rats, possibly by reducing proinflammatory cytokine levels and neutrophil infiltration. The increased intestinal permeability caused by 5-FU was ameliorated. These results were closely associated with the reestablishment of intestinal microbial homeostasis and alteration of the TLR2/TLR4 signaling pathway. *CONCLUSIONS*: Administration of the probiotic mixture DM#1 ameliorated 5-FU-induced intestinal mucositis and dysbiosis in rats.

Taylor, B. L., Woodfall, G. E., Sheedy, K. E., O'Riley, M. L., Rainbow, K. A., Bramwell, E. L., and Kellow, N. J. Effect of Probiotics on Metabolic Outcomes in Pregnant Women with Gestational Diabetes: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Nutrients. 5-5-2017; 9(5); PM: 28475161

ABSTRACT: The metabolic effects of probiotic administration in women with gestational diabetes mellitus (GDM) is unknown. The objective of this review was to investigate the effect of probiotics on fasting plasma glucose (FPG), insulin resistance (HOMA-IR) and LDL-cholesterol levels in pregnant women diagnosed with GDM. Seven electronic databases were searched for RCTs published in English between 2001 and 2017 investigating the metabolic effects of a 6-8 week dietary probiotic intervention in pregnant women following diagnosis with GDM. Eligible studies were assessed for risk of bias and subjected to qualitative and quantitative synthesis using a random effects model meta-analyses. Four high quality RCTs involving 288 participants were included in the review. Probiotic supplementation was not effective in decreasing FBG (Mean Difference = -0.13; 95% CI -0.32, 0.06, p = 0.18) or LDL-cholesterol (-0.16; 95% CI -0.45, 0.13, p = 0.67) in women with GDM. However, a significant reduction in HOMA-IR was observed following probiotic supplementation (-0.69; 95% CI -1.24, -0.14, p = 0.01). There were no significant differences in gestational weight gain, delivery method or neonatal outcomes between experimental and control groups, and no adverse effects of the probiotics were reported. Probiotic supplementation for 6-8 weeks resulted in a significant reduction in insulin resistance in pregnant women diagnosed with GDM. The use of probiotic supplementation is promising as a potential therapy to assist in the metabolic management of GDM. Further high quality studies of longer duration are required to determine the safety, optimal dose and ideal bacterial composition of probiotics before their routine use can be recommended in this patient group.

Thomas, J. P., Raine, T., Reddy, S., and Belteki, G. Probiotics for the prevention of necrotizing enterocolitis in very-low-birth-weight infants: A meta-analysis and systematic review. Acta Paediatr. 5-4-2017; PM: 28471478

ABSTRACT: We performed an updated meta-analysis incorporating the results of recent randomised controlled trials (RCTs) to measure the effectiveness of probiotic supplementation in preventing necrotizing enterocolitis (NEC) and death in very-low-birth-weight (VLBW) infants, and to investigate any differences in efficacy by probiotic agent. Using meta-regression analysis, we assessed the contribution of other measured variables on the overall effect size and between-study variability. CONCLUSION: Overall, probiotics lead to significant reductions in NEC incidence and mortality in VLBW infants. Differences in probiotic agents and the influence of prenatal steroids and feeding regimens may explain the differences in outcomes between studies. This article is protected by copyright. All rights reserved.

Thompson, M. E. and Noel, M. B. Issues in Nutrition: Dietary Supplements. FP.Essent. 2017; 452:18-25; PM: 28092150

ABSTRACT: The majority of American adults report use of one or more dietary supplements every day or occasionally. The Dietary Supplement Health and Education Act of 1994 defines dietary supplements and regulates their manufacture and distribution. One of the most commonly used supplements is vitamin D. Measurement of serum levels of vitamin D must be undertaken with the caveats that different laboratories

define normal levels differently, and that there is rarely a clinical correlation with the actual level. Patients should understand that supplements should not be used to excess, as there are toxicities and other adverse effects associated with most of them. There currently is considerable research being performed on probiotics and how the gut microbiome affects health and disease states. Protein supplements may be useful in reducing mortality rates in elderly patients but they do not appear to increase quality of life. If used, protein supplements should contain essential amino acids. Casein and whey supplements, derived from dairy sources, help transport essential amino acids to tissues. Although there have been many studies investigating the role of vitamin supplements in disease prevention, there have been few conclusive positive results.

Thongaram, T., Hoeflinger, J. L., Chow, J., and Miller, M. J. Prebiotic Galactooligosaccharide Metabolism by Probiotic Lactobacilli and Bifidobacteria. J.Agric.Food Chem. 5-12-2017; PM: 28466641

ABSTRACT: Galactooligosaccharides (GOS) are bifidogenic and lactogenic prebiotics; however, GOS utilization is strain-dependent. In this study, commercially available bifidobacteria and lactobacilli probiotic strains were evaluated for growth in the presence of GOS. Several bifidobacteria and lactobacilli grew on GOS; however, the specific GOS oligomers utilized for growth differed. A subset of probiotic bifidobacteria and lactobacilli revealed three different GOS utilization profiles delineated by the degrees of polymerization (DP) of GOS: (1) utilization of 2 DP GOS, (2) utilization of </=3 DP GOS, and (3) utilization of all DP GOS. Specifically, Lactobacillus acidophilus NCFM (LA_NCFM) was found to efficiently consume all GOS oligomers. Extracellular beta-galactosidase activity in the cell-free supernatant of LA_NCFM correlated with accumulation of galactose. In a LacL-deficient LA_NCFM strain, GOS utilization was abolished. This is the first report of LacL's role in GOS metabolism in LA_NCFM. In vitro GOS utilization should be considered when GOS are delivered with probiotic bifidobacteria and lactobacilli.

Thukral, A. and Sankar, M. J. Probiotics for prevention of suspected sepsis in low birthweight infants. Acta Paediatr. 2017; 106(4):681; PM: 28145021

No Abstract Available.

Todorov, S. D., Holzapfel, W., and Nero, L. A. In Vitro Evaluation of Beneficial Properties of Bacteriocinogenic Lactobacillus plantarum ST8Sh. Probiotics.Antimicrob.Proteins. 2017; 9(2):194-203; PM: 27943050

ABSTRACT: Lactobacillus plantarum ST8Sh, isolated from Bulgarian salami "shpek" and previously characterized as bacteriocin producer, was evaluated for its beneficial properties. Based on the PCR analysis, Lb. plantarum ST8Sh was shown to host a gene related to the production of adhesion proteins such as Mab, Mub, EF, and PrgB. Genetic and physiological tests suggest Lb. plantarum ST8Sh to represent a potential probiotic candidate, including survival in the presence of low levels of pH and high levels of ox bile, production of beta-galactosidase, bile salt deconjugation, high level of hydrophobicity, functional auto- and co-aggregation properties, and adhesion to cell lines. Application of semi-purified bacteriocin produced by Lb. plantarum ST8Sh in combination with ciprofloxacin presented synergistic effect on inhibition of Listeria monocytogenes Scott A. Based on observed properties, Lb. plantarum ST8Sh can be

considered as a potential probiotic candidate with additional bacteriocinogenic properties.

Todorov, S. D., Perin, L. M., Carneiro, B. M., Rahal, P., Holzapfel, W., and Nero, L. A. Safety of Lactobacillus plantarum ST8Sh and Its Bacteriocin. Probiotics.Antimicrob.Proteins. 2-23-2017; PM: 28233282

ABSTRACT: Total DNA extracted from Lb. plantarum ST8Sh was screened for the presence of more than 50 genes related to production of biogenic amines (histidine decarboxylase, tyrosine decarboxylase, and ornithine decarboxylase), virulence factors (sex pheromones, gelatinase, cytolysin, hyaluronidase, aggregation substance, enterococcal surface protein, endocarditis antigen, adhesion of collagen, integration factors), and antibiotic resistance (vancomycin, tetracycline, erythromycin, gentamicin, chloramphenicol, bacitracin). Lb. plantarum ST8Sh showed a low presence of virulence genes. Only 13 genes were detected (related to sex pheromones, aggregation substance, adhesion of collagen, tetracycline, gentamicin, chloramphenicol, erythromycin, but not to vancomycin, and bacitracin) and may be considered as indication of safety for application in fermented food products. In addition, interaction between Lb. plantarum ST8Sh and drugs from different groups were determined in order to establish possible application of the strain in combination with commercial drugs. Cytotoxicity of the semi-purified bacteriocins produced by Lb. plantarum ST8Sh was depended on applied concentration-highly cytotoxic when applied at 25 mug/mL and no cytotoxicity at 5 mug/mL.

Tonucci, L. B., Olbrich Dos Santos, K. M., Licursi de, Oliveira L., Rocha Ribeiro, S. M., and Duarte Martino, H. S. Clinical application of probiotics in type 2 diabetes mellitus: A randomized, double-blind, placebo-controlled study. Clin.Nutr. 2017; 36(1):85-92; PM: 26732026

ABSTRACT: BACKGROUND & AIMS: Type 2 diabetes has been associated with dysbiosis and one of the possible routes to restore a healthy gut microbiota is by the regular ingestion of probiotics. We aimed to investigate the effects of probiotics on glycemic control, lipid profile, inflammation, oxidative stress and short chain fatty acids in T2D. *METHODS*: In a double-blind, randomized, placebo-controlled trial, 50 volunteers consumed daily 120 g/d of fermented milk for 6 wk. Participants were assigned into two groups: probiotic group, consuming fermented milk containing Lactobacillus acidophilus La-5 and Bifidobacterium animalis subsp lactis BB-12 (109 colony-forming units/d, each) and control group, consuming conventional fermented milk. Anthropometric measurements, body composition, fasting blood and faecal samples were taken at baseline and after 6 wk. *RESULTS*: 45 subjects out of 50 (90%) completed follow-up. After 6 wk, there was a significant decrease in fructosamine levels (-9.91 mmol/L; p = 0.04) and hemoglobin A1c tended to be lower (-0.67%; p=0.06) in probiotic group. TNF-alpha and resistin were significantly reduced in probiotic and control groups (-1.5 and -1.3 pg/mL, -.1 and -2.8 ng/mL, respectively), while IL-10 was significantly reduced (- 0.65 pg/mL; p <0.001) only in the control group. Fecal acetic acid was increased in both groups (0.58 and 0.59% in probiotic and control groups, respectively; p <0.01). There was a significant difference between groups concerning mean changes of HbA1c (+0.31 for control group vs -0.65 for probiotic group; p=0.02), total cholesterol (+0.55 for control group vs -0.15 for probiotic group; p=0.04) and LDL-cholesterol (+0.36 for control group vs -0.20 for probiotic group p=0.03). *CONCLUSIONS*: Probiotic consumption improved the glycemic control in T2D subjects, however, the intake of fermented milk seems to be involved with

others metabolic changes, such as decrease in inflammatory cytokines (TNF-alpha and resistin) and increase in the acetic acid.

Toscano, M., De, Grandi R., Miniello, V. L., Mattina, R., and Drago, L. Ability of Lactobacillus kefiri LKF01 (DSM32079) to colonize the intestinal environment and modify the gut microbiota composition of healthy individuals. Dig.Liver Dis. 2017; 49(3):261-267; PM: 27939319

ABSTRACT: BACKGROUND: Probiotics have been observed to positively influence the host's health, but to date few data about the ability of probiotics to modify the gut microbiota composition exist. *AIMS*: To evaluate the ability of Lactobacillus kefiri LKF01 DSM32079 (LKEF) to colonize the intestinal environment of healthy subjects and modify the gut microbiota composition. *METHODS*: Twenty Italian healthy volunteers were randomized in pre-prandial and post-prandial groups. Changes in the gut microbiota composition were detected by using a Next Generation Sequencing technology (Ion Torrent Personal Genome Machine). *RESULTS*: L. kefiri was recovered in the feces of all volunteers after one month of probiotic administration, while it was detected only in three subjects belonging to the pre-prandial group and in two subjects belonging to the post-prandial group one month after the end of probiotic consumption. After one month of probiotic oral intake we observed a reduction of Bilophila, Butyricicomonas, Flavonifractor, Oscillibacter and Prevotella. Interestingly, after the end of probiotic administration Bacteroides, Barnesiella, Butyricicomonas, Clostridium, Haemophilus, Oscillibacter, Salmonella, Streptococcus, Subdoligranolum, and Veillonella were significantly reduced if compared to baseline samples. *CONCLUSION*: L. kefiri LKF01 showed a strong ability to modulate the gut microbiota composition, leading to a significant reduction of several bacterial genera directly involved in the onset of pro-inflammatory response and gastrointestinal diseases.

Toscano, M., De, Grandi R., Stronati, L., De, Vecchi E., and Drago, L. Effect of Lactobacillus rhamnosus HN001 and Bifidobacterium longum BB536 on the healthy gut microbiota composition at phyla and species level: A preliminary study. World J.Gastroenterol. 4-21-2017; 23(15):2696-2704; PM: 28487606

ABSTRACT: AIM: To evaluate the ability of Lactobacillus rhamnosus HN001 and Bifidobacterium longum BB536 to colonize the intestinal environment of healthy subjects and modify the gut microbiota composition. *METHODS*: Twenty healthy Italian volunteers, eight males and twelve females, participated in the study. Ten subjects took a sachet containing 4 x 109 colony-forming units (CFU) of Bifidobacterium longum BB536 and 109 CFU of Lactobacillus rhamnosus HN001, 30 min before breakfast (pre-prandial administration), while ten subjects took a sachet of probiotic product 30 min after breakfast (post-prandial administration). The ability of Lactobacillus rhamnosus HN001 and Bifidobacterium longum BB536 to colonize human gut microbiota was assessed by means of quantitative real-time PCR, while changes in gut microbiota composition were detected by using Ion Torrent Personal Genome Machine. *RESULTS*: Immediately after 1-mo of probiotic administration, B. longum BB536 and L. rhamnosus HN001 load was increased in the majority of subjects in both pre-prandial and post-prandial groups. This increase was found also 1 mo after the end of probiotic oral intake in both groups, if compared to samples collected before probiotic consumption. At phyla level a significant decrease in Firmicutes abundance was detected immediately after 1-mo of B. longum BB536 and L. rhamnosus HN001 oral intake. This reduction persisted up to 1 mo after the end of probiotic oral intake together with a significant decrease of

Proteobacteria abundance if compared to samples collected before probiotic administration. Whereas, at species level, a higher abundance of Blautia producta, Blautia wexlerae and Haemophilus ducrey was observed, together with a reduction of Holdemania filiformis, Escherichia vulneris, Gemmiger formicilis and Streptococcus sinensis abundance. In addition, during follow-up period we observed a further reduction in Escherichia vulneris and Gemmiger formicilis, together with a decrease in Roseburia faecis and Ruminococcus gnavus abundance. Conversely, the abundance of Akkermansia muciniphila was increased if compared to samples collected at the beginning of the experimental time course. *CONCLUSION*: B. longum BB536 and L. rhamnosus HN001 showed the ability to modulate the gut microbiota composition, leading to a significant reduction of potentially harmful bacteria and an increase of beneficial ones. Further studies are needed to better understand the specific mechanisms involved in gut microbiota modulation.

Tovar, A. R. and Herrera, G. Introduction to the Yogurt in Nutrition Initiative at the First Symposium of Yogurt in Mexico: The Balanced Diet Initiative. Adv.Nutr. 2017; 8(1):144S-145S; PM: 28096137

ABSTRACT: In some European countries, yogurt consumption is common. However, such consumption is not common in Latin America, particularly in Mexico, partially because of the lack of a cultural tradition of consuming yogurt. Moreover, we also know that little information about the health benefits associated with yogurt consumption has been provided to the Mexican population. Thus, there is an immediate need to provide, at least to the nutrition community in the country, current scientific evidence about the health benefits of yogurt, with the aim that yogurt be included as part of the functional foods recommended to the population. Currently, extensive research has been conducted to investigate the mechanisms through which yogurt generates beneficial effects. Gut microbiota appear to be an important factor that can be modified by dietary prebiotics, as well as probiotics such as yogurt. The prevention or attenuation of gut microbiota dysbiosis is now associated with improvements observed in individuals with metabolic syndrome and cardiovascular disease. Thus, it is important to establish guidelines for the consumption of dairy products, including yogurt. Such guidelines are necessary to increase the consumption of dairy products in Mexico and other countries.

Truong Thy, H. T., Tri, N. N., Quy, O. M., Fotedar, R., Kannika, K., Unajak, S., and Areechon, N. Effects of the dietary supplementation of mixed probiotic spores of Bacillus amyloliquefaciens 54A, and Bacillus pumilus 47B on growth, innate immunity and stress responses of striped catfish (Pangasianodon hypophthalmus). Fish.Shellfish.Immunol. 2017; 60:391-399; PM: 27836719

ABSTRACT: The study used the mixed probiotics of Bacillus amyloliquefaciens 54A and B. pumilus 47B isolated from striped catfish (Pangasianodon hypophthalmus) intestine aiming to stimulate growth performance, innate immunity, stress tolerance of striped catfish. The average weight gain (AWG), specific growth rate (SGR), and feed conversion ratio (FCR) were analyzed after fish were fed the mixture of probiotics (B. amyloliquefaciens 54A and B. pumilus 47B) at concentrations of 1 x 108, 3 x 108, and 5 x 108 CFU g-1 feed for 90 days. Immunity parameters, survival rate of fish challenged with Edwardsiella ictaluri and ammonia tolerance were also investigated. The amounts of B. amyloliquefaciens and B. pumilus were counted and identified by specific primer pairs of Ba1-F/Ba1-R, and 16-F/Bpu-R to confirm the presence of probiotics in fish intestine. The

AWG (476.6 +/- 7.81 g fish-1) of fish fed probiotics at 5 x 108 CFU g-1 was significant higher than the control (390 +/- 25.7 g fish-1) after 90 days of feeding, but there was no significant (P > 0.05) effect of probiotics on FCR and SGR. Fish fed diet containing probiotics at 5 x 108 CFU g-1 also expressed resistance to E. ictaluri infection and higher immune parameters such as phagocytic activity, respiratory bursts, and lysozyme activity than the control. Stress response with ammonia showed significantly lower mortality rate (25%, 20% and 27%) of fish fed probiotics at all three levels of 1, 3 and 5 x 108 CFU g-1 than the fish fed control diet (75%). The study also demonstrated that the probiotics survived in the intestine of striped catfish after 90 days of feeding. Therefore, the dietary supplementation of a mixture of B. amyloliquefaciens and B. pumilus at 5 x 108 CFU g-1 can be used to improve the health and growth rate of striped catfish.

Tsiouris, C. G., Kelesi, M., Vasilopoulos, G., Kalemikerakis, I., and Papageorgiou, E. G. The efficacy of probiotics as pharmacological treatment of cutaneous wounds: Meta-analysis of animal studies. Eur.J.Pharm.Sci. 4-7-2017; 104:230-239; PM: 28392493

ABSTRACT: The aim of the current meta-analysis of animal studies was to evaluate the efficacy of probiotics as pharmacological treatment of cutaneous wounds. A systematic electronic literature search was conducted and in total six animal studies which undertake twelve experiments met our inclusion criteria. We used the percentage (%) of wound area at the end of the first week after initial wounding to evaluate the efficacy of the probiotic treatment. The heterogeneity was estimated as statistically significant (p<0.0001) and therefore the meta-analysis was performed with the random-effect model. Based on the estimated Hedges' g (Hedges, 1982), the administration of probiotics was associated with acceleration of the wound contraction (g=-2.55; 95%CI=-3.59, -1.50; p<0.0001). The meta-regression analysis showed that the moderator sterile kefir extract has the greater effect on the overall estimated efficacy of probiotic treatment (g=-5.6983; p=0.0442) with bacteria probiotic therapies (70% kefir gel, L. brevis, L. fermentum, L. plantarum, L. reuteri) following (g=-2.3814; p=0.0003). For bacteria dose moderator, the results showed that increase in bacterial dose corresponds to increase of the estimated overall effect size (g=-10.2056; p=0.0053). The linear regression test of funnel plot asymmetry showed absence of publication bias. In conclusion, the results indicate that probiotics administration is an effective pharmacological treatment of cutaneous wounds. However, due to the heterogeneity among studies, further research is required.

Turner, R. B., Woodfolk, J. A., Borish, L., Steinke, J. W., Patrie, J. T., Muehling, L. M., Lahtinen, S., and Lehtinen, M. J. Effect of probiotic on innate inflammatory response and viral shedding in experimental rhinovirus infection - a randomised controlled trial. Benef.Microbes. 4-26-2017; 8(2):207-215; PM: 28343401

ABSTRACT: Ingestion of probiotics appears to have modest effects on the incidence of viral respiratory infection. The mechanism of these effects is not clear; however, there is evidence from animal models that the probiotic may have an effect on innate immune responses to pathogens. The purpose of this randomised, placebo-controlled study was to determine the effect of administration of Bifidobacterium animalis subspecies lactis BI-04 on innate and adaptive host responses to experimental rhinovirus challenge. The effect on the response of chemokine (C-X-C motif) ligand 8 (CXCL8) to rhinovirus infection was defined as the primary endpoint for the study. 152 seronegative volunteers who had been supplemented for 28 days, 73 with probiotic and 79 with placebo, were challenged with RV-A39. Supplement or placebo administration was then continued for

five days during collection of specimens for assessment of host response, infection, and symptoms. 58 probiotic and 57 placebo-supplemented volunteers met protocol-defined criteria for analysis. Probiotic resulted in higher nasal lavage CXCL8 on day 0 prior to virus challenge (90 vs 58 pg/ml, respectively, P=0.04, ANCOVA). The CXCL8 response to rhinovirus infection in nasal lavage was significantly reduced in the probiotic treated group (P=0.03, ANCOVA). Probiotic was also associated with a reduction in nasal lavage virus titre and the proportion of subjects shedding virus in nasal secretions (76% in the probiotic group, 91% in the placebo group, P=0.04, Fisher Exact test). The administration of probiotic did not influence lower respiratory inflammation (assessed by exhaled nitric oxide), subjective symptom scores, or infection rate. This study demonstrates that ingestion of BI-04 may have an effect on the baseline state of innate immunity in the nose and on the subsequent response of the human host to rhinovirus infection. Clinicaltrials.gov registry number: NCT01669603.

Uberos, J., guilera-Rodriguez, E., Jerez-Calero, A., Molina-Oya, M., Molina-Carballo, A., and Narbona-Lopez, E. Probiotics to prevent necrotising enterocolitis and nosocomial infection in very low birth weight preterm infants. Br.J.Nutr. 4-26-2017; 1-7; PM: 28443531

ABSTRACT: The aim of the study was to determine whether routine probiotic supplementation (RPS) with Lactobacillus rhamnosus GG (LGG) or Lactobacillus acidophilus +Lactobacillus bifidum is associated with reduced risk of necrotising enterocolitis (NEC)>/=Stage II in preterm neonates born at </=32 weeks' gestation. We conducted a retrospective cohort study on the effect of probiotic supplementation in very low birth weight infants in our neonatal unit by comparing two periods: before and after supplementation. The incidence of NEC>/=Stage II, late-onset sepsis and all-cause mortality was compared for an equal period 'before' (Period I) and 'after' (Period II) RPS with LGG or L. acidophillus+L. bifidum. Multivariate logistic regression analysis was conducted to adjust for relevant confounders. The study population was composed of 261 neonates (Period I v. II: 134 v. 127) with comparable gestation duration and birth weights. In <32 weeks, we observed a significant reduction in NEC>/=Stage II (11.3 v. 4.8 %), late-onset sepsis (16 v. 10.5 %) and mortality (19.4 v. 2.3 %). The benefits in neonates aged </=27 weeks did not reach statistical significance. RPS with LGG or L. acidophillus+L. bifidum is associated with a reduced risk of NEC>/=Stage II, late-onset sepsis and mortality in preterm neonates born at </=32 weeks' gestation.

Underwood, M. A. Impact of probiotics on necrotizing enterocolitis. Semin.Perinatol. 2017; 41(1):41-51; PM: 27836423

ABSTRACT: A large number of randomized placebo-controlled clinical trials and cohort studies have demonstrated a decrease in the incidence of necrotizing enterocolitis with administration of probiotic microbes. These studies have prompted many neonatologists to adopt routine prophylactic administration of probiotics while others await more definitive studies and/or probiotic products with demonstrated purity and stable numbers of live organisms. Cross-contamination and inadequate sample size limit the value of further traditional placebo-controlled randomized controlled trials. Key areas for future research include mechanisms of protection, optimum probiotic species or strains (or combinations thereof) and duration of treatment, interactions between diet and the administered probiotic, and the influence of genetic polymorphisms in the mother and infant on probiotic response. Next generation probiotics selected based on bacterial

genetics rather than ease of production and large cluster-randomized clinical trials hold great promise for NEC prevention.

Unterweger, C., Kahler, A., Gerlach, G. F., Viehmann, M., von, Altrock A., and Hennig-Pauka, I. Administration of non-pathogenic isolates of Escherichia coli and Clostridium perfringens type A to piglets in a herd affected with a high incidence of neonatal diarrhoea. Animal. 2017; 11(4):670-676; PM: 27574018

ABSTRACT: A bacterial cocktail of living strains of Clostridium perfringens type A (CPA) without beta2-toxin gene and non-pathogenic Escherichia coli was administered orally to newborn piglets before first colostrum intake and on 2 consecutive days on a farm with a high incidence of diarrhoea and antibiotic treatment in suckling piglets associated with E. coli and CPA. This clinical field study was driven by the hypothetic principle of competitive exclusion of pathogenic bacteria due to prior colonization of the gut mucosal surface by non-pathogenic strains of the same bacterial species with the aim of preventing disease. Although CPA strains used in this study did not produce toxins in vitro, their lack of pathogenicity cannot be conclusively confirmed. The health status of the herd was impaired by a high incidence of postpartum dysgalactia syndrome in sows (70%) and a high incidence of neonatal diarrhoea caused by enterotoxigenic E. coli and CPA during the study. No obvious adverse effect of the bacterial treatment occurred. On average, more piglets were weaned in litters treated (P=0.009). Visual pathological alterations in the small intestinal wall were more frequent in dead piglets of the control group (P=0.004) and necrotizing enteritis was only found in that group. A higher average daily weight gain of piglets in the control group (P<0.001) may be due to an increased milk uptake due to less competition in the smaller litters. The bacterial cocktail was tested under field conditions for its potential to stabilize gut health status in suckling piglets before disease development due to colibacillosis and clostridial infections; however, the gut flora stabilizing effect of the bacterial cocktail was not clearly discernible in this study. Further basic research is needed to confirm the positive effects of the bacterial treatment used and to identify additional potential bacterial candidates for competitive exclusion.

Upadhaya, S. D., Shanmugam, S. K., Kang, D. K., and Kim, I. H. Preliminary assessment on potentials of probiotic B. subtilis RX7 and B. methylotrophicus C14 strains as an immune modulator in Salmonella-challenged weaned pigs. Trop.Anim Health Prod. 2017; 49(5):1065-1070; PM: 28326485

ABSTRACT: A total of 40 crossbred weaned piglets (28 days old; [Landrace x Yorkshire] x Duroc) were used for preliminary assessment on potentials of Bacillus-based probiotics as an immune modulator in a Salmonella Typhimurium challenge model in a 3-week experiment. Pigs were randomly allotted to four experimental diets according to their initial body weight (9.21 +/- 1.1 kg) and sex (10 pigs per treatment; 5 barrows and 5 gilts). The dietary treatments were basal diet (CON), basal diet + oral administration of Salmonella enterica ser. Typhimurium at the dosage of 1 mL containing 1 x 1011 cfu/mL of viable cell concentrations at day 21 (SC), SC + Bacillus subtilis (BS), and SC+ Bacillus methylotrophicus (BM). After 12 h of Salmonella challenge, the red blood cell (RBC), immunoglobulin G (IgG), and immunoglobulin M (IgM) concentrations were reduced (P < 0.05) whereas haptoglobin and cortisol levels were greater (P < 0.05) in SC compared with CON. However, the concentrations of RBC, IgG, and IgM were increased whereas haptoglobin and cortisol levels were reduced in BS and BM compared with SC. The

probiotic-treated groups showed reduced (P < 0.05) IgM levels and increased (P < 0.05) WBC and cortisol levels compared with CON. The supplementation of probiotics showed increased (P < 0.05) fecal Lactobacillus counts and reduced Escherichia coli and Salmonella counts in piglets though there was no biological relevance compared with SC. Thus, in our preliminary study, Bacillus-based probiotic has shown some positive immunomodulatory effects in Salmonella-challenged pigs which provided a base for further studies.

Urquiaga, I., Echeverria, G., Dussaillant, C., and Rigotti, A. [Origin, components and mechanisms of action of the Mediterranean diet]. Rev.Med.Chil. 2017; 145(1):85-95; PM: 28393974

ABSTRACT: The Mediterranean diet is currently considered a healthy dietary pattern. It includes a great variety of foods, which are eaten in moderation and within a positive social environment. The generic term "Mediterranean diet" was born after the "Seven Countries Study" led by Ancel Keys around 1960. This dietary pattern is characterized by a high intake of fruits and vegetables, whole grains, legumes, nuts, fish, white meats and olive oil. It also includes moderate consumption of fermented dairy products, low intake of red meat and drinking wine with moderation during meals. Nutritionally, this diet is low in saturated fats and animal protein, high in antioxidants, fiber and monounsaturated fats, and exhibits an adequate omega-6/omega-3 fatty acid balance. The main bioactive compounds, which explain the health benefits of this dietary pattern, are antioxidants, fiber, monounsaturated and omega-3 fatty acids, phytosterols and probiotics. This diet is not exclusively confined to the Mediterranean Basin. Central Chile has a Mediterranean climate and our agriculture and culinary traditions are similar to those found in Mediterranean countries. Therefore, it is fundamental to increase awareness about the richness of our natural produce as well as our culinary culture, which may bring many health benefits and improve the quality of life in our population.

Vaghef-Mehrabany, E., Vaghef-Mehrabany, L., sghari-Jafarabadi, M., Homayouni-Rad, A., Issazadeh, K., and Alipour, B. Effects of probiotic supplementation on lipid profile of women with rheumatoid arthritis: A randomized placebo-controlled clinical trial. Health Promot.Perspect. 2017; 7(2):95-101; PM: 28326290

ABSTRACT: Background: Probiotics are live beneficial microorganisms which may exert hypolipidemic effects through many mechanisms. Lipid profile disturbances are frequently reported in rheumatoid arthritis (RA) patients. The objective of this study was to evaluate the effects of Lactobacillus casei on serum lipids of RA women. *Methods*: In the present parallel randomized double-blind placebo-controlled clinical trial, 60 RA patients were recruited and divided into 2 groups. They received either a daily capsule containing 108 CFU of L. casei 01, or identical capsules containing maltodextrin, for 8 weeks. Anthropometric parameters, dietary intake and physical activity were assessed at 2 ends of the study. Serum levels of total cholesterol (TC), high-density lipoprotein-cholesterol (HDL-C), low-density lipoprotein-cholesterol (LDL-C) and triglyceride (TG) were measured. Independent-samples t test and analysis of covariance (ANCOVA) test, and paired t test were used to test between- and within-group differences, respectively. *Results*: There were no significant between- or within-group differences for demographic and anthropometric parameters, physical activity and dietary intakes, throughout the study. No statistically significant within-group changes were observed for serum lipids in either group; between-group differences were also insignificant by the end of study period (TC: -0.18 [-0.65, 0.29], P = 0.801, HDL-C: -1.66 [-19.28, 15.59], P = 0.663, LDL-C: -2.73

[-19.17, 13.73], P = 0.666, TG: 0.12 [-19.76, 20.00], P = 0.900). *Conclusion*: Lactobacillus casei 01 could not improve serum lipids in RA patients. Further studies using probiotic foods and different probiotic strains are suggested.

Valcarce, D. G., Genoves, S., Riesco, M. F., Martorell, P., Herraez, M. P., Ramon, D., and Robles, V. Probiotic administration improves sperm quality in asthenozoospermic human donors. Benef.Microbes. 4-26-2017; 8(2):193-206; PM: 28343402

ABSTRACT: The objective of this study is to analyse the effect of the ingestion of two selected antioxidant probiotics strains (Lactobacillus rhamnosus CECT8361 and Bifidobacterium longum CECT7347) on sperm quality parameters in asthenozoospermic males after three and six weeks of administration. Nine asthenozoospermic men without any medical treatment under similar diet conditions participated in the study. The quality of individual sperm samples was evaluated before (previous to ingestion), during (after 3 and 6 weeks of ingestion) and after probiotic administration (3 and 6 weeks after finishing the treatment). Sperm motility was evaluated by computer-assisted sperm analysis system, DNA fragmentation by sperm chromatin structure assay, cell viability by flow cytometry and measurement of intracellular H2O2 (reactive oxygen species; ROS) by flow cytometry using dichloro-dihydrofluorescein diacetate. Sperm motility was drastically improved after the treatment (approximately 6 fold change), DNA fragmentation was statistically reduced after probiotic administration from (approximately 1.2 fold change) and intracellular H2O2 level was decreased (approximately 3.5 fold change). Cell viability was not affected by the treatment. The significant improvement in sperm motility and the decrease in DNA fragmentation reported in this study provide preliminary evidence that probiotics could be administrated to improve motility and decrease DNA fragmentation and ROS levels in asthenozoospermic human males.

Valdes-Varela, L., Ruas-Madiedo, P., and Gueimonde, M. In vitro fermentation of different fructo-oligosaccharides by Bifidobacterium strains for the selection of synbiotic combinations. Int.J.Food Microbiol. 2-2-2017; 242:19-23; PM: 27866040

ABSTRACT: The use of selected probiotics, prebiotics and/or synbiotics, constitute an interesting dietary strategy for intestinal microbiota modulation in case of dysbiosis. Species of the genus Bifidobacterium are among the most currently used probiotics for human consumption since they have shown beneficial effects in the prevention and treatment of some disorders. Bifidobacteria are saccharolytic microorganisms, but their ability to use different carbohydrates varies among strains. In this study, we investigate the utilization of three prebiotic substrates (two different short-chain fructo-oligosaccharides [scFOS] and inulin) by strains of Bifidobacterium, in order to determine the synbiotic potential of the different probiotic/prebiotic combinations. Batch culture fermentations from six Bifidobacterium strains (Bifidobacterium longum IPLA20021, B. longum IPLA20022, Bifidobacterium animalis IPLA20031, B. animalis IPLA20032, B. animalis IPLA20020 and B. animalis Bb12) were carried out in the presence of inulin or scFOS (Synergy or Actilight), or glucose, as carbon source. Bifidobacteria levels were quantified by plate counting. The pH and production of organic acids in the different batch-culture fermentations were also determined. Our results showed that all the studied strains of B. animalis and B. longum were able to utilize scFOS but not inulin. The use of scFOS as carbon source affected the pattern of metabolite's production, when compared with cultures carried out in glucose, particularly in the case of B. longum. The results indicated

that the scFOS are well suited to be used in combination with B. animalis or B. longum strains for the development of synbiotic foods or food supplements.

Valdovinos, M. A., Montijo, E., Abreu, A. T., Heller, S., Gonzalez-Garay, A., Bacarreza, D., Bielsa-Fernandez, M., Bojorquez-Ramos, M. C., Bosques-Padilla, F., Burguete-Garcia, A. I., Carmona-Sanchez, R., Consuelo-Sanchez, A., Coss-Adame, E., Chavez-Barrera, J. A., de, Arino M., Flores-Calderon, J., Gomez-Escudero, O., Gonzalez-Huezo, M. S., Icaza-Chavez, M. E., Larrosa-Haro, A., Morales-Arambula, M., Murata, C., Ramirez-Mayans, J. A., Remes-Troche, J. M., Rizo-Robles, T., Pelaez-Luna, M., Toro-Monjaraz, E. M., Torre, A., Urquidi-Rivera, M. E., Vazquez, R., Yamamoto-Furusho, J. K., and Guarner, F. The Mexican consensus on probiotics in gastroenterology. Rev.Gastroenterol.Mex. 2017; 82(2):156-178; PM: 28104319

ABSTRACT: INTRODUCTION: Probiotics are frequently prescribed in clinical practice. Their efficacy in treating gastrointestinal disorders is supported by a significant number of clinical trials. However, the correct prescription of these agents is hampered due to a lack of knowledge of the scientific evidence and to the different presentations and microbial compositions of the probiotics that are currently available. *AIM*: To provide the clinician with a consensus review of probiotics and recommendations for their use in gastroenterology. *MATERIALS AND METHODS*: Controlled clinical trials, meta-analyses, and systematic reviews published up to 2015 were selected, using the MESH terms: probiotics, gastrointestinal diseases, humans, adults, AND children. The Delphi method was employed. Eighteen gastroenterologists treating adult patients and 14 pediatric gastroenterologists formulated statements that were voted on until agreement>70% was reached. The level of evidence based on the GRADE system was evaluated for each statement. *RESULTS AND CONCLUSIONS*: Eleven statements on the general concepts of probiotics and 27 statements on the use of probiotics in gastrointestinal diseases in both adults and children were formulated. The consensus group recommends the use of probiotics under the following clinical conditions: the prevention of diarrhea associated with antibiotics, the treatment of acute infectious diarrhea, the prevention of Clostridium difficile infection and necrotizing enterocolitis, the reduction of adverse events from Helicobacter pylori eradication therapy, relief from irritable bowel syndrome symptoms, the treatment of functional constipation in the adult, and the induction and maintenance of remission in patients with ulcerative colitis and pouchitis, and the treatment of covert and overt hepatic encephalopathy.

Valeriano, V. D., Balolong, M. P., and Kang, D. K. Probiotic roles of Lactobacillus sp. in swine: insights from gut microbiota. J.Appl.Microbiol. 2017; 122(3):554-567; PM: 27914202

ABSTRACT: The use of lactobacilli as probiotics in swine has been gaining attention due to their ability to improve growth performance and carcass quality, prevent gastrointestinal infection and most importantly, their 'generally recognized as safe' status. Previous studies support the potential of lactobacilli to regulate host immune systems, enhance gut metabolic capacities and maintain balance in the gut microbiota. Research on swine gut microbiota has revealed complex gut microbial community structure and showed the importance of Lactobacillus to the host's health. However, the species- and strain-specific characteristics of lactobacilli that confer probiotic benefits are still not well understood. The diversity of probiotic traits in a complex gut ecosystem makes it challenging to infer the relationships between specific functions of Lactobacillus sp. and host health. In this review, we provide an overview of how lactobacilli play a

pivotal role in the swine gut ecosystem and identify key characteristics that influence gut microbial community structure and the health of pigs. In addition, based on recent and ongoing meta-omics and omics research on the gut microbiota of pigs, we suggest a workflow combining culture-dependent and culture-independent approaches for more effective selection of probiotic lactobacilli.

Valle Gottlieb, M. G., Closs, V. E., Junges, V. M., and Schwanke, C. H. Impact Of Human Aging And Modern Lifestyle On Microbiota. Crit Rev.Food Sci.Nutr. 1-13-2017; 0; PM: 28085494

ABSTRACT: Human evolution and lifestyle changes caused by the agricultural and industrial revolutions have led to great advances in medicine and increased life expectancy, whilst also profoundly altering the ecological relationships and disease patterns of populations. Studies involving populations that still enjoy a rural way of life and with traits similar to the Paleolithic period reveal them to present a more robust, resistant and diverse gut microbiota, in comparison to highly industrialized civilizations. The human diet has expanded and broadened to include the consumption of high-calorie foods, particularly from animal sources such as game, meat and eggs. For some time, the authors have been alert to the fact that a modern lifestyle leads to reduced intake of beneficial bacteria, suggesting that nonpathogenic bacteria are being eradicated. Furthermore, therapeutic procedures, including the use of probiotics and prebiotics, have been proposed to lead to recovery of this microbiota, which is altered due to both the ageing process and lifestyle related aspects. Accordingly, this article aims to review the impact of human aging and modern lifestyle on gut microbiota, within an evolutionary, ecological, epidemiological and therapeutic context.

van der Beek, C. M., Dejong, C. H., Troost, F. J., Masclee, A. A., and Lenaerts, K. Role of short-chain fatty acids in colonic inflammation, carcinogenesis, and mucosal protection and healing. Nutr.Rev. 4-10-2017; PM: 28402523

ABSTRACT: Short-chain fatty acids (SCFAs), mainly acetate, propionate, and butyrate, produced by microbial fermentation of undigested food substances are believed to play a beneficial role in human gut health. Short-chain fatty acids influence colonic health through various mechanisms. In vitro and ex vivo studies show that SCFAs have anti-inflammatory and anticarcinogenic effects, play an important role in maintaining metabolic homeostasis in colonocytes, and protect colonocytes from external harm. Animal studies have found substantial positive effects of SCFAs or dietary fiber on colonic disease, but convincing evidence in humans is lacking. Most human intervention trials have been conducted in the context of inflammatory bowel disease. Only a limited number of those trials are of high quality, showing little or no favorable effect of SCFA treatment over placebo. Opportunities for future research include exploring the use of combination therapies with anti-inflammatory drugs, prebiotics, or probiotics; the use of prodrugs in the setting of carcinogenesis; or the direct application of SCFAs to improve mucosal healing after colonic surgery.

Vanhaecke, T., Aubert, P., Grohard, P. A., Durand, T., Hulin, P., Paul-Gilloteaux, P., Fournier, A., Docagne, F., Ligneul, A., Fressange-Mazda, C., Naveilhan, P., Boudin, H., Le, Ruyet P., and Neunlist, M. L. fermentum CECT 5716 prevents stress-induced intestinal barrier dysfunction in newborn rats. Neurogastroenterol.Motil. 3-31-2017; PM: 28370715

ABSTRACT: BACKGROUND: Intestinal epithelial barrier (IEB) dysfunction plays a critical role in various intestinal disorders affecting infants and children, including the development of food allergies and colitis. Recent studies highlighted the role of probiotics in regulating IEB functions and behavior in adults, but their effects in the newborn remain largely unknown. We therefore characterized in rat pups, the impact of Lactobacillus fermentum CECT 5716 (L. fermentum) on stress-induced IEB dysfunction, systemic immune response and exploratory behavior. *METHODS*: Newborn rats received daily by gavage either L. fermentum or water. Intestinal permeability to fluorescein sulfonic acid (FSA) and horseradish peroxidase (HRP) was measured following maternal separation (MS) and water avoidance stress (WAS). Immunohistochemical, transcriptomic, and Western blot analysis of zonula occludens-1 (ZO-1) distribution and expression were performed. Anxiety-like and exploratory behavior was assessed using the elevated plus maze test. Cytokine secretion of activated splenocytes was also evaluated. KEY *RESULTS*: L. fermentum prevented MS and WAS-induced IEB dysfunction in vivo. L. fermentum reduced permeability to both FSA and HRP in the small intestine but not in the colon. L. fermentum increased expression of ZO-1 and prevented WAS-induced ZO-1 disorganization in ileal epithelial cells. L. fermentum also significantly reduced stress-induced increase in plasma corticosteronemia. In activated splenocytes, L. fermentum enhanced IFNgamma secretion while it prevented IL-4 secretion. Finally, L. fermentum increased exploratory behavior. *CONCLUSIONS & INFERENCES*: These results suggest that L. fermentum could provide a novel tool for the prevention and/or treatment of gastrointestinal disorders associated with altered IEB functions in the newborn.

Vasiee, A., Alizadeh, Behbahani B., Tabatabaei, Yazdi F., Mortazavi, S. A., and Noorbakhsh, H. Diversity and Probiotic Potential of Lactic Acid Bacteria Isolated from Horreh, a Traditional Iranian Fermented Food. Probiotics.Antimicrob.Proteins. 5-19-2017; PM: 28527125

ABSTRACT: The aim of this study was to evaluate the probiotic potential of lactic acid bacteria (LAB) strains isolated from Horreh. Some probiotic properties, e.g., resistance to acid, bile tolerance, antibacterial activity, and antibiotic susceptibility, were investigated. A total of 140 Gram-positive and catalase-negative isolates from Horreh were subjected to identification and grouping by cultural methods and the 16S rRNA sequencing. The new isolates were identified to be Lactobacillus (fermentum, plantarum, and brevis) Weissella cibaria, Enterococcus (faecium and faecalis), Leuconostoc (citreum and mesenteroides subsp. mesenteroides) and Pediococcus pentosaceus. Probiotic potential study of LAB isolates showed that Lb. plantarum and Leu. mesenteroides subsp. mesenteroides isolates were able to grow at pH 2.5 and 3.5. Lactobacillus plantarum (isolate A44) showed the highest cell hydrophobicity (84.5%). According to antibacterial activity tests, Listeria innocua and Staphylococcus aureus were the most sensitive indicators against the selected LAB strains, while Escherichia coli and Bacillus cereus were the most resistant. In addition, all the isolated LAB species were resistant to vancomycin. The results of the present study suggested that the Lactobacillus fermentum and plantarum isolated from Horreh, characterized in this study, have potential use for industrial purposes as probiotics.

Vemuri, R., Gundamaraju, R., and Eri, R. Role of lactic acid probiotic bacteria in IBD. Curr.Pharm.Des. 2-6-2017; PM: 28176664

ABSTRACT: BACKGROUND: IBD is considered as one of the major public health concerns

worldwide. The pathophysiology and gut microbial alteration during inflammatory bowel disease (IBD) are still not completely understood. Gut microbiota is implicated in most of the gastro-intestinal (GI) diseases including IBD. From the time of gut microbiota establishment and through aging, it undergoes a lot of changes in the composition. *METHODS*: In a healthy state, the composition of beneficial microbes in the gut is comparatively higher and due to factors such as malnutrition, use of antibiotics and any underlying diseases allow the colonization and invasion of pathogens. *RESULTS*: A careful manipulation of gut microbiota during disease conditions such as IBD is required. Probiotics are natural, safe and useful interventions for GI diseases. *CONCLUSION*: Lactic acid probiotic bacteria have shown many beneficial effects in various gastrointestinal and inflammatory disorders. This review focuses on the use of probiotics in IBD and possible mechanism of probiotics in inflammation conditions.

Vemuri, R. C., Gundamaraju, R., Shinde, T., and Eri, R. Therapeutic interventions for gut dysbiosis and related disorders in the elderly: antibiotics, probiotics or faecal microbiota transplantation? Benef.Microbes. 4-26-2017; 8(2):179-192; PM: 28008784

ABSTRACT: Ageing and physiological functions of the human body are inversely proportional to each other. The gut microbiota and host immune system co-evolve from infants to the elderly. Ageing is accompanied by a decline in gut microbial diversity, immunity and metabolism, which increases susceptibility to infections. Any compositional change in the gut is directly linked to gastrointestinal disorders, obesity and metabolic diseases. Increase in opportunistic pathogen invasion in the gut like Clostridium difficile leading to C. difficile infection is more common in the elderly population. Frequent hospitalisation and high prevalence of nosocomial infections with the ageing is also well documented. Long-term utilisation of broad-spectrum antibiotic therapy is being followed in order to control these infections. Nosocomial infections and antibiotic therapy in combination or alone is leading to gastroenteritis followed by Clostridium associated diarrhoea or antibiotic associated diarrhoea. Above all, use of broad-spectrum antibiotics is highly debated all over the world due to growing antimicrobial resistance. The use of narrow spectrum antibiotics could be helpful to some extent. Dietary supplementation of probiotics with prebiotics (synbiotics) or without prebiotics has improved gut commensal diversity and regulated the immune system. The recent emergence of faecal microbiota transplantation has played an important role in treating recurrent Clostridium associated diarrhoea. This review focuses on various therapeutic interventions for gut dysbiosis and gastrointestinal diseases in the elderly. The possible mechanism for antimicrobial resistance and mechanism of action of probiotics are also discussed in detail.

Venema, K. Foreword - Probiotics and prebiotics - important dietary components for health. Benef.Microbes. 2-7-2017; 8(1):1-2; PM: 28168883

No Abstract Available.

Vernaya, M., McAdam, J., and Hampton, M. D. Effectiveness of probiotics in reducing the incidence of Clostridium difficile-associated diarrhea in elderly patients: a systematic review. JBI.Database.System.Rev.Implement.Rep. 2017; 15(1):140-164; PM: 28085732

ABSTRACT: BACKGROUND: Clostridium difficile bacteria are a leading cause of infectious

diarrhea. This is an anaerobic, gram-positive and spore-forming rod responsible for significant morbidity and mortality, especially among elderly hospitalized patients. Standard management of C. difficile-associated diarrhea (CDAD) consists of discontinuing a causative antibiotic, correcting fluid-electrolytes imbalance and initiating an antibiotic treatment for CDAD. Alternative approaches for prevention of CDAD include probiotics. This systematic review will provide a comprehensive, unbiased summary of the available research on the effectiveness of probiotics in decreasing the incidence of infectious diarrhea in elderly hospitalized patients. *OBJECTIVES*: To conduct a systematic review to determine the best available evidence related to the effectiveness of probiotics in the prevention of CDAD in elderly hospitalized patients. The review question was: are probiotics effective in decreasing the incidence of CDAD in elderly hospitalized patients? *INCLUSION CRITERIA TYPES OF PARTICIPANTS*: The current review included studies of participants who were aged 60 years and more and who were residents of acute- and post-acute care facilities undergoing or planning to undergo antibiotic treatment for the management of any infectious conditions, except CDAD. *TYPES OF INTERVENTION(S):* The current review included studies that evaluated the effectiveness of probiotics for prevention of CDAD in elderly hospitalized patients in acute- and post-acute care settings compared to usual care. OUTCOMES: The current review included studies examining the following outcome measures: incidence or relapse of CDAD. Cases of CDAD were defined by presence of diarrhea and verified by positive results for stool enzyme immunoassay for toxins A and B. *TYPES OF STUDIES*: The current review included only experimental study designs including randomized controlled trials. *SEARCH STRATEGY*: The search strategy included studies published in English between 1978, when the first case of CDAD was reported, and 2015. *ASSESSMENT OF METHODOLOGICAL QUALITY*: Papers selected for retrieval were assessed by two independent reviewers for methodological quality prior to inclusion in the review using standardized critical appraisal instruments from the Joanna Briggs Institute (JBI). *DATA EXTRACTION*: Data were extracted from papers included in the review using the standardized data extraction tool from the JBI Meta-Analysis of Statistics Assessment and Review Instrument. The data extracted included specific details about the interventions, populations, study methods and outcomes of significance to the review question and specific objectives. *DATA SYNTHESIS*: Quantitative data were pooled using statistical meta-analysis. Effect sizes were expressed as odds ratios, and their 95% confidence intervals were calculated to determine if probiotic treatment was superior to placebo in reducing CDAD incidence. Heterogeneity was assessed using the standard I statistic. *RESULTS*: Five studies were included in the review. The individual study results were conflicting, including non-significant results for four studies and statistically significant results in one that demonstrated fewer cases of CDAD among patients receiving probiotics compared to placebo. The meta-analysis finding indicated that there was no statistically significant difference in CDAD incidence in elderly hospitalized patients taking probiotics when compared to a placebo. *CONCLUSION*: Probiotics were not found to be more effective than placebo for reducing CDAD incidence in elderly hospitalized patients. However, studies that demonstrate improved outcomes must be examined to determine future needs for research. Studies varied with regard to the dose, frequency, method of administration (probiotic drinks versus capsule), length of administration and the number of strains of bacteria administered. Further studies are needed to evaluate the effectiveness of probiotics for CDAD prevention in this population. Clinical trials with evidence-based administration methods and meta-analyses that pool the results of studies with congruent methodologies are needed to enable conclusions to be drawn on the effectiveness of probiotic administration for CDAD prevention.

Villa, C. R., Ward, W. E., and Comelli, E. M. Gut microbiota-bone axis. Crit Rev.Food Sci.Nutr. 5-24-2017; 57(8):1664-1672; PM: 26462599

ABSTRACT: The gut microbiota (GM) is an important regulator of body homeostasis, including intestinal and extra-intestinal effects. This review focuses on the GM-bone axis, which we define as the effect of the gut-associated microbial community or the molecules they synthesize, on bone health. While research in this field is limited, findings from preclinical studies support that gut microbes positively impact bone mineral density and strength parameters. Moreover, administration of beneficial bacteria (probiotics) in preclinical models has demonstrated higher bone mineralization and greater bone strength. The preferential bacterial genus that has shown these beneficial effects in bone is Lactobacillus and thus lactobacilli are among the best candidates for future clinical intervention trials. However, their effectiveness is dependent on stage of development, as early life constitutes an important time for impacting bone health, perhaps via modulation of the GM. In addition, sex-specific difference also impacts the efficacy of the probiotics. Although auspicious, many questions regarding the GM-bone axis require consideration of potential mechanisms; sex-specific efficacy; effective dose of probiotics; and timing and duration of treatment.

Viramontes, Horner D., Avery, A., and Stow, R. The Effects of Probiotics and Symbiotics on Risk Factors for Hepatic Encephalopathy: A Systematic Review. J.Clin.Gastroenterol. 2017; 51(4):312-323; PM: 28059938

ABSTRACT: Alterations in the levels of intestinal microbiota, endotoxemia, and inflammation are novel areas of interest in the pathogenesis of hepatic encephalopathy (HE). Probiotics and symbiotics are a promising treatment option for HE due to possible beneficial effects in modulating gut microflora and might be better tolerated and more cost-effective than the traditional treatment with lactulose, rifaximin or L-ornithine-L-aspartate. A systematic search of the electronic databases PubMed, ISI Web of Science, EMBASE, and Cochrane Library was conducted for randomized controlled clinical trials in adult patients with cirrhosis, evaluating the effect of probiotics and symbiotics in changes on intestinal microflora, reduction of endotoxemia, inflammation, and ammonia, reversal of minimal hepatic encephalopathy (MHE), prevention of overt hepatic encephalopathy (OHE), and improvement of quality of life. Nineteen trials met the inclusion criteria. Probiotics and symbiotics increased beneficial microflora and decreased pathogenic bacteria and endotoxemia compared with placebo/no treatment, but no effect was observed on inflammation. Probiotics significantly reversed MHE [risk ratio, 1.53; 95% confidence interval (CI): 1.14, 2.05; P=0.005] and reduced OHE development (risk ratio, 0.62; 95% CI: 0.48, 0.80; P=0.0002) compared with placebo/no treatment. Symbiotics significantly decreased ammonia levels compared with placebo (15.24; 95% CI: -26.01, -4.47; P=0.006). Probiotics did not show any additional benefit on reversal of MHE and prevention of OHE development when compared with lactulose, rifaximin, and L-ornithine-L-aspartate. Only 5 trials considered tolerance with minimal side effects reported. Although further research is warranted, probiotics and symbiotics should be considered as an alternative therapy for the treatment and management of HE given the results reported in this systematic review.

Viswanathan, S., Lau, C., Akbari, H., Hoyen, C., and Walsh, M. C. Survey and evidence based review of probiotics used in very low birth weight preterm infants within the United States. J.Perinatol. 2017; 37(1):104; PM: 28050019

No Abstract Available.

Vitetta, L., Coulson, S., Thomsen, M., Nguyen, T., and Hall, S. Gut Microbes manuscript type: Commentary and views submission probiotics, D-Lactic acidosis, oxidative stress and strain specificity. Gut Microbes. 1-12-2017; 1-12; PM: 28080206

ABSTRACT: The existence of an implicit living microscopic world, composed primarily of bacteria, has been known for centuries. The exact mechanisms that govern the contribution of bacteria to human health and disease have only recently become the subject of intense research efforts. Within this very evident shift in paradigms, the rational design of probiotic formulations has led to the creation of an industry that seeks to progress the engineering of probiotic bacteria that produce metabolites that may enhance human host health and prevent disease. The promotion of probiotics is often made in the absence of quality scientific and clinically plausible data. The latest incursions into the probiotic market of claims have posited the amelioration of oxidative stress via potent antioxidant attributes or limiting the administration of probiotics to those species that do not produce D-Lactic acid (i.e., claims that D-Lactic acid acidosis is linked to chronic health conditions) or are strain-specific (shaping an industry point of difference) for appraising a therapeutic effect. Evidence-based research should guide clinical practice, as there is no place in science and medicine that supports unsubstantiated claims. Extravagant industry based notions continue to fuel the imprimatur of distrust and skepticism that is leveled by scientists and clinicians at an industry that is already rife with scientific and medical distrust and questionable views on probiotics. Ignoring scientifically discordant data, when sorting through research innovations and false leads relevant to the actions of probiotics, drives researcher discomfit and keeps the bar low, impeding the progress of knowledge. Biologically plausible posits are obligatory in any research effort; companies formulating probiotics often exhibit a lack of analytical understanding that then fuels questionable investigations failing to build on research capacity.

Vitko, H. A., Sekula, L. K., and Schreiber, M. A. Probiotics for Trauma Patients: Should We Be Taking a Precautionary Approach? J.Trauma Nurs. 2017; 24(1):46-52; PM: 28033143

ABSTRACT: The use of probiotics in the hospital setting is largely understudied and highly controversial. Probiotics are living organisms that, when taken internally, can produce an immunomodulating effect and improve the gastrointestinal (GI) mucosal barrier. Although used for centuries by healthy individuals for GI health, their use in the hospital setting is now gaining wide attention for the prevention of infectious complications such as antibiotic-associated diarrhea, Clostridium difficile infections, multiple-organ dysfunction syndrome, and ventilator-associated pneumonia. However, current understanding of the efficacy of probiotics in the acute care setting is confounded by the inconsistencies in the literature with regard to the strain of probiotic being studied, optimal dosage, and timing and duration of dosing, which make the formulation of clinical practice guidelines difficult. Although the safety of probiotics has been confirmed when used for the prevention and treatment of certain diseases, practitioners remain hesitant to administer them to their patients, citing the lack of high-quality studies clearly demonstrating efficacy and safety. Infection is a cause of late death in trauma patients, but only recently has research been conducted on the use of probiotics specifically for the prevention of hospital-acquired infections in trauma patients. In the face of such

limited but promising research, is it reasonable to use probiotics for the prevention of infection in hospitalized trauma patients and improve outcomes? Use of the "precautionary principle" may be useful in this instance.

Vogt, S. L. and Finlay, B. B. Gut microbiota-mediated protection against diarrheal infections. J.Travel.Med. 4-1-2017; 24(suppl_1):S39-S43; PM: 28520994

ABSTRACT: Background: The mammalian gut microbiota is a highly abundant and diverse microbial community that resides in the gastrointestinal tract. One major benefit that the gut microbiota provides to its host is colonization resistance-the ability to prevent colonization by foreign microbes, including diarrheal pathogens such as Clostridium difficile , Salmonella enterica serovar Typhimurium and diarrheagenic Escherichia coli . *Methods*: We conducted a literature review of the effects of the gut microbiota on infection by diarrheal pathogens. We used PubMed to search for relevant articles published before July 2016, as well as incorporated data from our laboratory. *Results*: The gut microbiota provides protection from diarrheal infections both by direct inhibition of pathogens and by indirect effects on host functions. Direct effects of the microbiota on diarrheal pathogens include competing for nutrients and producing metabolites that inhibit pathogen growth or virulence. Indirect effects of the gut microbiota include promoting maintenance of the gut mucosal barrier and stimulating innate and adaptive immunity. *Conclusions*: Human epidemiological studies and experimental infections of laboratory animals both demonstrate that antibiotic treatment can alter the gut microbial community and thereby reduce colonization resistance against diarrheal pathogens. Further research might lead to the development of next-generation probiotics that could be used to bolster colonization resistance and thus prevent travellers' diarrheal. Introduction.

Wallace, C. J. K. and Milev, R. The effects of probiotics on depressive symptoms in humans: a systematic review. Ann.Gen.Psychiatry. 2017; 16:14; PM: 28239408

ABSTRACT: BACKGROUND: Patients suffering from depression experience significant mood, anxiety, and cognitive symptoms. Currently, most antidepressants work by altering neurotransmitter activity in the brain to improve these symptoms. However, in the last decade, research has revealed an extensive bidirectional communication network between the gastrointestinal tract and the central nervous system, referred to as the "gut-brain axis." Advances in this field have linked psychiatric disorders to changes in the microbiome, making it a potential target for novel antidepressant treatments. The aim of this review is to analyze the current body of research assessing the effects of probiotics, on symptoms of depression in humans. *METHODS*: A systematic search of five databases was performed and study selection was completed using the preferred reporting items for systematic reviews and meta-analyses process. *RESULTS*: Ten studies met criteria and were analyzed for effects on mood, anxiety, and cognition. Five studies assessed mood symptoms, seven studies assessed anxiety symptoms, and three studies assessed cognition. The majority of the studies found positive results on all measures of depressive symptoms; however, the strain of probiotic, the dosing, and duration of treatment varied widely and no studies assessed sleep. *CONCLUSION*: The evidence for probiotics alleviating depressive symptoms is compelling but additional double-blind randomized control trials in clinical populations are warranted to further assess efficacy.

Wallace, C. J. K. and Milev, R. Erratum to: The effects of probiotics on depressive symptoms in humans: a systematic review. Ann.Gen.Psychiatry. 2017; 16:18; PM: 28286538

ABSTRACT: [This corrects the article DOI: 10.1186/s12991-017-0138-2.].

Walsh, A. M., Crispie, F., Claesson, M. J., and Cotter, P. D. Translating Omics to Food Microbiology. Annu.Rev.Food Sci.Technol. 2-28-2017; 8:113-134; PM: 28125344

ABSTRACT: This review examines the applications of omics technologies in food microbiology, with a primary focus on high-throughput sequencing (HTS) technologies. We discuss the different sequencing approaches applicable to the study of food-related microbial isolates and mixed microbial communities in foods, and we provide an overview of the sequencing platforms suitable for each approach. We highlight the potential for genomics, metagenomics, and metatranscriptomics to guide efforts to optimize food fermentations. Additionally, we explore the use of comparative and functional genomics to further our understanding of the mechanisms of probiotic action and we describe the applicability of HTS as a food safety measure. Finally, we consider the use of HTS to investigate the effects that ingested microbes have on the human gut microbiota.

Wanchai, K., Pongchaidecha, A., Chatsudthipong, V., Chattipakorn, S. C., Chattipakorn, N., and Lungkaphin, A. Role of Gastrointestinal Microbiota on Kidney Injury and the Obese Condition. Am.J.Med.Sci. 2017; 353(1):59-69; PM: 28104104

ABSTRACT: Obesity is associated with kidney disease, probably due to obesity-mediated inflammation, podocyte injury and oxidative stress in the kidney It is also linked to other diseases, for example, diabetes and hypertension, which are associated with the development and progression of chronic kidney disease. Interestingly, gastrointestinal dysbiosis has been demonstrated in cases of obesity with the development and progression of kidney disease. Thus, modification of gastrointestinal microbiota using probiotics or prebiotics or both to improve the balance of bacterial flora is a potential approach for the management of obesity-associated kidney disease. This review covers information regarding the association between obesity and kidney injury, and it examines evidence for a hypothesized role of gastrointestinal microbiota in this setting. Studies describing the effects of probiotic and prebiotic treatments on kidney disease show mixed results, although several suggest benefits indicated by biomarkers associated with kidney injury, uremia and inflammation. Additional studies are needed to determine whether these interventions are clinically effective in managing kidney injury and kidney disease.

Wang, B., Chen, J., Wang, S., Zhao, X., Lu, G., and Tang, X. Lactobacillus plantarum L9 but not Lactobacillus acidophilus LA reduces tumour necrosis factor induced bacterial translocation in Caco-2 cells. Benef.Microbes. 4-26-2017; 1-10; PM: 28441885

ABSTRACT: Translocation of bacteria across the intestinal barrier is important in the pathogenesis of systemic sepsis and multiple organ dysfunction syndromes. Inflammatory cytokines increase paracellular permeability that allows increased luminal bacteria to translocate across mucosal epithelium and further deteriorate the gut barrier. In order to reduce this risk, the prophylactic use of probiotics has been recently addressed. In this

paper, we investigate the protective role toward tumour necrosis factor (TNF)-alpha induced non-pathogenic Escherichia coli translocation across Caco-2 monolayers of Lactobacillus strains. According to our experimental data, Lactobacillus plantarum L9 and Lactobacillus acidophilus LA have good capacities to adhere to Caco-2 cells. Addition of L. plantarum L9 and L. acidophilus LA to the enterocyte monolayer surface result in significant inhibition of E. coli adhesion and cell internalisation. However, L. plantarum L9 and L. acidophilus LA did not inhibit the growth of the non-pathogenic E. coli B5 after 24 h incubation. Exposure to TNF-alpha for 6 h caused a dramatic increase in E. coli B5 translocation across Caco-2 cells, which was uncoupled from increases in paracellular permeability. Pretreatment with L. plantarum L9 prevent TNF-alpha induced transcellular bacterial translocation and IL-8 production in Caco-2 cells. L. plantarum L9 also did not affect the integrity of the monolayers, as indicated by lactate dehydrogenase release, horseradish peroxidase permeability, and transepithelial electrical resistance. L. plantarum L9 showed the potential to protect enterocytes from an acute inflammatory response and therefore could be good potential prophylactic agents in counteracting bacterial translocation.

Wang, H., Jatmiko, Y. D., Bastian, S. E., Mashtoub, S., and Howarth, G. S. Effects of Supernatants from Escherichia coli Nissle 1917 and Faecalibacterium prausnitzii on Intestinal Epithelial Cells and a Rat Model of 5-Fluorouracil-Induced Mucositis. Nutr.Cancer. 2017; 69(2):307-318; PM: 28094590

ABSTRACT: Faecalibacterium prausnitzii (Fp) and Escherichia coli Nissle 1917 (EcN) are probiotics, which have been reported to ameliorate certain gastrointestinal disorders. We evaluated the effects of supernatants (SN) derived from Fp and EcN on 5-fluorouracil (5-FU)-treated intestinal cells and in a rat model of mucositis. In vitro: IEC-6, Caco-2, and T-84 cells were analyzed for viability and monolayer permeability. In vivo: Female dark agouti rats were gavaged with Fp or EcN SN and injected intraperitoneally with saline (control) or 5-FU to induce mucositis. Rats were euthanized and intestinal tissues collected for myeloperoxidase assay and histological analyses. In vitro: Caco-2 cell viability was further reduced when treated with Fp SN + 5-FU compared to 5-FU controls. In both Caco-2 and T-84 cells, Fp SN partially prevented the decrease in transepithelial electrical resistance (TER) caused by 5-FU administration. In vivo: 5-FU-injected rats administered Fp SN or EcN SN partly prevented body weight loss and normalized water intake compared to 5-FU controls. These results suggest a growth inhibitory mechanism of Fp SN action on transformed epithelial cells that could be mediated by effects on tight junctions. Factors derived from Fp SN and EcN SN could have a role in reducing the severity of intestinal mucositis.

Wang, L., Si, W., Xue, H., and Zhao, X. A fibronectin-binding protein (FbpA) of Weissella cibaria inhibits colonization and infection of Staphylococcus aureus in mammary glands. Cell Microbiol. 1-26-2017; PM: 28125161

ABSTRACT: Staphylococcus aureus (S. aureus) is a frequent cause of infections in both humans and animals. Probiotics are known to inhibit colonization of pathogens on host tissues. However, mechanisms for the inhibition are still elusive due to complex host-microbe and microbe-microbe interactions. Here, we show that reduced abilities of S. aureus to infect mammary glands in the presence of Weissella cibaria (W. cibaria) were correlated with its poor adherence to mammary epithelial cells. Such inhibition by W.

cibaria isolates was at least partially attributed to a fibronectin-binding protein (FbpA) on this lactic acid bacterium. Three W. cibaria isolates containing fbpA had higher inhibitory abilities than other three LAB isolates without the gene. The fbpA-deficient mutant of W. cibaria isolate LW1, LW1DeltafbpA, lost the inhibitory activity to reduce the adhesion of S. aureus to mammary epithelial cells and was less able to reduce the colonization of S. aureus in mammary glands. Expression of FbpA to the surface of LW1DeltafbpA reversed its inhibitory activities. Furthermore, addition of purified FbpA inhibited S. aureus biofilm formation. Our results suggest that W. cibaria FbpA hinders S. aureus colonization and infection through interfering with the S. aureus invasion pathway mediated by fibronectin-binding proteins and inhibiting biofilm formation of S. aureus.

Wang, W., Xin, H., Fang, X., Dou, H., Liu, F., Huang, D., Han, S., Fei, G., Zhu, L., Zha, S., Zhang, H., and Ke, M. Isomalto-oligosaccharides ameliorate visceral hyperalgesia with repair damage of ileal epithelial ultrastructure in rats. PLoS.One. 2017; 12(4):e0175276; PM: 28437458

ABSTRACT: BACKGROUND: Treatment of irritable bowel syndrome (IBS) with probiotics has achieved effectiveness to a certain extent. Whether prebiotics will work is still unclear. This study aimed to investigate the therapeutic effects of the prebiotic isomalto-oligosaccharides (IMO) on visceral hypersensitivity (VHS) in rats and to explore potential mechanism. *METHODS*: Water avoidance stress (WAS) was used to induce VHS in rats. The score for the abdominal withdrawal reflex (AWR) was determined while colorectal distension and compared between VHS group and control group in order to validate VHS preparation. Rats with VHS were then divided into an IMO-treated group (intragastric 5% IMO, 2 mL/d, 14 days) and a water-control group (intragastric water). After treatment, AWR score and intestinal transit rate (ITR) were determined, stool culture was performed, the ultrastructure of the ileum epithelium was observed with scanning electron microscopy (SEM), and serum cytokines were measured. *RESULTS*: WAS significantly increased AWR score responding to colorectal distension, and lowered the pain threshold. IMO treatment improved VHS with a reduction in AWR score on graded colorectal distension and an increase in pain threshold. SEM showed damages on the ileal epithelial ultrastructure in VHS rats, which was attenuated by IMO treatment. ITR, fecal microbiota and serum cytokine levels were comparable among control group, water-control group, and IMO-treated rats. *CONCLUSION*: In this randomized placebo-controlled study, the results showed that IMO ameliorated WAS-induced visceral hyperalgesia in rats, this effect may be attributed to the repair of damages on intestinal epithelial ultrastructure.

Wang, Y., Wu, Y., Wang, Y., Fu, A., Gong, L., Li, W., and Li, Y. Bacillus amyloliquefaciens SC06 alleviates the oxidative stress of IPEC-1 via modulating Nrf2/Keap1 signaling pathway and decreasing ROS production. Appl.Microbiol.Biotechnol. 2017; 101(7):3015-3026; PM: 27957629

ABSTRACT: Oxidative stress (OS) plays a major role in the gastrointestinal disorders. Although probiotics were reported to repress OS, few researches compared the antioxidant ability of different Bacillus strains and deciphered the mechanisms. To select a Bacillus strain with higher antioxidant capacity, we used H2O2 to induce intestinal porcine epithelial cell 1 (IPEC-1) OS model. The most suitable H2O2 concentration and incubation time were determined by the half lethal dose and methyl thiazolyl tetrazolium. Correlation analysis was performed to choose a sensitive indicator for OS. As

for the comparison of Bacillus, cells were divided into control, Bacillus treatment, H2O2 treatment, and Bacillus pre-protection + H2O2 treatment. Bacillus were co-cultured with IPEC-1 for 3 h in Bacillus and Bacillus pre-protection + H2O2 treatments. Then, based on OS model, 300 mumol/L H2O2 was added into medium of H2O2 and Bacillus pre-protection + H2O2 treatments for another 12 h. Antioxidant and apoptosis gene expressions were detected to screen the target strain. Nuclear factor erythroid-derived 2-related factor 2 (Nrf2)/Kelch-like ECH-associated protein1 (Keap1) pathway, reactive oxygen species (ROS) production, mitochondrial membrane potential (Deltapsim), apoptosis, and necrosis were analyzed. Results revealed that heme oxygenase-1 (HO-1) gene expression had a positive correlation with H2O2 induction. Moreover, Bacillus amyloliquefaciens SC06 (SC06)-meditated IPEC-1 showed the best antioxidant capacity though modulating Nrf2 phosphorylation. Deltapsim was elevated, while ROS generation was reduced with SC06 pre-protection, resulting in decreased apoptosis and necrosis. Altogether, HO-1 expression could be regarded as an OS indicator. The regulation of Nrf2/Keap1 pathway and ROS production by SC06 are involved in alleviating OS of IPEC-1.

Warland, J., Mitchell, E. A., and O'Brien, L. M. Novel strategies to prevent stillbirth. Semin.Fetal Neonatal Med. 2-2-2017; PM: 28162972

ABSTRACT: This article reviews three new and emerging risk factors for stillbirth that may be modifiable or might identify a compromised fetus. We focus on fetal movements, maternal sleep, and maternal diet. Recent studies have suggested than a sudden increase in vigorous fetal activity may be associated with increased risk of stillbirth. We review the papers that have reported this finding and discuss the implications as well as potential future directions for research. There is emerging literature to suggest that maternal sleep position may be a risk for stillbirth, especially if the woman settles to sleep supine. This risk is biologically plausible. How this knowledge may be utilized to assist stillbirth reduction strategies is discussed. Finally, we examine the somewhat limited literature regarding maternal diet and pregnancy outcome. Introducing probiotics into the diet may prove useful, but further work is required. The possible next steps for research are considered, as well as some potential intervention strategies that may ultimately lead to stillbirth reduction.

Watson, S. Meibomian gland disease and the microbiotome: is it time for ocular probiotics? Clin.Exp.Ophthalmol. 2017; 45(2):103-104; PM: 28297170

No Abstract Available.

Wei, C. Y., Liao, N. B., Zhang, Y., Ye, X. Q., Li, S., Hu, Y. Q., Liu, D. H., Linhardt, R. J., Wang, X., and Chen, S. G. In vitro fermentation behaviors of fucosylated chondroitin sulfate from Pearsonothuria graeffei by human gut microflora. Int.J.Biol.Macromol. 4-18-2017; 102:1195-1201; PM: 28431945

ABSTRACT: A fucosylated chondroitin sulfate (FCS-pg) with highly repeated structure from Pearsonothuria graeffei was subjected to a in vitro fermentation model to investigate its fermentability and effects on human gut microflora. High performance liquid chromatography (HPLC) measurement found FCS-pg can be fermented to short chain fatty acids (SCFAs) by gut microflora from partial human fecal samples. 16S rRNA gene-

based polymerase chain reaction-based denaturing gradient gel electrophoresis (PCR-DGGE) profiling and real-time quantitative PCR analysis showed that FCS-pg mainly increased the proportions of Clostridium cluster XI, Bacteriodes prevotella group, Bifidobacterium genus, Clostridium cluster I and Clostridium cluster XIVab, whereas the numbers of the Enterobacteriaceae and Lactobacillus decreased. These results indicated that FCS-pg was mainly fermented by Bacteroides, Bifidobacterium and Clostridium. It increased the content of probiotics bacteria in achieving health-enhancing effect, was slightly different than most sulfated polysaccharides from marine animals. The current study provides useful new information on the mechanism of absorption and functional activity on FCS-pg within the gastrointestinal tract of the human body.

Wei, Z., Tan, B., Cao, S., Liu, S., Tan, X., Yao, Z., Yin, N., Li, J., Zhang, D., and Zhou, Y. The influence of neoadjuvant chemotherapy on gastric cancer patients' postoperative infectious complications: What is the negative role played by the intestinal barrier dysfunction? Oncotarget. 1-18-2017; PM: 28118611

ABSTRACT: Evidence has shown that neoadjuvant chemotherapy (NACT) is correlated with patients' overall postoperative complications. But investigations on relationship between NACT and postoperative infectious complications, which is closely linked to intestinal barrier damage, were scanty. Accordingly, 90 patients with advanced gastric cancer were included in this study. The differences in postoperative infectious complications were determined between NACT group in which patients received NACT before surgery and SURG group in which received surgical treatment immediately after diagnosis. The damage of mechanical structure of intestinal barrier was assessed by hematoxylin and eosin staining, transmission electron microscopy, and immunohistochemistry. Mucosal microbiota changes were determined by using a 16S rRNA gene sequencing approach. Results showed that the incidence of postoperative infectious complications were significantly higher in the NACT group. Tight junctions were disrupted, and claudin-1, ZO-1 and occludin were down-regulated in patients with infectious complications in overall compared with those without. And similarly, the patients in the NACT group also showed damaged intestinal barrier compared with those in SURG group. Besides, the total diversity of mucosal related bacteria was decreased and relative abundance of some probiotics, such as Bifidobacterium, Faecalibacterium and Ruminococcus, was reduced in the NACT group as well. In conclusion, our study identifies a higher incidence of postoperative infection in gastric cancer patients who underwent NACT treatment, and these changes might be caused by a significant damage in the intestinal barrier as well as reduced probiotics.

Weng, F. C., Shaw, G. T., Weng, C. Y., Yang, Y. J., and Wang, D. Inferring Microbial Interactions in the Gut of the Hong Kong Whipping Frog (Polypedates megacephalus) and a Validation Using Probiotics. Front Microbiol. 2017; 8:525; PM: 28424669

ABSTRACT: The concerted activity of intestinal microbes is crucial to the health and development of their host organisms. Investigation of microbial interactions in the gut should deepen our understanding of how these micro-ecosystems function. Due to advances in Next Generation Sequencing (NGS) technologies, various bioinformatic strategies have been proposed to investigate these microbial interactions. However, due to the complexity of the intestinal microbial community and difficulties in monitoring their interactions, at present there is a gap between the theory and biological application. In

order to construct and validate microbial relationships, we first induce a community shift from simple to complex by manipulating artificial hibernation (AH) in the treefrog Polypedates megacephalus. To monitor community growth and microbial interactions, we further performed a time-course screen using a 16S rRNA amplicon approach and a Lotka-Volterra model. Lotka-Volterra models, also known as predator-prey equations, predict the dynamics of microbial communities and how communities are structured and sustained. An interaction network of gut microbiota at the genus level in the treefrog was constructed using Metagenomic Microbial Interaction Simulator (MetaMIS) package. The interaction network obtained had 1,568 commensal, 1,737 amensal, 3,777 mutual, and 3,232 competitive relationships, e.g., Lactococcus garvieae has a commensal relationship with Corynebacterium variabile. To validate the interacting relationships, the gut microbe composition was analyzed after probiotic trials using single strain (L. garvieae, C. variabile, and Bacillus coagulans, respectively) and a combination of L. garvieae, C. variabile, and B. coagulans, because of the cooperative relationship among their respective genera identified in the interaction network. After a 2 week trial, we found via 16S rRNA amplicon analysis that the combination of cooperative microbes yielded significantly higher probiotic concentrations than single strains, and the immune response (interleukin-10 expression) also significantly changed in a manner consistent with improved probiotic effects. By taking advantage of microbial community shift from simple to complex, we thus constructed a reliable microbial interaction network, and validated it using probiotic strains as a test system.

Wickens, K. L., Barthow, C. A., Murphy, R., Abels, P. R., Maude, R. M., Stone, P. R., Mitchell, E. A., Stanley, T. V., Purdie, G. L., Kang, J. M., Hood, F. E., Rowden, J. L., Barnes, P. K., Fitzharris, P. F., and Crane, J. Early pregnancy probiotic supplementation with Lactobacillus rhamnosus HN001 may reduce the prevalence of gestational diabetes mellitus: a randomised controlled trial. Br.J.Nutr. 2017; 117(6):804-813; PM: 28367765

ABSTRACT: The study aims to assess whether supplementation with the probiotic Lactobacillus rhamnosus HN001 (HN001) can reduce the prevalence of gestational diabetes mellitus (GDM). A double-blind, randomised, placebo-controlled parallel trial was conducted in New Zealand (NZ) (Wellington and Auckland). Pregnant women with a personal or partner history of atopic disease were randomised at 14-16 weeks' gestation to receive HN001 (6x109 colony-forming units) (n 212) or placebo (n 211) daily. GDM at 24-30 weeks was assessed using the definition of the International Association of Diabetes and Pregnancy Study Groups (IADPSG) (fasting plasma glucose >/=5.1 mmol/l, or 1 h post 75 g glucose level at >/=10 mmol/l or at 2 h >/=8.5 mmol/l) and NZ definition (fasting plasma glucose >/=5.5 mmol/l or 2 h post 75 g glucose at >/=9 mmol/l). All analyses were intention-to-treat. A total of 184 (87 %) women took HN001 and 189 (90 %) women took placebo. There was a trend towards lower relative rates (RR) of GDM (IADPSG definition) in the HN001 group, 0.59 (95 % CI 0.32, 1.08) (P=0.08). HN001 was associated with lower rates of GDM in women aged >/=35 years (RR 0.31; 95 % CI 0.12, 0.81, P=0.009) and women with a history of GDM (RR 0.00; 95 % CI 0.00, 0.66, P=0.004). These rates did not differ significantly from those of women without these characteristics. Using the NZ definition, GDM prevalence was significantly lower in the HN001 group, 2.1 % (95 % CI 0.6, 5.2), v. 6.5 % (95 % CI 3.5, 10.9) in the placebo group (P=0.03). HN001 supplementation from 14 to 16 weeks' gestation may reduce GDM prevalence, particularly among older women and those with previous GDM.

Wiest, R., Albillos, A., Trauner, M., Bajaj, J., and Jalan, R. 'Targeting the gut-liver axis in liver disease'. J.Hepatol. 5-16-2017; PM: 28526488

ABSTRACT: The gut is open to the outer environment, harbours the microbiome containing several fold more genetic material than the human genome and produces a myriad of metabolites as well as hormones/peptides. The liver is at the nexus between this vast source of nutrients, toxins and hormones and the remaining human body. Not surprisingly, this liver-gut-axis has hence, been demonstrated in experimental models and in-vitro systems to contribute to the pathogenesis of most liver diseases such as alcoholic and non-alcoholic fatty liver disease (NAFLD), -steatohepatitis (NASH), cholestatic liver diseases, hepatocellular carcinoma, acute-on-chronic liver failure, progression to fibrosis/cirrhosis and complications of cirrhosis. Therapeutic approaches can be grouped into modulation of the microbiota, the bile acid pool and/or its signaling, gut-lumen adsorptive strategies, bariatric procedures, incretins and miscellaneous (e.g.prokinetics). However, in order to proof these concepts investigations in humans are key and thus, this article will highlight the most recent human studies and clinical trials targeting the liver-gut-axis. A list of ongoing (not yet published) trials is presented in table 1. Moreover, we will take the liberty to encourage clinical trials on concepts that are so far not yet established.

Williamson, C. B., Burns, C. M., Gossard, C. M., Pizano, J. M., Dolan, K. E., Finley, H. J., Gasta, M. G., Parker, E. C., and Lipski, E. A. Probiotics and Disease: A Comprehensive Summary-Part 3, Cardiometabolic Disease and Fatigue Syndromes. Integr.Med.(Encinitas.). 2017; 16(1):30-41; PM: 28223906

ABSTRACT: This article series provides a literature review of the disease-specific probiotic strains, associated with cardiometabolic diseases and fatigue syndromes, studied in published clinical trials in humans and animals. This is not an exhaustive review. The table design allows for quick access to supportive data and will be helpful as a guide for both researchers and clinicians. The goal of the probiotics and disease series is to provide clinically useful tools. The first article (part 1) focused on mental health and neurological conditions and the second article (part 2) explored cultured and fermented foods that are commonly available in the United States. This third article (part 3) explores the relationship between bacterial strains and 2 of the most prevalent diseases we have in modern society: cardiometabolic disease and fatigue syndromes. Future articles will review conditions related to respiratory, ear, nose, and throat infections and infectious diseases; autoimmunity and dermatological conditions; cancer; and gastrointestinal and genitourinary, followed by an article focused on probiotic supplements. This literature review is specific to disease condition, probiotic classification, and individual strain.

Wojtyniak, K., Horvath, A., Dziechciarz, P., and Szajewska, H. Lactobacillus casei rhamnosus Lcr35 in the Management of Functional Constipation in Children: A Randomized Trial. J.Pediatr. 2017; 184:101-105; PM: 28284477

ABSTRACT: OBJECTIVE: To assess the effectiveness of Lactobacillus casei rhamnosus Lcr35 (Lcr35) in the management of functional constipation in children. *STUDY DESIGN*: A randomized, double-blind, placebo-controlled trial was conducted in 94 children aged <5 years with functional constipation according to the Rome III criteria. Children were assigned to receive Lcr35 (8 x 108 colony-forming units, n = 48) or placebo (n = 46), twice daily, for 4 weeks. The primary outcome measure was treatment success, defined as 3 or

more spontaneous stools per week, without episodes of fecal soiling, in the last week of the intervention. Analyses were by intention to treat. *RESULTS*: Eighty-one (86%) children completed the study. There was no significant difference in treatment success between the placebo and the Lcr35 group (28/40 vs 24/41, respectively; relative risk, 0.6, 95% CI 0.24-1.5, P = .4). There was a significant increase in the frequency of defecation from baseline to week 4 in both the placebo group (median [IQR] 2.0 [1.0, 2.0] to 6.0 [4.0, 9.0], P < .001) and in the Lcr35 group (2.0 [1.0, 2.0] to 4.0 [3.0, 5.0], P < .001), but the defecation frequency in the placebo group was significantly greater than that in the Lcr35 group at weeks 1, 2, 3, and 4. *CONCLUSION*: Lcr35 as a sole treatment was not more effective than placebo in the management of functional constipation in children <5 years. This study adds to current recommendations that do not support the use of probiotics in the treatment of childhood constipation. *TRIAL REGISTRATION*: ClinicalTrials.gov: NCT01985867.

Wollina, U. Microbiome in atopic dermatitis. Clin.Cosmet.Investig.Dermatol. 2017; 10:51-56; PM: 28260936

ABSTRACT: Atopic dermatitis (AD) is a common chronic inflammatory skin disease affecting ~10-20% of the general population. AD is characterized by disturbances in epidermal barrier function and hyperactive immune response. Recently, changes in the skin and intestinal microbiome have been analyzed in more detail. The available data suggest a link between disturbed skin microbiome and course of the disease. Flares of the disease are associated with an expansion of Staphylococcus aureus on lesional skin and a substantial loss of biodiversity in skin microbiome. Staphylococci exoproteins and superantigens evoke inflammatory reactions in the host. Skin microbiome includes superficial stratum corneum that is affected by environmental factors such as exposure to germs and cleansing. Available evidence argues for a link between epidermal barrier impairment and disturbances in skin microbiome in AD. In contrast to skin microbiome, intestinal microbiome seems to become stabilized after infancy. There is also a significant heritable component for intestinal microbiome. The microbial taxa, relative percentages and quantities vary remarkably between the different parts of the intestinal tract. Early intestinal microbial colonization may be a critical step for prevention of further development of AD. Skin barrier-aimed topical treatments help to develop a neo-microbiome from deeper compartments. Probiotics, prebiotics and synbiotics have been investigated for the treatment of AD, but further investigations are needed. Targeted treatment options to normalize skin and intestinal microbiome in AD are under investigation.

Wu, W., Wang, Y., Zou, J., Long, F., Yan, H., Zeng, L., and Chen, Y. Bifidobacterium adolescentis protects against necrotizing enterocolitis and upregulates TOLLIP and SIGIRR in premature neonatal rats. BMC.Pediatr. 1-5-2017; 17(1):1; PM: 28056921

ABSTRACT: BACKGROUND: Necrotizing enterocolitis (NEC) is a serious gastrointestinal disorder that is often seen in premature infants. Probiotics decrease the risk of NEC; however, the mechanism by which probiotics work is not clear. The goal of this study was to evaluate the preventive effect of Bifidobacterium adolescentis in an NEC rat model. *METHODS*: Sprague-Dawley neonatal rats were obtained by caesarean section after 20-21 d gestation and randomly divided into the following 3 groups: dam fed (DF), formula fed (FF), and formula + B. adolescentis (FB). Those in the FF and FB groups developed

NEC after exposure to asphyxia and cold stress. All rats were sacrificed 72 h after birth and intestinal injury and mRNA expression of TLR4, TOLLIP and SIGIRR were assessed. *RESULTS*: B. adolescentis significantly increased the 72-h survival rate from 56.3% in the FF group to 86.7% in the FB group. B. adolescentis significantly reduced the histological score from a median of 3.0 in the FF group to a median of 1.0 in the FB group,and significantly decreased the rate of NEC-like intestinal injury from 77.8% in the FF group to 23.1% in the FB group. The mRNA expression of TLR4 increased 3.6 fold in the FF group but decreased by 2 fold from B. adolescentis treatment. mRNA expression of TOLLIP and SIGIRR decreased 4.3 and 3.7 fold, respectively, in the FF group. B. adolescentis significantly increased mRNA expression of TOLLIP and SIGIRR by 3.7 fold and 2.6 fold, respectively. *CONCLUSIONS*: This study demonstrated B. adolescentis prevents NEC in preterm neonatal rats and that the mechanism for this action might be associated with the alteration of TLR4, TOLLIP, and SIGIRR expression.

Wu, Y., Wang, Y., Zou, H., Wang, B., Sun, Q., Fu, A., Wang, Y., Wang, Y., Xu, X., and Li, W. Probiotic Bacillus amyloliquefaciens SC06 Induces Autophagy to Protect against Pathogens in Macrophages. Front Microbiol. 2017; 8:469; PM: 28382029

ABSTRACT: Probiotics are increasingly applied in popularity in both humans and animals. Decades of research has revealed their beneficial effects, including the immune modulation in intestinal pathogens inhibition. Autophagy-a cellular process that involves the delivery of cytoplasmic proteins and organelles to the lysosome for degradation and recirculation-is essential to protect cells against bacterial pathogens. However, the mechanism of probiotics-mediated autophagy and its role in the elimination of pathogens are still unknown. Here, we evaluated Bacillus amyloliquefaciens SC06 (Ba)-induced autophagy and its antibacterial activity against Escherichia coli (E. coli) in murine macrophage cell line RAW264.7 cells. Western blotting and confocal laser scanning analysis showed that Ba activated autophagy in a dose- and time-dependent manner. Ba-induced autophagy was found to play a role in the elimination of intracellular bacteria when RAW264.7 cells were challenged with E. coli. Ba induced autophagy by increasing the expression of Beclin1 and Atg5-Atg12-Atg16 complex, but not the AKT/mTOR signaling pathway. Moreover, Ba pretreatment attenuated the activation of JNK in RAW264.7 cells during E. coli infection, further indicating a protective role for probiotics via modulating macrophage immunity. The above findings highlight a novel mechanism underlying the antibacterial activity of probiotics. This study enriches the current knowledge on probiotics-mediated autophagy, and provides a new perspective on the prevention of bacterial infection in intestine, which further the application of probiotics in food products.

Xiao, L., Ding, G., Ding, Y., Deng, C., Ze, X., Chen, L., Zhang, Y., Song, L., Yan, H., Liu, F., and Ben, X. Effect of probiotics on digestibility and immunity in infants: A study protocol for a randomized controlled trial. Medicine (Baltimore). 2017; 96(14):e5953; PM: 28383398

ABSTRACT: The gastrointestinal (GI) tract of a fetus in utero is sterile but it becomes colonized with environmental microorganisms shortly after birth. Since the gut microbiota undergoes substantial changes in early life, healthy gut microflora is essential to an infant's gut health and immune system and probably also has an effect on overall health status in later life. Probiotics, defined as viable microbial preparations that have a beneficial effect on the health of the host, represent a rapidly expanding field. Although

randomized controlled trials using probiotics in infants have shown promising results in the prevention and treatment of common diseases such as diarrhea and allergy, little is known about whether probiotics could offer benefits to healthy infants. We have designed a randomized controlled trial to test the hypothesis that an oral preparation of probiotics is superior to placebo in improving digestive and immune function in healthy infants.The trial will be a randomized, double-blind, placebo-controlled, 2-parallel-group study in Shanghai, China. After a 2-week run-in period, 200 exclusively formula-fed healthy infants aged 4 to 6 months will be randomly allocated to receive either a probiotic product containing Bifidobacterium infantis R0033, Bifidobacterium bifidum R0071, and Lactobacillus helveticus R0052 or an identical placebo once daily for 4 weeks and will be followed up for 8 weeks. The duration of the subject's participation will be 14 weeks, with a total of 5 visits: inclusion (Visit 1, Day 1), start of intervention (V2, D15), end of intervention (V3, D44), and follow-up (V4 and V5, D72 and D100). Stool and saliva samples will be collected at the first 3 visits to measure microbial populations and secretory immunoglobulin A (SIgA), respectively. Physical examination will be performed at each visit, and tolerance records will be completed 1 day prior to each visit. The primary endpoints will be the changes in the composition of fecal microbiota, particularly the Bifidobacterium bifidum population. The secondary endpoints will include the change in salivary SIgA level, growth parameters, digestive tolerance, and adverse events.An effective, practical, and acceptable probiotic intervention in manipulating the gut microbiota and boosting the immune system in formula-fed infants would represent a major clinical advance. The administration of probiotic supplementation or follow-on formula to infant may be associated with some clinic benefits.

Xiong, S., Li, Q., Liu, D., and Zhu, Z. Gastrointestinal Tract: a Promising Target for the Management of Hypertension. Curr.Hypertens.Rep. 2017; 19(4):31; PM: 28349378

ABSTRACT: The pathogenesis of hypertension remains elusive. Current treatments on hypertension have only achieved modest reductions. Facilitating theoretical research and looking for new therapeutic strategy are urgently needed. Besides food digestion and nutrients absorption, the gastrointestinal tract (GI) has been shown to influence the status of the central nervous system, immune system, metabolism, and cardiovascular homeostasis. Emerging findings demonstrate that endogenous factors derived from GI including gut hormones, autonomic nerve, and gut microbiota play important roles in the regulation of vascular function and/or blood pressure. Meanwhile, evidences from clinical practice and experimental study have found that intervention in GI through metabolic surgery, probiotics consumption, and dietary modification can efficiently ameliorate or even remit hypertension and related cardiometabolic diseases. Thus, we propose that GI might be an initiating organ of hypertension and a promising target for the management of hypertension. Further, illuminating this concept may aid to understand the pathogenesis and control of hypertension.

Xue, L., He, J., Gao, N., Lu, X., Li, M., Wu, X., Liu, Z., Jin, Y., Liu, J., Xu, J., and Geng, Y. Probiotics may delay the progression of nonalcoholic fatty liver disease by restoring the gut microbiota structure and improving intestinal endotoxemia. Sci.Rep. 3-28-2017; 7:45176; PM: 28349964

ABSTRACT: Gut-derived bacterial lipopolysaccharide (LPS) and subsequent hepatic toll-like receptor 4 (TLR4) activation have been recognized to be involved in the onset of diet-induced nonalcoholic fatty liver disease (NAFLD), but little is known about the

variation of LPS and TLR4 during the progression of NAFLD. Probiotics were able to inhibit proliferation of harmful bacteria and improve gastrointestinal barrier function. However, it's unclear whether LPS/TLR4 is involved in the protection effect of probiotics on NAFLD. In this study, we described characteristic of gut microbiota structure in the progression of NAFLD, and we also analyzed the relationship between gut microbiota and LPS/TLR4 in this process. Furthermore, we applied probiotics intervention to investigate the effect of probiotics on gut flora structure, intestinal integrity, serum LPS, liver TLR4 and liver pathology. Our results showed that serum LPS and liver TLR4 were highly increased during progression of NAFLD, with gut flora diversity and gut mircobiological colonization resistance (B/E) declining. Furthermore, probiotics could improve gut microbiota structure and liver pathology. Probiotics could also downregulate serum LPS and liver TLR4. Our results suggested that both gut flora alteration and endotoxemia may be involved in the progression of NAFLD. Probiotics may delay the progression of NAFLD via LPS/TLR4 signaling.

Yadav, R., Singh, P. K., Puniya, A. K., and Shukla, P. Catalytic Interactions and Molecular Docking of Bile Salt Hydrolase (BSH) from L. plantarum RYPR1 and Its Prebiotic Utilization. Front Microbiol. 2016; 7:2116; PM: 28111569

ABSTRACT: Prebiotics are the non-digestible carbohydrate, which passes through the small intestine into unmetabolized form, reaches the large intestine and undergoes fermentation by the colonic bacteria thus; prebiotics stimulate the growth of probiotic bacteria. Further, bile salt hydrolase (BSH) is an enzyme that catalyses the deconjugation of bile salt, so it has enormous potential toward utilizing such capability of Lactobacillus plantarum RYPR1 toward detoxifying through BSH enzyme activity. In the present study, six isolates of Lactobacillus were evaluated for the co-aggregation assay and the isolate Lactobacillus plantarum RYPR1 was further selected for studies of prebiotic utilization, catalytic interactions and molecular docking. The prebiotic utilization ability was assessed by using commercially available prebiotics lactulose, inulin, xylitol, raffinose, and oligofructose P95. The results obtained revealed that RYPR1 is able to utilize these probiotics, maximum with lactulose by showing an increase in viable cell count (7.33 +/- 0.02 to 8.18 +/- 0.08). In addition, the molecular docking of BSH from Lactobacillus plantarum RYPR1 was performed which revealed the binding energy -4.42 and 7.03 KJ/mol. This proves a considerably good interactions among BSH and its substrates like Taurocholic acid (-4.42 KJ/mol) and Glycocholic acid (-7.03 KJ/mol). These results from this study establishes that Lactobacillus plantarum RYPR1 possesses good probiotic effects so it could be used for such applications. Further, molecular dynamics simulations were used to analyze the dynamic stability of the of modeled protein to stabilize it for further protein ligand docking and it was observed that residues Asn12, Ile8, and Leu6 were interacting among BSH and its substrates, i.e., Taurocholic acid and Lys88 and Asp126 were interacting with Glycocholic acid. These residues were interacting when the docking was carried out with stabilized BSH protein structure, thus, these residues may have a vital role in stabilizing the binding of the ligands with the protein.

Yadav, R., Kumar, V., Baweja, M., and Shukla, P. Gene editing and genetic engineering approaches for advanced probiotics: A Review. Crit Rev.Food Sci.Nutr. 1-10-2017; 0; PM: 28071925

ABSTRACT: The applications of probiotics are significant and thus resulted in need of genome analysis of probiotic strains. Various omics methods and systems biology approaches enables us to understand and optimize the metabolic processes. These

techniques have increased the researcher's attention towards gut microbiome and provided a new source for the revelation of uncharacterized biosynthetic pathways which enables novel metabolic engineering approaches. In recent years, the broad and quantitative analysis of modified strains relies on systems biology tools such as in silico design which are commonly used methods for improving strain performance. The genetic manipulation of probiotic microorganisms is crucial for defining their role in intestinal microbiota and exploring their beneficial properties. This review describes an overview of gene editing and system biology approaches, highlighting the advent of omics methods which allows the study of new routes for studying probiotic bacteria. We have also summarized gene editing tools like TALEN, ZFNs and CRISPR-Cas that edits or cleave the specific target DNA. Furthermore, in this review an overview of proposed design of advanced customized probiotic is also hypothesized to improvise the probiotics.

Yamamoto, T., Shimoyama, T., and Kuriyama, M. Dietary and enteral interventions for Crohn's disease. Curr.Opin.Biotechnol. 2017; 44:69-73; PM: 27940405

ABSTRACT: It is now widely acknowledged that the intestinal bacterial flora together with genetic predisposing factors significantly contribute to the immunopathogenesis of inflammatory bowel disease (IBD) as reflected by mucosal immune dysregulation. Recently, there has been an increased interest in nutraceutical therapies, including probiotics, prebiotics and synbiotics. Other dietary interventions with low carbohydrate diet, omega-3 polyunsaturated fatty acids and glutamine have been attempted to downregulate the gut inflammatory response and thereby alleviate gastrointestinal symptoms. Enteral nutrition has been widely used as induction and maintenance therapies in the management of Crohn's disease (CD). In this review, a critical assessment of the results of clinical trial outcomes and meta-analyses was conducted to evaluate the efficacy of dietary and enteral interventions for CD.

Yang, B., Xiao, L., Liu, S., Liu, X., Luo, Y., Ji, Q., Yang, P., and Liu, Z. Exploration of the effect of probiotics supplementation on intestinal microbiota of food allergic mice. Am.J.Transl.Res. 2017; 9(2):376-385; PM: 28337267

ABSTRACT: Environmental factor-induced alterations in intestinal microbiota have been demonstrated to be associated with increasing prevalence of food allergy. However, it is not clear to what extent oral administration of probiotics can affect gut microbiota composition, thus inhibiting food allergy development. Using ovalbumin (OVA)-sensitized murine model, it was demonstrated that probiotics ameliorated allergic symptoms, including reducing OVA specific-IgE, and -IgG1 levels in the serum, Th2 cytokines release in spleen, and occurrence of diarrhea. Moreover, 16S rRNA analysis showed that the probiotics-mediated protection was conferred by an enrichment of Coprococcus and Rikenella. The present study supports the theory that probiotics can treat food allergy by modulating specific genera of the gut microbiota.

Yang, D., Wu, X., Yu, X., He, L., Shah, N. P., and Xu, F. Mutual growth-promoting effect between Bifidobacterium bifidum WBBI03 and Listeria monocytogenes CMCC 54001. J.Dairy Sci. 2017; 100(5):3448-3462; PM: 28259400

ABSTRACT: In this study, Bifidobacterium bifidum WBBI03 and Listeria monocytogenes CMCC 54001 were selected to detect the changes in their growth pattern after mutual interaction between them. The proteomic changes after the interaction between the 2 bacteria were detected by the isobaric tags for relative and absolute quantitation method. The proteins related to the biosynthesis and cell reproduction were selected, and their changes at the transcriptional level were monitored by fluorescent quantitative PCR. Also, 3 other types of probiotic organisms and opportunistic pathogens were used to verify the results mentioned above. The results showed that growing the 2 organisms together could promote the growth of each other, resulting in earlier entry into the logarithmic phase. The results also showed that the expression of these proteins mostly tended to be upregulated at the translational and transcriptional level. The increase in the expression of these proteins might help promote the growth and reproduction of B. bifidum WBBI03 and L. monocytogenes CMCC 54001. One aspect of the biological significance of their presence in the normal intestine may be that the opportunistic pathogens promote the growth of the probiotics.

Yang, J., Chen, S., Chen, L., Ouyang, M., and Li, F. Chronic diarrhea associated with high serum level of immunoglobulin A and diffuse infiltration of plasma cell in small intestine: A case report. Medicine (Baltimore). 2017; 96(5):e6057; PM: 28151917

ABSTRACT: RATIONALE: Chronic diarrhea in adult patients due to various causes is very common in clinic, but patient suffering with mal-absorption due to immunoproliferative small intestinal disease was rarely reported in China. *PATIENT CONCERNS AND DIAGNOSES*: A 35-year-old female presented with more than three years history of chronic diarrhea, rickets, high serum value of immunoglobulin A protein, and anemia. Bone marrow aspiration suggested that the patient was in a sideropenic and megalobastic anemia stage. Duodenal and ileac biopsies revealed atrophy and blunting villi. The bowel lamina propria was infiltrated with slightly increased intraepithelial lymphocytes and mainly with diffuse plasma cells. The following enzyme labeling immunohistochemistry results were strongly positive to alpha-heavy-chain. Computed tomography manifested she had diffuse thickening of small intestine wall. At last a diagnosis of immunoproliferative small intestinal disease was made. *INTERVENTIONS AND OUTCOMES*: On the first month, the patient was treated with vitamin D supplements, calcium, magnesium, potassium, iron, folic acid, mecobalamin replacements and microflora probiotics. The patient frequency of water diarrhea alleviated slightly, but her weight loss, anxiety neurosis and other disorders were still severe. After taking with prednisone (40 mg per day, and gradually reduced to the lowest dose) for another month, the symptoms was gradually subsided. *LESSONS*: The study shows that immunohistochemical staining for alpha-heavy chain proteins should be completed on small intestine biopsy specimens if the patient is suspected a diagnosis of immunoproliferative small intestinal disease.

Yang, W. C., Hsu, T. C., Cheng, K. C., and Liu, J. R. Expression of the Clonostachys rosea lactonohydrolase gene by Lactobacillus reuteri to increase its zearalenone-removing ability. Microb.Cell Fact. 4-24-2017; 16(1):69; PM: 28438205

ABSTRACT: BACKGROUND: Mycotoxins are secondary metabolites produced by filamentous fungi that can contaminate agricultural crops in the field as well as during harvest, transportation, processing, or storage. Zearalenone (ZEN), a non-steroidal

estrogenic mycotoxin, produced by Fusarium species, has been shown to be associated with reproductive disorders in farm animals and to a lesser extent in hyperoestrogenic syndromes in humans. Thus, the decontamination of ZEN in foods and feeds is an important issue. *RESULTS*: In this study, the gene encoding ZHD101, a ZEN-degrading enzyme produced by Clonostachys rosea IFO 7063, was cloned into an Escherichia coli-Lactobacillus shuttle vector, pNZ3004, and the resultant plasmid pNZ-zhd101 was then introduced via electroporation into Lactobacillus reuteri Pg4, a probiotic strain isolated from the gastrointestinal tract of broilers. The transformed strain L. reuteri pNZ-zhd101 acquired the capacity to degrade ZEN. In addition, the production of recombinant ZHD101 did not affect cell growth, acid and bile salt tolerance, and had only a minor effect on the adhesion ability of L. reuteri pNZ-zhd101. *CONCLUSIONS*: To the best of our knowledge, this is the first report of successful expression of a ZEN-degrading enzyme by intestinal lactobacilli.

Yang, Y., Huang, S., Wang, J., Jan, G., Jeantet, R., and Chen, X. D. Mg2+ improves the thermotolerance of probiotic Lactobacillus rhamnosus GG, Lactobacillus casei Zhang and Lactobacillus plantarum P-8. Lett.Appl.Microbiol. 2017; 64(4):283-288; PM: 28100014

ABSTRACT: Food-related carbohydrates and proteins are often used as thermoprotectants for probiotic lactobacilli during industrial production and processing. However, the effect of inorganic salts is rarely reported. Magnesium is the second-most abundant cation in bacteria, and commonly found in various foods. Mg2+ homeostasis is important in Salmonella and has been reported to play a critical role in their thermotolerance. However, the role of Mg2+ in thermotolerance of other bacteria, in particular probiotic bacteria, still remains a hypothesis. In this study, the effect of Mg2+ on thermotolerance of probiotic lactobacilli was investigated in three well-documented probiotic strains, Lactobacillus rhamnosus GG, Lactobacillus casei Zhang and Lactobacillus plantarum P-8, in comparison with Zn2+ and Na+ . Concentrations of Mg2+ between 10 and 50 mmol l-1 were found to increase the bacterial survival upon heat challenge. Remarkably, Mg2+ addition at 20 mmol l-1 led to a 100-fold higher survival of L. rhamnosus GG upon heat challenge. This preliminary study also showed that Mg2+ shortened the heat-induced extended lag time of bacteria, which indicated the improvement in bacterial recovery from thermal injury. SIGNIFICANCE AND IMPACT OF THE STUDY: In order to improve the productivity and stability of live probiotics, extensive investigations have been carried out to improve thermotolerance of probiotics. However, most of these studies focused on the effects of carbohydrates, proteins or amino acids. The roles of inorganic salts in various food materials, which have rarely been reported, should be considered when incorporating probiotics into these foods. In this study, Mg2+ was found to play a significant role in the thermotolerance of probiotic lactobacilli. A novel strategy may be available in the near future by employing magnesium salts as protective agents of probiotics during manufacturing process.

Yang, Y., Chen, G., Yang, Q., Ye, J., Cai, X., Tsering, P., Cheng, X., Hu, C., Zhang, S., and Cao, P. Gut microbiota drives the attenuation of dextran sulphate sodium-induced colitis by Huangqin decoction. Oncotarget. 3-22-2017; PM: 28415628

ABSTRACT: The gut microbiota, including probiotics and pathogenic microorganisms, is involved in ulcerative colitis (UC) by regulating pathogenic microorganisms and the production of intestinal mucosal antibodies. Huangqin decoction (HQD), a traditional Chinese formula chronicled in the Shanghan lun, has been recognized as an effective

drug for UC, owing to its anti-inflammatory and anti-oxidative properties. In the present study, we investigated whether HQD ameliorates dextran sulphate sodium (DSS)-induced colitis through alteration of the gut microbiota. We found that HQD significantly inhibited colitis, alleviating the loss of body weight, disease activity index, colon shortening, tissue injury, and inflammatory cytokine changes induced by DSS treatment. Principal component analysis and principal co-ordinate analysis showed an obvious difference among the groups, with increased diversity in the DSS and DSS+HQD groups. Linear discriminant analysis effect size was used to determine differences between the groups. The relative abundance of Lactococcus was higher in the DSS+HQD group than in the DSS group, whereas Desulfovibrio and Helicobacter were decreased. Furthermore, the protective effect of HQD was attenuated only in antibiotic-treated mice. In conclusion, our results suggest that HQD could ameliorate DSS-induced inflammation through alteration of the gut microbiota.

Yao, P., Tan, F., Gao, H., Wang, L., Yang, T., and Cheng, Y. Effects of probiotics on Tolllike receptor expression in ulcerative colitis rats induced by 2,4,6trinitrobenzene sulfonic acid. Mol.Med.Rep. 2017; 15(4):1973-1980; PM: 28260106

ABSTRACT: The present study aimed to investigate the regulatory effect of probiotics on the expression of Tolllike receptors (TLRs) in an ulcerative colitis (UC) rat model, and to determine the role of probiotics in the underlying mechanisms through which UC develops and progresses in rat models. Rats were randomly allocated to one of the four following groups: i) The healthy control, ii) the model, iii) the Golden bifid treatment group, and iv) the TLR4 monoclonal antibody (TLR4mAb) intervention group. The UC rat model was established using 2,4,6trinitrobenzene sulfonic acid. The general status and histological changes of rats were scored using the disease activity index and the histopathological scoring method, respectively. In these rats, the expression of TLR4 and TLR2 was measured using reverse transcriptionquantitative polymerase chain reaction. The expression of TLR4 and TLR2 in the model group was significantly higher than that in the healthy control group. However, when compared with the model rats, those that received either Golden bifid treatment or TLR4mAb intervention exhibited significantly decreased mRNA expression levels of TLR4 and TLR2 ($P<0.05$). The development of UC is characterized by an abnormal immune response in the intestines. Probiotics alleviated inflammatory reactions in rats with UC. The underlying mechanism of UC may be associated with the expression of TLRs and the subsequent release of inflammatory cytokines.

Yates, A. A., Erdman, J. W., Jr., Shao, A., Dolan, L. C., and Griffiths, J. C. Bioactive nutrients - Time for tolerable upper intake levels to address safety. Regul.Toxicol.Pharmacol. 2017; 84:94-101; PM: 28110066

ABSTRACT: There is increasing interest by consumers, researchers, and regulators into the roles that certain bioactive compounds, derived from plants and other natural sources, can play in health maintenance and promotion, and even prolonging a productive quality of life. Research has rapidly emerged suggesting that a wide range of compounds and mixtures in and from plants (such as fruits and vegetables, tea and cocoa) and animals (such as fish and probiotics) may exert substantial health benefits. There is interest in exploring the possibility of establishing recommended intakes or dietary guidance for certain bioactive substances to help educate consumers. A key aspect of establishing dietary guidance is the assessment of safety/toxicity of these substances.

Toxicologists need to be involved in both the development of the safety framework and in the evaluation of the science to establish maximum intake/upper limits.

Yin, Y., Hountras, P., and Wunderink, R. G. The microbiome in mechanically ventilated patients. Curr.Opin.Infect.Dis. 2017; 30(2):208-213; PM: 28067677

ABSTRACT: *PURPOSE OF REVIEW*: Discovery of a normal lung microbiome requires reassessment of our concepts of HAP/VAP pathogenesis and has important implications for clinical diagnosis and management. *RECENT FINDINGS*: Changes in the microbiome of dental plaque are associated with increased risk of HAP/VAP. A transition to a lung microbiome enriched with gut flora is found in ARDS with an increased inflammatory response in patients with this change in microbial flora. A characteristic microbiome pattern of higher amounts of bacterial DNA, lower community diversity, and greater relative abundance of a single species characterize pneumonia and occasionally identify bacteria not found in culture. The influence of the microbiome makes probiotics a logical strategy to prevent or ameliorate HAP/VAP but so far clinical support is unclear. *SUMMARY*: The presence of a normal lung microbiome and the interaction of that microbiome with other microbiota have an important but previously overlooked impact on the pathogenesis of HAP/VAP. Deep sequencing suggests that the repertoire of microorganisms and the pattern of bacterial communities associated with HAP/VAP remains incompletely understood but recent studies are adding greater clarity.

Youn, S. Y., Ji, G. E., Han, Y. R., and Park, M. S. Development of Strain-Specific Primers for Identification of Bifidobacterium bifidum BGN4. J.Microbiol.Biotechnol. 2-24-2017; PM: 28237995

ABSTRACT: Bifidobacterium bifidum BGN4 (BGN4) has many proven beneficial effects including antiallergy and anti-cancer properties. It has been commercialized and used in several probiotic products and thus, strain-specific identification of this strain is very valuable for further strain dependent physiological study. For this purpose, we developed novel multiplex polymerase chain reaction (PCR) primer sets for strain specific detection of BGN4 in the commercial product and fecal sample of animal model. The primer set was tested on seven strains of B. bifidum and 75 strains of the other Bifidobacterium species. The BGN4-specific regions were derived using megablast against genome sequences of various B. bifidum databases and four sets of primers were designed. As a result, only BGN4 produced four PCR products simultaneously while other strains did not. The PCR detection limit using BGN4-specific primer sets were 2.8 x 10(1) CFU/ml of BGN4. Those primer sets also detected and identified BGN4 in the probiotic products containing BNG4 and fecal samples from BGN4-fed animal model with high specificity. Our results indicate that the PCR assay from this study is an efficient tool for simple, rapid and reliable identification of BGN4, for which probiotic strains are known.

Yuan, F., Ni, H., Asche, C. V., Kim, M., Walayat, S., and Ren, J. Efficacy of Bifidobacterium infantis 35624 in patients with irritable bowel syndrome: a meta-analysis. Curr.Med.Res.Opin. 3-7-2017; 1-7; PM: 28166427

ABSTRACT: BACKGROUND: The treatment of irritable bowel syndrome (IBS) is a challenge because its cause remains unknown. Previous clinical trials to examine the efficacy of probiotic Bifidobacterium infantis 35624 (B. infantis) in patients with IBS have shown inconsistent findings. This study aimed to assess the combined effect of B. infantis on reducing the symptom severity of IBS based on the published data. *METHODS*: A meta-analysis was conducted using fixed-effect models to estimate the combined effect of B. infantis on primary outcomes, which included abdominal pain, bloating/distention, and bowel habit satisfaction. A systematic review was performed based on PubMed, Cochrane Library, and EMBASE databases to identify the randomized controlled trials comparing probiotic B. infantis with placebo in treating IBS symptoms, published up until 31 December 2016. The standardized mean difference (SMD) method was used to combine data since scales to measure the efficacy of probiotics were different among studies. *RESULTS*: A total of five studies were identified as suitable for inclusion, including three studies with single probiotic B. infantis and two studies with composite probiotics containing B. infantis. Treatment with single probiotic B. infantis didn't impact on abdominal pain, bloating/distention, or bowel habit satisfaction among IBS patients. However, patients who received composite probiotics containing B. infantis had significantly reduced abdominal pain (SMD, 0.22; 95% CI, 0.03-0.41) and bloating/distention (SMD, 0.30; 95% CI, 0.04-0.56). After combining the data from six studies, the improvement of bloating/distention among IBS patients remained significant (SMD, 0.21; 95% CI, 0.07-0.35). *CONCLUSION*: Composite probiotics containing B. infantis might be an effective therapeutic option for IBS patients, which could significantly alleviate the symptoms of IBS without significant adverse effects. However, the efficacy of single probiotic B. infantis on IBS has not been confirmed yet, which needs to be further validated by more large-sized randomized clinical trials.

Yucel, Falco C., Sotres, J., Rascon, A., Risbo, J., and Cardenas, M. Design of a potentially prebiotic and responsive encapsulation material for probiotic bacteria based on chitosan and sulfated beta-glucan. J.Colloid Interface Sci. 2-1-2017; 487:97-106; PM: 27756004

ABSTRACT: HYPOTHESIS: Chitosan and sulfated oat beta-glucan are materials suitable to create a prebiotic coating for targeted delivery to gastrointestinal system, using the layer by layer technology. *EXPERIMENT*: Quartz crystal microbalance with dissipation (QCM-D), spectroscopic ellipsometry (SE) and atomic force microscopy (AFM) were used to assess the multilayer formation capacity and characterize the resulting coatings in terms of morphology and material properties such as structure and rigidity. The coating of colloidal materials was proven, specifically on L. acidophilus bacteria as measured by changes in the bacterial suspension zeta potential. Viability of coated cells was shown using plate counting method. The coatings on solid surfaces were examined after exposure to mimics of gastrointestinal fluids and a commercially available beta-glucanase. *FINDINGS*: Successful build-up of multilayers was confirmed with QCM-D and SE. Zeta potential values proved the coating of cells. There was 2 log CFU/mL decrease after coating cells with four alternating layers of chitosan and sulfated beta-glucan when compared to viability of uncoated cells. The coatings were partially degraded after exposure to simulated intestinal fluid and restructured as a result of beta-glucanase treatment, mimicking enzymes present in the microflora of the human gut, but seemed

to resist acidic gastric conditions. Therefore, coatings of chitosan and sulfated beta-glucan can potentially be exploited as carriers for probiotics and delicate nutraceuticals.

Zanjani, S. Y., Eskandari, M. R., Kamali, K., and Mohseni, M. The effect of probiotic bacteria (Lactobacillus acidophilus and Bifidobacterium lactis) on the accumulation of lead in rat brains. Environ.Sci.Pollut.Res.Int. 2017; 24(2):1700-1705; PM: 27796979

ABSTRACT: Lead is a toxic metal present in different concentrations in a wide variety of food products. Exposure to lead, even to low levels, causes acute and chronic toxicities. Lead can cross the blood-brain barrier and accumulate in the nervous system. Probiotics are live microorganisms that, when used in adequate amounts, confer a health benefit on the host. Although a recent study demonstrated that the studied bacteria have a protective effect against acute lead toxicity, no research has been found that shows the long-term impact of these bacteria in vivo. The current study surveyed the protective effects of two species of probiotics, Lactobacillus acidophilus LA-5 and Bifidobacterium lactis BB-12, that are most widely used in many functional foods against oral lead exposure (4 weeks) in rat brains. The results revealed that, at the end of the second week of chronic exposure to lead and probiotic bacteria, the lowest level of lead belonged to the Lactobacillus group. At the end of the fourth week, the lowest amount of lead was related to the group receiving both types of probiotics. With the physiological benefits of probiotic consumption, the bacterial solution in this study did not show high efficacy in reducing brain lead concentrations.

Zarate, G., Saez, G. D., and Perez, Chaia A. Dairy propionibacteria prevent the proliferative effect of plant lectins on SW480 cells and protect the metabolic activity of the intestinal microbiota in vitro. Anaerobe. 2017; 44:58-65; PM: 28161414

ABSTRACT: Plant lectins are specific carbohydrate-binding proteins that are widespread in legumes such as beans and pulses, seeds, cereals, and many plants used as farm feeds. They are highly resistant to cooking and digestion, reaching the intestinal lumen and/or blood circulation with biological activity. Since many legume lectins trigger harmful local and systemic reactions after their binding to the mucosal surface, these molecules are generally considered anti-nutritive and/or toxic substances. In the gut, specific cell receptors and bacteria may interact with these dietary components, leading to changes in intestinal physiology. It has been proposed that probiotic microorganisms with suitable surface glycosidic moieties could bind to dietary lectins, favoring their elimination from the intestinal lumen or inhibiting their interaction with epithelial cells. In this work, we assessed in vitro the effects of two representative plant lectins, concanavalin A (Con A) and jacalin (AIL) on the proliferation of SW480 colonic adenocarcinoma cells and metabolic activity of colonic microbiota in the absence or presence of Propionibacterium acidipropionici CRL 1198. Both lectins induced proliferation of colonic cells in a dose-dependent manner, whereas ConA inhibited fermentative activities of colonic microbiota. Pre-incubation of propionibacteria with lectins prevented these effects, which could be ascribed to the binding of lectins by bacterial cells since P. acidipropionici CRL 1198 was unable to metabolize these proteins, and its adhesion to colonic cells was reduced after reaction with Con A or AIL. The results suggest that consumption of propionibacteria at the same time as lectins could reduce the incidence of lectin-induced alterations in the gut and may be a tool to protect intestinal physiology.

Zhang, H. Q., Fan, R., Zhang, J. J., Tao, X. J., and Sun, X. [Association between risk factors during maternal pregnancy and the neonatal period and childhood bronchial asthma]. Zhongguo Dang.Dai Er.Ke.Za Zhi. 2017; 19(1):49-53; PM: 28100322

ABSTRACT: OBJECTIVE: To study the association of the risk factors during maternal pregnancy and the neonatal period with childhood bronchial asthma. *METHODS*: A total of 306 children with asthma (asthma group) and 250 healthy children (control group) were enrolled. Their clinical data during the neonatal period and the maternal data during pregnancy were retrospectively studied. *RESULTS*: The univariate analysis showed that there were significant differences in the rates of maternal use of antibiotics during pregnancy, use of antibiotics and probiotics during the neonatal period, preterm birth, cesarean section, low birth weight, and breast feeding (>6 months) between the asthma and control groups (P<0.05). The multivariate logistic regression analysis showed that use of antibiotics during pregnancy (OR=3.908, 95%CI: 1.277-11.962), use of antibiotics during neonatal period (OR=24.154, 95%CI: 7.864-74.183), preterm birth (OR=8.535, 95%CI: 2.733-26.652), and cesarean section (OR=4.588, 95%CI: 2.887-7.291) were independent risk factors for childhood asthma. The use of probiotics during the neonatal period (OR=0.014, 95%CI: 0.004-0.046) and breast feeding (>6 months) (OR=0.161, 95%CI: 0.103-0.253) were protective factors for childhood asthma. *CONCLUSIONS*: The early prevention of childhood asthma can be improved by reducing the use of antibiotics during pregnancy, reducing cesarean section, avoiding abuse of antibiotics during the neonatal period, trying breast feeding and taking probiotics in early stage.

Zhang, J., Su, H., Li, Q., Wu, H., Liu, M., Huang, J., Zeng, M., Zheng, Y., and Sun, X. Oral administration of Clostridium butyricum CGMCC0313-1 inhibits beta-lactoglobulin-induced intestinal anaphylaxis in a mouse model of food allergy. Gut Pathog. 2017; 9:11; PM: 28250847

ABSTRACT: BACKGROUND: Probiotic bacteria can induce immune regulation or immune tolerance in patients with allergic diseases, but the underlying mechanisms are still unclear. There has been a growing interest in the use of beneficial bacteria for allergic diseases recently. This study aimed at exploring whether Clostridium butyricum CGMCC0313-1 (C. butyricum) can reduce beta-lactoglobulin(BLG)-induced intestinal anaphylaxis in a murine model of food allergy. *METHODS*: The preventive and therapeutic effects of oral C. butyricum on anaphylactic symptoms induced via BLG in food allergy mice were investigated. Intestinal anaphylaxis, T helper (Th)-specific cytokines and transcription factors, secretory IgA (sIgA), CD4+ CD25+ Foxp3Treg cell and histopathological alterations were examined. *RESULTS*: Clostridium butyricum significantly ameliorated intestinal anaphylaxis symptoms in the food allergy mice. sIgA and CD4+ CD25+ Foxp3Treg cell were increased by oral C. butyricum. It also reversed the imbalance of Th1/Th2 andTh17/Treg. *CONCLUSIONS*: Clostridium butyricum reduces BLG-induced intestinal anaphylaxis in mice and might be an additional or supplementary therapy for food allergy.

Zhang, R., Dong, X., Zhou, M., Tu, Y., Zhang, N., Deng, K., and Diao, Q. Oral administration of Lactobacillus plantarum and Bacillus subtilis on rumen fermentation and the bacterial community in calves. Anim Sci.J. 2017; 88(5):755-762; PM: 27628956

ABSTRACT: The objective of this study was to assess the effect of dietary probiotics on rumen fermentation and the bacterial community in dairy calves. Twelve Holstein calves

were randomly allocated to three treatments: a basal diet, the basal diet supplemented with Lactobacillus plantarum GF103 (LB) or basal diet supplemented with a mixture of Lactobacillus plantarum GF103 and Bacillus subtilis B27 (LBS). A milk replacer was fed to calves from 8 days of age. A starter and alfalfa hay was offered ad libitum from 21 and 28 days of age, respectively, and the orts were weighted daily. The ruminal fluid was sampled at 56 and 83 days of age to determine the rumen fermentation characteristics. The bacterial community was analyzed by denaturing gradient gel electrophoresis (DGGE) and the number of certain bacteria was quantified by real-time polymerase chain reaction. The ratio of total dry matter intake to average body wieght was higher in the control ($P < 0.05$). The DGGE fingerprint of the 16S ribosomal RNA gene was affected by the blended probiotics at 83 days of age. The number of Ruminococcus albus was lower in the LB and LBS treatment ($P < 0.05$). Oral administration of the probiotics affected the rumen bacterial community and the numbers of cellulolytic bacteria decreased.

Zhang, W., Zhu, Y. H., Zhou, D., Wu, Q., Song, D., Dicksved, J., and Wang, J. F. Oral Administration of a Select Mixture of Bacillus Probiotics Affects the Gut Microbiota and Goblet Cell Function following Escherichia coli Challenge in Newly Weaned Pigs of Genotype MUC4 That Are Supposed To Be Enterotoxigenic E. coli F4ab/ac Receptor Negative. Appl.Environ.Microbiol. 2-1-2017; 83(3); PM: 27881419

ABSTRACT: Structural disruption of the gut microbiota and impaired goblet cell function are collateral etiologic factors in enteric diseases. Low, moderate, or high doses of a Bacillus licheniformis-B. subtilis mixture (BLS mix) were orally administered to piglets of genotype MUC4 that are supposed to be F4-expressing enterotoxigenic Escherichia coli strain (F4+ ETEC) F4ab/ac receptor negative (i.e., MUC4-resistant piglets) for 1 week before F4+ ETEC challenge. The luminal contents were collected from the mucosa of the colon on day 8 after F4+ ETEC challenge. The BLS mix attenuated E. coli-induced expansion of Bacteroides uniformis, Eubacterium eligens, Acetanaerobacterium, and Sporobacter populations. Clostridium and Turicibacter populations increased following F4+ ETEC challenge in pigs pretreated with low-dose BLS mix. Lactobacillus gasseri and Lactobacillus salivarius populations increased after administration of BLS mix during E. coli infection. The beneficial effects of BLS mix were due in part to the expansion of certain Clostridium, Lactobacillus, and Turicibacter populations, with a corresponding increase in the number of goblet cells in the ileum via upregulated Atoh1 expression, in turn increasing MUC2 production and thus preserving the mucus barrier and enhancing host defenses against enteropathogenic bacteria. However, excessive BLS mix consumption may increase the risk for enteritis, partly through disruption of colonic microbial ecology, characterized by expansion of Proteobacteria and impaired goblet cell function in the ileum. Our findings suggest that oral administration of BLS mix reprograms the gut microbiota and enhances goblet cell function to ameliorate enteritis. IMPORTANCE: The present study is important for improving our understanding of the protective role of probiotics against Escherichia coli infection in piglets. Structural disruption of the gut microbiota and impaired goblet cell function are collateral etiologic factors in enteric diseases. In this study, low, moderate, or high doses of a Bacillus licheniformis-B. subtilis mixture (BLS mix) were orally administered to MUC4-resistant piglets for 1 week before the F4-expressing ETEC strain (F4+ ETEC) challenge. Our findings suggest that oral administration of BLS mix reprograms the gut microbiota and enhances goblet cell function to ameliorate enteritis.

Zhao, S., Liu, W., Wang, J., Shi, J., Sun, Y., Wang, W., Ning, G., Liu, R., and Hong, J. Akkermansia muciniphila improves metabolic profiles by reducing inflammation in chow diet-fed mice. J.Mol.Endocrinol. 2017; 58(1):1-14; PM: 27821438

ABSTRACT: Abnormal shifts in the composition of gut microbiota contribute to the pathogenesis of metabolic diseases, including obesity and type 2 diabetes (T2DM). The crosstalk between gut microbes and the host affects the inflammatory status and glucose tolerance of the individuals, but the underlying mechanisms have not been elucidated completely. In this study, we treated the lean chow diet-fed mice with Akkermansia muciniphila, which is thought to be inversely correlated with inflammation status and body weight in rodents and humans, and we found that A. muciniphila supplementation by daily gavage for five weeks significantly alleviated body weight gain and reduced fat mass. Glucose tolerance and insulin sensitivity were also improved by A. muciniphila supplementation compared with the vehicle. Furthermore, A. muciniphila supplementation reduced gene expression related to fatty acid synthesis and transport in liver and muscle; meanwhile, endoplasmic reticulum (ER) stress in liver and muscle was also alleviated by A. muciniphila. More importantly, A. muciniphila supplementation reduced chronic low-grade inflammation, as reflected by decreased plasma levels of lipopolysaccharide (LPS)-binding protein (LBP) and leptin, as well as inactivated LPS/LBP downstream signaling (e.g. decreased phospho-JNK and increased IKBA expression) in liver and muscle. Moreover, metabolomics profiling in plasma also revealed an increase in anti-inflammatory factors such as alpha-tocopherol, beta-sitosterol and a decrease of representative amino acids. In summary, our study demonstrated that A. muciniphila supplementation relieved metabolic inflammation, providing underlying mechanisms for the interaction of A. muciniphila and host health, pointing to possibilities for metabolic benefits using specific probiotics supplementation in metabolic healthy individuals.

Zhao, Y., Duan, C., Gao, L., Yu, X., Niu, C., and Li, S. Genome shuffling of Lactobacillus plantarum C88 improves adhesion. Biosci.Biotechnol.Biochem. 2017; 81(1):184-193; PM: 27691905

ABSTRACT: Genome shuffling is an important method for rapid improvement in microbial strains for desired phenotypes. In this study, ultraviolet irradiation and nitrosoguanidine were used as mutagens to enhance the adhesion of the wild-type Lactobacillus plantarum C88. Four strains with better property were screened after mutagenesis to develop a library of parent strains for three rounds of genome shuffling. Fusants F3-1, F3-2, F3-3, and F3-4 were screened as the improved strains. The in vivo and in vitro tests results indicated that the population after three rounds of genome shuffling exhibited improved adhesive property. Random Amplified Polymorphic DNA results showed significant differences between the parent strain and recombinant strains at DNA level. These results suggest that the adhesive property of L. plantarum C88 can be significantly improved by genome shuffling. Improvement in the adhesive property of bacterial cells by genome shuffling enhances the colonization of probiotic strains which further benefits to exist probiotic function.

Zheng, H., Gao, M., Ren, Y., Lou, R., Xie, H., Yu, W., Liu, X., and Ma, X. An improved pH-responsive carrier based on EDTA-Ca-alginate for oral delivery of Lactobacillus rhamnosus ATCC 53103. Carbohydr.Polym. 1-2-2017; 155:329-335; PM: 27702519

ABSTRACT: A pH-responsive carrier based on an ethylenediaminetetraacetic-calcium-alginate (EDTA-Ca-Alg) system was developed by controlling the release of Ca2+. The

system remained in the solution state at neutral pH since EDTA completely chelated the Ca2+. In contrast, a hydrogel immediately formed when the pH was below 4.0, which triggered the in situ release of Ca2+ from the EDTA-Ca compound and led to alginate-Ca binding. Taking advantage of the pH sensitivity, we prepared hydrogel microspheres with uniform size to entrap Lactobacillus rhamnosus ATCC 53103 through emulsification. In an acidic environment, the hydrogel structure remained compact with negligible pores to protect L. rhamnosus ATCC 53103. However, in a neutral intestinal environment, the hydrogel structure gradually disassembled because of the Ca2+ release from the hydrogel, which caused cell release. Therefore, a pH-responsive carrier was developed for the protection and the controlled release of cells in gastrointestinal tract, thus providing potential for oral delivery of probiotics.

Zhong, C., Qu, C., Wang, B., Liang, S., and Zeng, B. Probiotics for Preventing and Treating Small Intestinal Bacterial Overgrowth: A Meta-Analysis and Systematic Review of Current Evidence. J.Clin.Gastroenterol. 2017; 51(4):300-311; PM: 28267052

ABSTRACT: The present study conducted a meta-analysis and systematic review of current evidence to assess the efficacy of probiotics in preventing or treating small intestinal bacterial overgrowth (SIBO). Relevant studies from PubMed, Embase, and the Cochrane Central Register of Controlled Trials, until May 2016, were assimilated. The prevention efficacy was assessed by the incidence of SIBO in the probiotic group, and the treatment efficacy by the SIBO decontamination rate, reduction in H2 concentration, and symptom improvement. The relative risk (RR) and weighted mean difference (WMD) were used as effect measures and the random-effects model used for meta-analysis. A total of 14 full-text articles and 8 abstracts were included for the systematic review, and 18 studies were eligible for data synthesis. Patients on probiotic usage showed an insignificant trend toward low SIBO incidence [RR=0.54; 95% confidence intervals (CI), 0.19-1.52; P=0.24]. The pooled SIBO decontamination rate was 62.8% (51.5% to 72.8%). The probiotics group showed a significantly higher SIBO decontamination rate than the nonprobiotic group (RR=1.61; 95% CI, 1.19-2.17; P<0.05). Also, the H2 concentration was significantly reduced among probiotic users (WMD=-36.35 ppm; 95% CI, -44.23 to -28.47 ppm; P<0.05). Although probiotics produced a marked decrease in the abdominal pain scores (WMD=-1.17; 95% CI, -2.30 to -0.04; P<0.05), it did not significantly reduce the daily stool frequency (WMD=-0.09; 95% CI, -0.47 to 0.29). Therefore, the present findings indicated that probiotics supplementation could effectively decontaminate SIBO, decrease H2 concentration, and relieve abdominal pain, but were ineffective in preventing SIBO.

Zhu, F. Encapsulation and delivery of food ingredients using starch based systems. Food Chem. 8-15-2017; 229:542-552; PM: 28372213

ABSTRACT: Functional ingredients can be encapsulated by various wall materials for controlled release in food and digestion systems. Starch, as one of the most abundant natural carbohydrate polymers, is non-allergenic, GRAS, and cheap. There has been increasing interest of using starch in native and modified forms to encapsulate food ingredients such as flavours, lipids, polyphenols, carotenoids, vitamins, enzymes, and probiotics. Starches from various botanical sources in granular or amorphous forms are modified by chemical, physical, and/or enzymatic means to obtain the desired properties for targeted encapsulation. Other wall materials are also employed in combination with starch to facilitate some types of encapsulation. Various methods of

crafting the starch-based encapsulation such as electrospinning, spray drying, antisolvent, amylose inclusion complexation, and nano-emulsification are introduced in this mini-review. The physicochemical and structural properties of the particles are described. The encapsulation systems can positively influence the controlled release of food ingredients in food and nutritional applications.

Zhu, L., Qin, S., Zhai, S., Gao, Y., and Li, L. Inulin with different degrees of polymerization modulates composition of intestinal microbiota in mice. FEMS Microbiol.Lett. 4-12-2017; PM: 28407078

ABSTRACT: The study aimed to analyse the global influences of dietary inulin with different degrees of polymerization (DP) on intestinal microbial communities. 6-week-old male C57BL/6J mice were treated with fructo-oligosaccharides (FOS) and inulin for 6 weeks. Fecal samples were obtained at time point 0 and 6th week. 16S rRNA sequence analysis was used to measure intestinal microbiota performed on Illumina MiSeq platform. Influences of dietary inulin on intestinal microbiota were more complex effects than bifidogenic effects, relative abundance of butyrate-producing bacteria increased after interventions. Akkermansia muciniphila, belonging to mucin-degrading species, became a dominant species in Verrucomicrobia phylum after treatment with FOS and inulin. Modulation effects of intestinal microbiota were positively correlated with DP. Lower DP interventions exhibited better effects than higher DP treatment on stimulation of probiotics. We hypothesized that Akkermansia muciniphila played an important role on maintaining balance between mucin and short chain fatty acids.

Zhu, X. and Liu, F. Probiotics as an adjuvant treatment in Helicobacter pylori eradication therapy. J.Dig.Dis. 3-10-2017; PM: 28294543

ABSTRACT: Over 80% population with Helicobacter pylori (H. pylori) infection is asymptomatic. H. pylori was considered as a primary reason for various natural gastric physiopathology. Increased antibiotic resistance and less medication compliance lead to the failure of antibiotic eradication therapy. Probiotics have been applied as a supplementary treatment in H. pylori eradication therapy in recent years. They have direct and indirect inhibitory effects on H. pylori in both animal models and clinical trials. Because of the improvement in eradication rates and therapy-related side effects, probiotics have been considered as the useful supplementation to current eradication therapy although the treatment outcomes were controversial due to the heterogeneity of probiotics in species, strains, doses and therapeutic duration. Despite the positive role of probiotics, several factors need to be further considered during the application of probiotics. At last, the adverse effects of probiotics are notable. Further investigation into the safety of adjuvant probiotics to present H. pylori eradication therapy is still needed.

Zoghi, A., Khosravi-Darani, K., Sohrabvandi, S., Attar, H., and Alavi, S. A. Effect of probiotics on patulin removal from synbiotic apple juice. J.Sci.Food Agric. 2017; 97(8):2601-2609; PM: 27785791

ABSTRACT: BACKGROUND: Studies have reported the occurrence of the mycotoxin patulin in apple products. The aim of this study was to produce synbiotic apple juice and investigate the detoxification of patulin by Lactobacillus acidophilus and Lactobacillus plantarum as probiotic strains. The impact of seven process variables on efficiency of

toxin removal was investigated using Plackett-Burman design and presence of the surface-layer proteins as binding site of probiotics to patulin was confirmed during 6 weeks of cold storage. *RESULTS*: Results showed that the removal of patulin by probiotic bacteria from apple juice depends significantly ($P < 0.05$) on the fructooligosaccharide content (as a prebiotic), concentration of patulin and the addition of ascorbic acid. Sodium dodecyl sulfate polyacrylamide gel electrophoresis of cell surface proteins of probiotic strains revealed that surface layer proteins have an important role in patulin removal from apple juice. In the best conditions, 91.23% of initial patulin concentration was removed from juice during 6 weeks refrigerated storage. No significant difference was observed in organoleptic properties of the synbiotic apple juice and raw sample. *CONCLUSION*: In the best condition reported in this study, contaminated synbiotic apple juice by patulin will be safe for consumers after the first day of probiotic inoculation. (c) 2016 Society of Chemical Industry.

Zubiria, M. G., Gambaro, S. E., Rey, M. A., Carasi, P., Serradell, M. L. A., and Giovambattista, A. Deleterious Metabolic Effects of High Fructose Intake: The Preventive Effect of Lactobacillus kefiri Administration. Nutrients. 5-17-2017; 9(5); PM: 28513533

ABSTRACT: Modern lifestyle and diets have been associated with metabolic disorders and an imbalance in the normal gut microbiota. Probiotics are widely known for their health beneficial properties targeting the gut microbial ecosystem. The aim of our study was to evaluate the preventive effect of Lactobacillus kefiri (L. kefiri) administration in a fructose-rich diet (FRD) mice model. Mice were provided with tap water or fructose-added (20% w/v) drinking water supplemented or not with L. kefiri. Results showed that probiotic administration prevented weight gain and epididymal adipose tissue (EAT) expansion, with partial reversion of the adipocyte hypertrophy developed by FRD. Moreover, the probiotic prevented the increase of plasma triglycerides and leptin, together with the liver triglyceride content. Leptin adipocyte secretion was also improved by L. kefiri, being able to respond to an insulin stimulus. Glucose intolerance was partially prevented by L. kefiri treatment (GTT) and local inflammation (TNFalpha; IL1beta; IL6 and INFgamma) was completely inhibited in EAT. L. kefiri supplementation generated an impact on gut microbiota composition, changing Bacteroidetes and Firmicutes profiles. Overall, our results indicate that the administration of probiotics prevents the deleterious effects of FRD intake and should therefore be promoted to improve metabolic disorders.

Zupancic, K., Kriksic, V., Kovacevic, I., and Kovacevic, D. Influence of Oral Probiotic Streptococcus salivarius K12 on Ear and Oral Cavity Health in Humans: Systematic Review. Probiotics.Antimicrob.Proteins. 2017; 9(2):102-110; PM: 28236205

ABSTRACT: Traditionally, probiotics are linked to the good health of the intestine and most clinical studies focus on that field. Evidence of oral probiotic use for ear and oral cavity disease prevention with impact on human health is limited. This work reviews existing studies and literature on Streptococcus salivarius K12 as an oral probiotic and effects of S. salivarius K12 on human ear and oral cavity human health. The studies were accessed via database searches: MEDLINE, PubMed, and Elsevier. The search included/focused on/encompassed publications from 2003 to 2016 with keywords related to K12 Streptococcus salivarius, bacteriocin-like inhibitory substances (BLIS) K12, probiotic K12 salivarius, and K12 probiotic health effects. Only a small amount of studies was identified: the total of 68 studies was identified, 35 of which were relevant after screening, and 9

were included in the final analysis. Very little literature is available about the association/correlation between/connection/interrelation of S. salivarius K12 with/and human ear and oral cavity health. S. salivarius K12 may have a role in reducing the occurrence and/or severity of secretory otitis media (SOM) and also in prevention of streptococcal and viral pharyngotonsillitis in children. Research highlights that S. salivarius K12 has shown promising results in treatment of halitosis, but data are still deficient. Further studies need to be initiated to improve understanding of the association of oral probiotic S. salivarius K12 with human ear and oral cavity health.



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