Biotherapy Journal Review

Volume 3, Number 3; Fall 2017



BioTherapeutics, Education & Research Foundation

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The BTER Foundation's

Biotherapy Journal Review

Vol 3, No 3; Fall 2017

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From the Editor's Desk:

Dear Readers,

The current issue of Biotherapy Journal Review was a long time in coming. What follows are hundreds of pages of abstracts from newly published biotherapy research. Three of those abstracts are featured in the review section: one maggot therapy article, one bacteriophage article, and one leech therapy article.

The maggot therapy paper - **Viabililty of *Lucilia sericata* maggots after exposure to wound antiseptics** by Daeschlein et al - provides additional data regarding maggots and their interaction with common and not-so-common disinfectants. There have already been a couple of published studies examining the effect of antibiotics on maggots, as used in maggot therapy, but the present study examines the effects of topical disinfectants on maggot viability and disinfection potential.

The reviewed publication by Leitner and colleagues (**Bacteriophages for treating urinary tract infections in patients undergoing transurethral resection of the prostate: a randomized, placebo-controlled, double-blind clinical trial**) is unusual on several levels. Not only does it offer the hope of additional much-needed controlled, clinical trial data, but it presents and analyzes the study protocol rather than the study results.

The third publication being reviewed in this issue of BJR is by Rothenberger et al, entitled: "**Determining the appropriate number and duration of leech therapy in congested tissues using tissue spectrophotometry and laser Doppler flowmetry**." Here we learn how tissue spectrophotometry and laser Doppler flowmetry can be used to help monitor the progress or benefits of leech therapy.

In this issue's reviewed publications, we see researchers advancing their respective fields. The three highlighted articles are not so much about clinical efficacy or biochemistry as they are about methodology: the nitty-gritty details of how to perform the treatments or how to execute the studies. Indeed, these authors present us with knowledge and tools that they believe will allow us to do our jobs better, whether we are focused on patient care or biotherapy research.

If you, too, would like to review a publication, or suggest an article for review, or even publish your own research, let us know. Sharing information is the best and fastest way to advance biotherapy, and, in turn, advance health care.



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

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Section I: Journal Reviews

The BTER Foundation's

Biotherapy Journal Review

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Title: Viability of *Lucilia sericata* maggots after exposure to wound antiseptics.
Authors: Daeschlein G, Napp M, Assadian O, von Podewils S, Reese K, Hinz P, Matiasek J, Spitzmueller R, Humphreys P, Jünger M, Kramer A.
Reviewer: Anonymous
To view the article review, visit page 5

Title: Bacteriophages for treating urinary tract infections in patients undergoing transurethral resection of the prostate: a randomized, placebo-controlled, double-blind clinical trial.
Authors: Leitner L, Sybesma W, Chanishvili N, Goderdzishvili M, Chkhotua A, Ujmajuridze A, Schneider MP, Sartori A, Mehnert U, Bachmann LM, Kessler TM.
Reviewer: Ronald Sherman, MD
To view the article review, visit page 9

Title: Determining the appropriate number and duration of leech therapy in congested tissues using tissue spectrophotometry and laser Doppler flowmetry.
Authors: Rothenberger J, Petersen W, Schaller HE, Held M.
Reviewer: Ronald Sherman, MD
To view the article review, visit page 12

Maggot Therapy Reviews

Journal Citation

Daeschlein G, Napp M, Assadian O, von Podewils S, Reese K, Hinz P, Matiasek J, Spitzmueller R, Humphreys P, Jünger M, Kramer A. **Viability of *Lucilia sericata* maggots after exposure to wound antiseptics.** Int Wound J. 2017; 14:512–515

Published 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.

Context (why and how the research was carried out)

In clinical practice wounds may be treated with antiseptics prior to application of maggot therapy. The effect of these antiseptics on medicinal maggots has been unclear and this research sought to determine whether fly maggots remain viable during and after exposure to the following commonly used wound and skin antiseptics, hand rubs and disinfectants:

Octenisept®	0·1% octenidine dihydrochloride, 2% phenoxyethanole
Lavasept®	0·04% polyhexanide
Betaisodona®	10%povidone-iodine
Manorapid synergy®	57·6% of ethanol 96%, 10% 1-propanol
Ethanol	70% ethanol
Lysoformin 3000®	7.5% glyoxal, 9.5% glutaral, 9.6% didecyldimethyl-ammoniumchloride
Descogen F®	60% potassium peroxymonosulfate
Disifin med® (powder)	90% tosylchloramine sodium
Wofasteril®	35% peracetic acid
Wofasept®	5% chlorocresol, 2%chlorofen, 5–15%anionic tensides
Control	0.9% Sterile saline

In the experiment, maggots were fully immersed for either 1, 2, 5, 10, 30 or 60 minutes in the antiseptic product made up to recommended concentration. Thereafter, maggots were washed three times and placed for 2 hours on Columbia agar for viability monitoring. Follow-up observations for up to three days were made for initially immobile larvae.

In an additional experiment, larvae treated with 70% ethanol, Betaisodona®, Octenisept®, Lavasept®, Disifin med®, Descogen F® and sterile saline were placed in bacterial suspensions containing *Staphylococcus aureus* to assess their ability to control infection after exposure to antiseptics.

Findings

The three wound antiseptics impacted somewhat on maggot motility and caused up to 19% reduction in the efficacy of maggots to control *S. aureus*. However, the other antiseptics used for surface and/or instrument disinfection had far greater detrimental impact on larval morbidity and mortality and the maggots' ability to control S. aureus. With the exception of ethanol and Lysoformin 3000®, these antiseptics led to variable reduction in motility as soon as 1 or 2 minutes from exposure and major maggot mortality of up to 50% in the case of Wolfasteril® and Wolfasept®. Ethanol neither reduced maggot motility nor ability to reduce *S. aureus* burden. The 1-propanol containing hand rub caused obvious morbidity and mortality due to the toxicity of propanol compared to ethanol. The two surface sterilizers Descogen F® and Disifin med® not only had an obvious effect on maggot wellbeing but also reduced the maggots' ability to control infection in the order of 74% for Descogen F® and 61% for Disifin med®.

Discussion

This paper has been an important first step in answering the question whether treatment of wounds with antiseptics is compatible with maggot therapy. The results presented here suggest that maggots may be sufficiently resilient to withstand temporary exposure. However, further research is necessary that aligns more closely with true wound conditions, clinical practice and calliphorid biology before the green light can be given for the concomitant use of wound antiseptics with maggot therapy.

To that end, the paper would have been enriched by more detailed information as to the use of wound antiseptics in clinical practice, either by themselves or in conjunction with maggot debridement therapy. The reader would have benefited from learning when topical wound antiseptics are indicated and in what manner they are applied, including quantity and frequency. These practical considerations are important when discussing concomitant use of antiseptics with maggot therapy in clinical practice. Consideration of clinical practice may also have led to the exclusion of hand-rubs and disinfectants from the experimental protocol because they are unlikely to pose a relevant risk to medicinal maggots in clinical practice.

The authors briefly mention that wound antiseptics may be used before the application of medicinal maggots and that the experiments were conducted with third instar maggots, which ought to be much more resilient to environmental insults than are early-stage maggots. Importantly, given the ability of medicinal maggots to control wound infection, it is probably rare that clinicians would consider applying topical antiseptics during maggot therapy. The compatibility of antibiotics, however, has been shown to be safe and indeed synergistic (Cazander et al., 2010, Peck and Kirkup, 2012, Sherman et al., 1995). Consequently, in clinical practice, fragile small early second instar larvae are typically applied to wounds for maggot therapy, not third instars as were used in this study. For this reason, future studies should align experiments closer with the use of antiseptics in the treatment cycle and match the corresponding maggot development stage in the experiment.

The wound is unlike a test-tube that maintains content volume and concentration. The wounds treated with maggot therapy often produce lots of exudate which further increases in the presence of medicinal maggots. Given the diluting effect of exudate and maggot excretions/secretions, and liquefaction of necrotic wound tissue, the concentration of any antiseptic would quickly decrease provided the medicinal maggots survive the first few hours in the wound and are well enough to convey therapeutic benefit.

The paper reports on the initial mortality and morbidity, as expressed in reduced motility, but not on the performance of medicinal maggots over the likely maggot therapy treatment time of 2 to 4 days. It is plausible that the antibiotic effect measured is the result of the briefly remaining ability to produce secretions and void excretions, which may rapidly decrease along with the health of the maggot. It is not clear how severely the longer-term health of exposed medicinal maggots is affected and whether they are able to survive and provide therapeutic benefits for the full period of debridement (2-4 days depending on dressing modality), especially because it is in all likelihood early second instar maggots that are exposed to antiseptics. In addition to immediate exposure, the chronic low-level presence of these chemicals in the wound and dressing materials also needs to be considered. Moreover, the reviewer notes the absence of any statistical analysis of results which weakens the relevance of reported results considerably.

In summary, it may be premature of the authors to conclude that "*Concomitant short-term application of wound antiseptics together with maggots on wound beds is tolerated by larvae and does not impair their viability*". This research would have been more conclusive and practice-relevant if early second instar maggots had been used and if the experimental protocol had allowed for morbidity, mortality and performance testing of maggots over a period of four days. Moreover, debridement efficacy ought to be a good proxy for overall maggot health and the ability of maggots to produce excretions and secretions that control pathogens in the wound. It may therefore be instructive in future experiments to focus on performance and viability testing of antiseptic-treated maggots using artificial wound models as in Blake et al. (2007) and Čičková et al. (2015).

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"Caution! Maggots [baby flies] on Board"
Making a delivery in Ronald Sherman's car; 1998

Phage Therapy Reviews

Journal Citation

Leitner L, Sybesma W, Chanishvili N, Goderdzishvili M, Chkhotua A, Ujmajuridze A, Schneider MP, Sartori A, Mehnert U, Bachmann LM, Kessler TM. **Bacteriophages for treating urinary tract infections in patients undergoing transurethral resection of the prostate: a randomized, placebo-controlled, double-blind clinical trial**. BMC Urol. 2017;17:90.

Published Abstract

BACKGROUND: Urinary tract infections (UTI) are among the most prevalent microbial diseases and their financial burden on society is substantial. The continuing increase of antibiotic resistance worldwide is alarming. Thus, well-tolerated, highly effective therapeutic alternatives are urgently needed. Although there is evidence indicating that bacteriophage therapy may be effective and safe for treating UTIs, the number of investigated patients is low and there is a lack of randomized controlled trials.

METHODS AND DESIGN: This study is the first randomized, placebo-controlled, double-blind trial investigating bacteriophages in UTI treatment. Patients planned for transurethral resection of the prostate are screened for UTIs and enrolled if in urine culture eligible microorganisms $\geq 10^4$ colony forming units/mL are found. Patients are randomized in a double-blind fashion to the three study treatment arms in a 1:1:1 ratio to receive either: a) bacteriophage (i.e. commercially available Pyo bacteriophage) solution, b) placebo solution, or c) antibiotic treatment according to the antibiotic sensitivity pattern. All treatments are intended for 7 days. No antibiotic prophylaxes will be given to the double-blinded treatment arms a) and b). As common practice, the Pyo bacteriophage cocktail is subjected to periodic adaptation cycles during the study. Urinalysis, urine culture, bladder and pain diary, and IPSS questionnaire will be completed prior to and at the end of treatment (i.e. after 7 days) or at withdrawal/drop out from the study. Patients with persistent UTIs will undergo antibiotic treatment according to antibiotic sensitivity pattern.

DISCUSSION: Based on the high lytic activity and the potential of resistance optimization by direct adaptation of bacteriophages, and considering the continuing increase of antibiotic resistance worldwide, bacteriophage therapy is a very promising treatment option for UTIs. Thus, our randomized controlled trial investigating bacteriophages for treating UTIs will provide essential insights into this potentially revolutionizing treatment option.

Context

Urinary tract infections (UTIs) are very common. In the U.S., as the authors point out, UTIs account for over 7 million doctor visits and cost $1.6 billion annually. Typically, treatment

involves increased fluid intake, usually accompanied by antibiotics. The problem is that those antibiotics are often associated with adverse events and the development of antibiotic resistance.

The authors describe, in brief, the history of bacteriophages during the past century, including the fact that bacteriophage use and study has continued in Eastern Europe, while essentially disappearing from the literature in Western Europe and North America. Within the past two decades, however, there has been an increasing interest in bacteriophage therapy in the west, with a few very small studies of phage for urinary and diabetic foot wound infections.

This team of researchers have therefore designed a prospective, controlled and randomized clinical trial of intra-vesicular phage therapy (phage directly into the bladder) for the treatment of UTI/s. Their operating hypotheses are: 1) intravesical bacteriophage treatment in patients with UTIs due to *E. coli* and other uropathogens, will show a 40% increase in success rate (normalization of urine culture defined as no evidence of bacteria, i.e. $<10^4$ colony forming units/mL) as compared to placebo treatment within 7 days. 2) bacteriophage treatment will be non-inferior to antibiotic treatment in terms of treatment success rates, with a non-inferiority margin of 35%.

There is another issue that must be considered when discussing the context of this publication: This article describes a research project which has not yet been performed. It is a study that has not even yet been started (at least not at the time it was written). This is most uncommon for several reasons. First and foremost, many researchers do not want to publicize their research plans and designs for fear that others may perform the work before they themselves have a chance to finish and publish it. Second, there is often less interest by readers and publishers in seeing study protocols than there is in reviewing study results.

Findings

The "findings" of this publication are really the methods by which the researches have decided to pursue their investigation. So here is what they plan to do: a randomized, placebo-controlled, double-blinded three-armed clinical trial of intravesicular bacteriophage (Pyo bacteriophage solution: commercially available and registered in Georgia) vs placebo vs antibiotics, for the treatment of UTI in patients undergoing transurethral prostatectomy with susceptible microorganisms (*Enterococcus* spp., *Escherichia coli, Proteus mirabilis, Pseudomonas aeruginosa, Staphylococcus* spp., and *Streptococcus* spp.). The study will be carried out at at the Tzulukidze National Center of Urology (TNCU), Tbilisi, Georgia. Pyo bacteriophage solution is produced by the Eliava Institute of Bacteriophages, Microbiology, and Virology in Tbilisi (EIBMV), Georgia. During the study, continuous adaption cycles will be carried out at EIBMV to enhance the treatment effect. Study design and statistical analysis will be performed by staff at the Neuro-Urology, Spinal Cord Injury Center & Research, University of Zürich, Balgrist University Hospital, Zürich, Switzerland. Based on a set of performance assumptions and a power goal of 0.8, the sample size was calculated to be 27 subjects in each arm, for a total of 81 evaluable patients. Rather than enroll a larger set number of patients to

compensate for whatever attrition may occur, the researchers plan simply to "replace" those subjects lost prematurely with new enrollees.

Discussion

Urinary tract infections are common, and many can pose a serious threat to life. The clinical situation being studied in this proposed research (namely, UTI's in men undergoing trans-urethral resection of the prostate - TURP) is not common, but does fall into the category of serious and difficult-to-treat UTI. Many have had multiple infections by the time they are scheduled for TURP, and therefore frequently have infections with antibiotic-resistant organisms. So, in that sense, the study population being addressed is representative of the patients in whom phage therapy should be considered. This is a strong "plus" for the study.

Actually, I cannot think of a strong negative with regard to this study design. I find it unusual that the team would not set out to enroll 85 or 90 patients to ensure that they still meet their goal of 81 evaluable patients, despite the few who are likely not to complete the study. Enrolling more patients to make up for those who drop out is an unusual way to design the study, but as long as the replacements are invited to participate in a random fashion (for example, the very next patients who are eligible, in order of presentation), then the study can maintain its status as a randomized trial. The fact that study duration is so short (just one week from initiation to final data collection) means that recruiting additional subjects should not delay the completion of the study by any appreciable amount of time.

Throughout my reading of the manuscript, I have been wondering: why is this group publishing their study methods before they actually conduct the study? The study group is from Tbilisi, Georgia, where phage therapy is already well accepted. One of the participants (Eliava Institute) is the manufacturer of the product being tested. By publishing this manuscript, which is essentially a study protocol, the authors are essentially providing a template as well as a stimulus for other researchers to do the same or similar studies. This could have significant benefit for the study participants . . . and significant benefits for the rest of us. Sincerely, I hope others in the infectious disease community consider doing phage studies like this or on other populations. The authors are correct in drawing our attention to the fact that we need more prospective, randomized clinical trials. But we particularly need more trials in the West.

So I am now inspired to do what I can, independently or through the BTER Foundation, to support more well-designed clinical trials of phage therapy in North America. What about you??

Hirudotherapy Reviews

Journal Citation

Rothenberger J, Petersen W, Schaller HE, Held M. **Determining the appropriate number and duration of leech therapy in congested tissues using tissue spectrophotometry and laser Doppler flowmetry.** Wound Repair Regen. 2016;24:1023-1029.

Published Abstract

A universal protocol determining the number of leeches and their application time does not exist. The aim of this study, therefore, is to quantify perfusion dynamics in venous congested tissues after leech application to get more detailed information about changes due to leech-induced skin microcirculation and to evaluate the usability of the Oxygen to See (O2C) device in terms of determining the appropriate number of leeches and the duration of therapy. Twelve patients with the need for leech therapy participated in the study. Perfusion dynamics of the congested tissue was assessed using the O2C device, which determines blood flow (BF), the relative amount of hemoglobin (rHB), and the oxygen saturation (SO2). Measurements were carried out before leech application and on various intervals like 10 minutes, one hour, and three hours after leech application. The leech application effectuated after 10 minutes a nonsignificant perfusion improvement, which further increased after one hour with a significant reduction of the relative amount of hemoglobin and a significant increase of blood flow and oxygen saturation (BF5 156.7%; rHB5 225.5%; SO25 153.7%). After three hours, the values returned to the levels before leech administration. In two cases, in which further administration of leeches within the measurement period was necessary, no substantial perfusion changes were obtained. The results of this study forms a more precise pattern of microcirculatory changes of leech therapy in congested tissues. According to our measurements a venous drainage improvement can be expected in congested tissue one hour after leech administration. The O2C seems to be a useful method to determine the appropriate number and duration of leech therapy.

Context

In reconstructive and transplant surgery, arterial circulation can be established or repaired surgically; but surgical repair of venous circulation (to carry the blood back to the heart) is rarely feasible. Usually, the patient and the doctor must wait for nature to reconnect (anastomose) the venous drainage. When venous drainage is not re-established quickly enough, the blood pools in the affected area and this vascular congestion can prevent fresh oxygenated blood from reaching the area. In order to decompress or remove the pooled venous blood, leech therapy is often used. The leeches suck the blood and secrete vasodilatory and anticoagulant proteins which allow the blood to continue draining, even after the leech finishes feeding and drops off.

One common dilemma for surgeons is how many leeches to place, and how often the leeches should be placed, in order to provide adequate drainage. To date, the answers to these questions have been guided by clinical observation. But doctors like objective measures – tests – that can guide if not dictate their treatment decisions. This is the origin of this study: the search for objective measures of circulatory integrity which can inform the surgeon about the number, frequency, and duration of leech phlebotomy to relieve post-surgical congestion.

In this project, the researchers investigated the use of the Oxygen to See (O2C) device, which can determine blood flow, flow velocity, relative amount of hemoglobin, and oxygen saturation, using a combination of white light and laser light (830 nm and 30 mW). Twelve patients who needed leech therapy for compromised flaps had their perfusion dynamics assessed with the O2C device before and after leeching. It should be noted that the decision to continue or halt leeching for these patients was reached based on clinical data. The spectrophotometric and doppler flowmetry data that was collected was not used to decide how many total leeches or leech treatments.

Findings

A total of 12 patients were enrolled in this study. Their surgical interventions differed; their outcomes differed. Four subjects underwent sural flaps. All four flaps survived, but one experienced a major necrosis. One of these subjects (not the one suffering major necrosis) was assessed clinically and determined to need additional leech treatments, so he was treated accordingly. Four subjects had successful anterior lateral thigh flaps. One of these subjects required additional leech treatments, based on clinical evaluation. Two subjects had random pattern flaps, one of which survived with only minor necrosis, the other was lost. One subject underwent a dorsal metacarpal artery flap, which survived with only minor necrosis. One subject had a digit replantation which, unfortunately, was not successful.

For the two subjects who required more than a single application of leeches, tissue spectrophotometry and laser Doppler flowmetry was not continued throughout the entire 3 hour study period. Within 10 minutes for one patient and within 1 hour for the second patient, blood flow and relative amount of hemoglobin failed to change, although hemoglobin oxygenation may have arguably increased slightly. Nevertheless, on the basis of clinical evaluation of the patients (still very poor circulation and oxygenation), measurements were halted and further leech treatments were administered.

For the remaining 10 subjects who were treated with only one application of leeches, their average blood flow and hemoglobin oxygenation increased within 1 hour and relative amount of hemoglobin decreased within an hour, consistent with decompression of the vascular congestion (stagnation of blood) and increased flow of fresh arterial blood into the area. After 3 hours, these values, on average, returned to baseline.

Discussion

This study clearly adds objective measurements that corroborate our understanding of the benefits of leech therapy for post-operative venous congestion: stagnated venous blood is removed by the leeches, resulting in decreased local pressure and consequently increased in-flow of fresh, oxygenated arterial blood. These findings are not unique; they have been demonstrated multiple times by other researchers, as reviewed by the current authors. What is unique is their use of this particular piece of technology, the O2C device, which measures both tissue photometrics and doppler flow.

But what of their stated goal: using this or a similar technology to help guide decisions concerning the need for additional leeching? This moves us a little closer to that point, by pointing out the fact that we can monitor these meaningful physiological changes, but we are still a far way away from being able to predict or recommend optimal dosage and treatment schedule ahead of time, based on objective clinical measures. The reasons we are still so far away are related to limitations that can be seen even in this study.

One obvious limitation is the technology itself. While the O2C appears to be a fine piece of equipment, it was not a simple matter to adjust the probes such that they could reliably and consistently perform optimally, given the anatomy of these post-surgical sites and the reality of live leeches hanging from the tissue.

Additionally, one must remember that what was described was not a test of the hypothesis that O2C could help decide whether or not additional leeching was necessary. That promise may have driven the researchers forwards, but the published study described only the feasibility of gathering meaningful physiological data in this way. The researchers proved that this was possible. In order to determine whether or not the data can predict outcomes or drive clinical decisions, a study should be performed in which the decisions to leech or not to leech are actually made on the basis of this data, and outcomes are then evaluated to determine whether or not the data and decision parameters were successful. Hopefully a study like that will be forthcoming; admittedly it will not be an easy study to design or perform.

What else could be done with this data? Perhaps the authors could re-examine the data they have (or collect additional data) to evaluate not the average results for each study subject, but the specific results, with an eye towards cut-off points. The fact that patients who required only one leech treatment, on average, had increased blood flow or decreased relative hemoglobin does not tell us whether or not these markers are predictive, if in fact many of the subjects had blood flow that did not increase, or relative hemoglobin that did not fall. In the world of useful decision points, "average" is not as meaningful as sensitivity and specificity: HOW MANY of the subjects actually had blood flow that increased? What percent of subjects actually had relative hemoglobin measurements that decreased? By how much? This is the next step that has to take place before we can determine whether or not this physiologic data could

be useful in directing the course of leech therapy. It looks like the data may be at hand. If so, I hope to hear more from them about this study or future studies.

Despite the data that this new device can provide, still I am left feeling that our technology is not yet advanced enough to assist us any more than what we already have at our fingertips: leeches to help with the problem of venous congestion, and a trained human brain to observe the patient and make the decision – intuitive or not – as to whether the patient needs the leech's help.



Leech and Cocoon,
from the BTER Foundation's Leech Therapy Research Laboratory



BTER Foundation's Biotherapy Exhibit at SAWC 2007

Looking to delve deeper into Biotherapy? The BTER Foundation maintains a presence at a variety of biotherapy conferences, and periodically offers webinars and workshops. Learn more at http://www.bterfoundation.org/education

Section II: Biotherapy Citations for Fall 2017

A. Apitherapy and Bee Venom Therapy

No new citations for Fall 2017.



Herbal medicine in jars ©iStock #000015960273

B. Helminthic Therapy

Haarder, S., Kania, P. W., Holm, T. L., von Gersdorff, Jorgensen L., and Buchmann, K. Effect of ES products from Anisakis (Nematoda: Anisakidae) on experimentally induced colitis in adult zebrafish. Parasite Immunol. 8-5-2017; PM: 28779539

ABSTRACT: Inflammatory bowel disease (IBD) in developed countries is linked with elevated hygienic standards. One of the several factors involved in this question may be reduced exposure to the immunomodulatory effects of parasitic helminths. Several investigations on treatment of mice and humans with helminth-derived substances have supported this notion, but underlying mechanisms remain unclear. This study therefore dissects to what extent a series of immune-related genes are modulated in zebrafish with experimentally induced colitis following exposure to excretory-secretory (ES) products isolated from larval Anisakis, a widely distributed fish nematode. Adult zebrafish intrarectally exposed to the colitis-inducing agent TNBS developed severe colitis leading to 80% severe morbidity, but if co-injected (ip) with Anisakis ES products, the morbidity rate was 50% at the end of the experiment (48 hours post-exposure). Gene expression studies of TNBS-treated zebrafish showed clear upregulation of a range of genes encoding inflammatory cytokines and effector molecules and some induction of genes related to the adaptive response. A distinct innate-driven immune response was seen in both TNBS and TNBS + ES groups, but expression values were significantly depressed for several important pro-inflammatory genes in the TNBS + ES group, indicating protective mechanisms of Anisakis ES compounds on intestinal immunopathology in zebrafish.

Wegener, Parfrey L., Jirku, M., Sima, R., Jalovecka, M., Sak, B., Grigore, K., and Jirku, Pomajbikova K. A benign helminth alters the host immune system and the gut microbiota in a rat model system. PLoS.One. 2017; 12(8):e0182205; PM: 28771620

ABSTRACT: Helminths and bacteria are major players in the mammalian gut ecosystem and each influences the host immune system and health. Declines in helminth prevalence and bacterial diversity appear to play a role in the dramatic rise of immune mediated inflammatory diseases (IMIDs) in western populations. Helminths are potent modulators of immune system and their reintroduction is a promising therapeutic avenue for IMIDs. However, the introduction of helminths represents a disturbance for the host and it is important to understand the impact of helminth reintroduction on the host, including the immune system and gut microbiome. We tested the impact of a benign tapeworm, Hymenolepis diminuta, in a rat model system. We find that H. diminuta infection results in increased interleukin 10 gene expression in the beginning of the prepatent period, consistent with induction of a type 2 immune response. We also find induction of humoral immunity during the patent period, shown here by increased IgA in feces. Further, we see an immuno-modulatory effect in the small intestine and spleen in patent period, as measured by reductions in tissue immune cells. We observed shifts in microbiota community composition during the patent period (beta-diversity) in response to H. diminuta infection. However, these compositional changes appear to be minor; they occur within families and genera common to both treatment groups. There was no change in alpha diversity. Hymenolepis diminuta is a promising model for helminth therapy because it establishes long-term, stable colonization in rats and modulates the immune system without causing bacterial dysbiosis. These results suggest that the goal of engineering a therapeutic helminth that can safely manipulate the mammalian immune system without disrupting the rest of the gut ecosystem is in reach.

Williams, A. R., Dige, A., Rasmussen, T. K., Hvas, C. L., Dahlerup, J. F., Iversen, L., Stensvold, C. R., Agnholt, J., and Nejsum, P. Immune responses and parasitological observations induced during probiotic treatment with medicinal Trichuris suis ova in a healthy volunteer. Immunol.Lett. 2017; 188:32-37; PM: 28602842

ABSTRACT: Ingestion of eggs (ova) of the porcine nematode parasite Trichuris suis (TSO) may reduce the severity of autoimmune disorders, however the development of TSO treatment as a useful therapy for autoimmune diseases is hampered by a lack of knowledge on the development of the parasite and the nature of the local immune responses in humans. Here, we used colonoscopy to investigate the development of T. suis and related mucosal and systemic immune responses during TSO treatment in an intestinally healthy male volunteer. TSO treatment induced T. suis-specific serum antibodies, a transient blood eosinophilia, and increases in IFNgamma+ and IL4+ cells within the circulating CD4+ T-cell population. Increased expression of genes encoding cytokines (IL4, IL10, IL17 and TGF-beta), and transcription factors (FOXP3, GATA3 and RORC) were apparent in the ascending and transverse colon (the predilection site of the worms), whereas only limited changes in gene expression were observed proximally (ileum) and distally (descending colon) to the infected tissue. We further show that T. suis is able to colonise the human colon, with a number of worms developing to a similar size and morphology observed in the natural pig host, and a small number of unembryonated eggs were passed in the faeces, indicating patent infection. Notably, the volunteer experienced a substantial improvement in psoriasis during the course of TSO treatment. Thus, TSO treatment induced a mixed Th1/Th2/T regulatory response at the local site of infection, which was also reflected to some extent in the peripheral circulation. These results, together with the first definitive observations that T. suis can mature to adult size and reproduce in humans, shed new light on the interaction between the human immune system and probiotic helminth treatment, which should facilitate further development of this novel therapeutic option.



Necator americanus larva (L3), 100 X
Photo by Jasper Lawrence, 2007; Nikon E200 Trinocular microscope;
Sony HDV-A1U HD digital video camera.

C. Ichthyotherapy

No New Publications for Fall 2017



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D. Leech Therapy

Asgari, S. A., Rostami, S., and Teimoori, M. Leech Therapy for Treating Priapism: Case Report. Iran J.Public Health. 2017; 46(7):985-988; PM: 28845411

ABSTRACT: Priapism is well-defined by persistent, painful penile erection which happens without sexual stimulation. Currently, the hirudotherapy is practiced to treat venous congestion and subsequent compartment syndrome. Here we will report a case of a male with priapism treated by leeches. The case was a 26 yr old young single male referred to the Razi Hospital Emergency Department, Guilan University of Medical Sciences, Rasht, Iran due to long-time spontaneous erections. The patient had no history of mental disorders, trauma or sickle cell anemia. we insert two leeches in each side of penile shaft for two hours, after a one hour break we insert do in same manner for another cycle. At follow-up two days later he had significantly decreased pain, though still had cavernosal swelling and tenderness to palpation. The patient was subsequently discharged after three days of admission. The pain and perineal swelling completely resolved over the course of one month. In this case, chronology indicates that leech therapy was possibly treatment option for priapism. This procedure seems to be non-invasive treatment strategy worth to discussing in such patients.

Cooper, E. L. and Mologne, N. Exploiting leech saliva to treat osteoarthritis: A provocative perspective. J.Tradit.Complement Med. 2017; 7(3):367-369; PM: 28725633

ABSTRACT: Plant and animal-derived products are crucial components in complementary and alternative medicine. Although modern medicine has provided numerous innovations and advancements, these often fail to reveal new and dependable, inexpensive treatments nor real cures that are relatively free of adverse side effects. We present evidence that hirudotherapy, which utilizes leeches, improves certain diseases, including osteoarthritis. Osteoarthritis, a disease in joints, could benefit from use of medicinal peptides found in leech saliva, components of its immune system.

Cornejo, A., Shammas, R. L., Poveromo, L. P., Lee, H. J., and Hollenbeck, S. T. Institutional Outcomes of Leech Therapy for Venous Congestion in 87 Patients. J.Reconstr.Microsurg. 7-4-2017; PM: 28675913

No Abstract Available.

Hamidizadeh, N., Azizi, A., Zarshenas, M. M., and Ranjbar, S. Leech therapy in treatment of cutaneous leishmaniasis: a case report. J.Integr.Med. 2017; 15(5):407-410; PM: 28844218

No Abstract Available.

Kotick, J. D. and Taghinia, A. Prolonged Bleeding after a Single Leech Application in Pediatric Hand Surgery. J.Hand Microsurg. 2017; 9(2):98-100; PM: 28867911

ABSTRACT: Use of the medicinal leech in microsurgery is common place for venous decongestion and can be associated with the need for transfusion over time and multiple applications. Here the authors present a case of profound, ongoing, life-

threatening bleeding after a single leech application in pediatric microscopic surgery. There are no reports of such profound bleeding in the literature, and this case serves as a warning of the need for close surveillance in this subset of patients.



Application of Leech
BTER Foundation Leech Therapy Research Center

E. Mammals- Service & Therapeutic Animals

Chubak, J., Hawkes, R., Dudzik, C., Foose-Foster, J. M., Eaton, L., Johnson, R. H., and Macpherson, C. F. Pilot Study of Therapy Dog Visits for Inpatient Youth With Cancer. J.Pediatr.Oncol.Nurs. 2017; 34(5):331-341; PM: 28614971

ABSTRACT: This study assessed the feasibility of studying animal-assisted activities (AAA) in inpatient pediatric oncology and collected preliminary data on potential benefits of AAA for this population. Patients at a large pediatric hospital were identified using electronic medical records and approached with physician approval. Patients completed surveys before and after a therapy dog visit in their private hospital room. Data on infections were ascertained by electronic medical record review. Provider surveys were placed in provider common areas and distributed through a link in an e-mail. We summarized resultsusing descriptive statistics and estimated mean changes in pre- and postintervention distress and conducted hypothesis tests using the paired t test. The study population (mean age = 12.9 years) consisted of 9 females and 10 males. Following the therapy dog visit, patients had lower distress and significant decreases in worry, tiredness, fear, sadness, and pain. Providers were generally supportive of the intervention. Eight patients developed infections during the 14 days after the dog visit but none could be clearly attributed to the therapy dog visit. The study's primary limitation was that there was no control group. However, results support the feasibility of and need for future studies on AAA in pediatric oncology.

Crowe, T. K., Sanchez, V., Howard, A., Western, B., and Barger, S. Veterans transitioning from isolation to integration: a look at veteran/service dog partnerships. Disabil.Rehabil. 8-13-2017; 1-9; PM: 28805082

*ABSTRACT: **BACKGROUND***: This study explored the dynamics of veteran/service dog partnerships by gathering the perspectives of veterans with a history of post-traumatic stress disorder and/or traumatic brain injury. ***METHODS***: Exploratory qualitative methods (focus groups and individual interviews) were used to investigate veteran/service dog relationships related to community involvement, family and friend relationships, self-care, work, and leisure. Nine male veterans, Paws, and Stripes program graduates participated. Data were audio recorded and transcribed by two research team members who used qualitative analytic software to manage and code the data. The full research team discussed themes and reached consensus on the themes that emerged from analysis. ***RESULTS***: Five themes emerged about the perceived benefit of veteran/service dog relationship: Secluded but Seeking Society (moving from isolation to reconnection); Opening Opportunities (navigating daily life); Bridging the Gap (facilitating social opportunities); and Reclaiming Life (transforming sense of worth and purpose). An overarching theme, Calming Catalyst, connected the other four themes. ***CONCLUSIONS***: Veterans in this study reported that their goal was to reclaim and develop key aspects of their lives and they perceived service dogs as a support in their transition from isolation to reintegration. This study found that service dogs supported the veterans to meet their goal. Implications for rehabilitation There are a significant number of veterans with post-traumatic stress disorder and/or traumatic brain injury who are facing life challenges including self-care, securing work, participating in leisure activities, and integrating into the community. Service dogs are an emerging intervention used to assist veterans with reintegration into civilian life. There is a need for professionals to be aware of potential benefits of service dog/veteran partnerships. Based on our findings,

veterans could benefit from being paired with a service dog to facilitate their successful return to community life.

Gonder-Frederick, L. A., Grabman, J. H., Shepard, J. A., Tripathi, A. V., Ducar, D. M., and McElgunn, Z. R. Variability of Diabetes Alert Dog Accuracy in a Real-World Setting. J.Diabetes Sci.Technol. 2017; 11(4):714-719; PM: 28627305

*ABSTRACT**: BACKGROUND***: Diabetes alert dogs (DADs) are growing in popularity as an alternative method of glucose monitoring for individuals with type 1 diabetes (T1D). Only a few empirical studies have assessed DAD accuracy, with inconsistent results. The present study examined DAD accuracy and variability in performance in real-world conditions using a convenience sample of owner-report diaries. ***METHOD***: Eighteen DAD owners (44.4% female; 77.8% youth) with T1D completed diaries of DAD alerts during the first year after placement. Diary entries included daily BG readings and DAD alerts. For each DAD, percentage hits (alert with BG </= 5.0 or >/= 11.1 mmol/L; </=90 or >/=200 mg/dl), percentage misses (no alert with BG out of range), and percentage false alarms (alert with BG in range) were computed. Sensitivity, specificity, positive likelihood ratio (PLR), and true positive rates were also calculated. ***RESULTS***: Overall comparison of DAD Hits to Misses yielded significantly more Hits for both low and high BG. Total sensitivity was 57.0%, with increased sensitivity to low BG (59.2%) compared to high BG (56.1%). Total specificity was 49.3% and PLR = 1.12. However, high variability in accuracy was observed across DADs, with low BG sensitivity ranging from 33% to 100%. Number of DADs achieving >/= 60%, 65% and 70% true positive rates was 71%, 50% and 44%, respectively. ***CONCLUSIONS***: DADs may be able to detect out-of-range BG, but variability across DADs is evident. Larger trials are needed to further assess DAD accuracy and to identify factors influencing the complexity of DAD accuracy in BG detection.

Herlache-Pretzer, E., Winkle, M. Y., Csatari, R., Kolanowski, A., Londry, A., and Dawson, R. The Impact of Service Dogs on Engagement in Occupation among Females with Mobility Impairments: A Qualitative Descriptive Study. Int.J.Environ.Res.Public Health. 6-16-2017; 14(6); PM: 28621752

ABSTRACT: It is becoming more common for people with disabilities to procure service dogs as a form of assistive technology (AT). However, there is little qualitative research examining the impact of service dogs on engagement in valued daily activities (occupations) among persons with mobility impairments. This study used a qualitative descriptive methodology to learn about the experiences of four female service dog owners with mobility impairments, with a focus on the impact of service dog use on the performance of daily occupations and participation in social activities, and their experiences utilizing a service dog as a form of AT. Data analysis indicated that each participant's service dog made a significant impact on their everyday lives and their ability to independently perform everyday activities; however, there are also unique challenges associated with service dog ownership that must be considered when evaluating benefits of service dog partnership. Overall, the positive outcomes reported by participants indicate that service dogs can be considered a beneficial, adaptable form of AT for some persons with mobility impairments.

Kramlich, D. Complementary Health Practitioners in the Acute and Critical Care Setting: Nursing Considerations. Crit Care Nurse. 2017; 37(3):60-65; PM: 28572102

ABSTRACT: In response to the rising demand by patients and their families for complementary health approaches, hospitals are increasingly integrating complementary health approaches with their conventional medical practices to create healing environments. Results of the 2010 Complementary and Alternative Medicine Survey of Hospitals indicated that the top 6 inpatient modalities included pet therapy, massage therapy, music or art therapy, guided imagery, relaxation therapy, and Reiki and therapeutic touch. Whether complementary health approaches are provided by complementary health practitioners through hospital-based integrative medicine programs, volunteer practitioners, or bedside nurses, the regulatory, legal, ethical, and safety concerns remain constant. Previous articles in this column of Critical Care Nurse provided an overview of complementary health approaches that nurses may encounter in their practices, with specific attention to implications for acute and critical care nurses, as well as important legal, ethical, safety, quality, and financial implications that acute and critical care nurses should consider when integrating complementary health approaches with conventional care. This column provides the acute and critical care nurse with key information about validation of credentials, experience, and competence of nurses and volunteers providing complementary health approaches, as well as about institutional policies and scope of practice.

Lee, J. and Yun, C. K. Effects of hippotherapy on the thickness of deep abdominal muscles and activity of daily living in children with intellectual disabilities. J.Phys.Ther.Sci. 2017; 29(4):779-782; PM: 28533630

ABSTRACT: [***Purpose***] The purpose of this study is to investigate the effect of hippotherapy exercise on the thickness of deep abdominal muscles and daily activities of children with intellectual disabilities. [***Subjects and Methods***] Seven children with intellectual disabilities were treated with hippotherapy for 30 minutes twice a week for 6 weeks. The thickness of deep abdominal muscles and Functional Independence Measure (FIM) of the subjects were measured by ultrasonography before and after the experiment. [***Results***] There was no significant change in the thickness of the External Oblique and Internal Oblique muscles, but there was a statistically significant change in Transverse Adbominis thickness and FIM score after treatment compared to before treatment. [***Conclusion***] Hippotherapy exercise has a positive effect on the improvement of Transverse Abdominis (TrA) and activity of daily livings of children with intellectual disabilities.

Linder, D. E., Siebens, H. C., Mueller, M. K., Gibbs, D. M., and Freeman, L. M. Animal-assisted interventions: A national survey of health and safety policies in hospitals, eldercare facilities, and therapy animal organizations. Am.J.Infect.Control. 8-1-2017; 45(8):883-887; PM: 28673680

*ABSTRACT****: BACKGROUND***: Animal-assisted intervention (AAI) programs are increasing in popularity, but it is unknown to what extent therapy animal organizations that provide AAI and the hospitals and eldercare facilities they work with implement effective animal health and safety policies to ensure safety of both animals and humans. Our study objective was to survey hospitals, eldercare facilities, and therapy animal organizations on their AAI policies and procedures. ***METHODS***: A survey of United States hospitals, eldercare facilities, and therapy animal organizations was administered to assess existing health and safety policies related to AAI programs. RESULTS: Forty-five eldercare facilities, 45 hospitals, and 27 therapy animal organizations were surveyed. Health and safety

policies varied widely and potentially compromised human and animal safety. For example, 70% of therapy animal organizations potentially put patients at risk by allowing therapy animals eating raw meat diets to visit facilities. In general, hospitals had stricter requirements than eldercare facilities. ***DISCUSSION***: This information suggests that there are gaps between the policies of facilities and therapy animal organizations compared with recent guidelines for animal visitation in hospitals. ***CONCLUSIONS***: Facilities with AAI programs need to review their policies to address recent AAI guidelines to ensure the safety of animals and humans involved.

McDaniel Peters, B. C. and Wood, W. Autism and Equine-Assisted Interventions: A Systematic Mapping Review. J.Autism Dev.Disord. 7-21-2017; PM: 28733851

ABSTRACT: This systematic mapping review mapped current knowledge of equine-assisted interventions for people with autism to help guide future practice and research. Thirty-three studies including children and adolescents with autism, 3 of which confirmed diagnoses, were reviewed. Five types of equine-assisted activities were identified across 25 studies, with reported improvements in behavior, social interaction, and communication. Four types of equine-assisted therapies were identified across 8 studies, with reported improvements in motor control and self-care. Different approaches to therapeutic riding and hippotherapy, the most studied interventions, were evident. While this literature reflected early scientific development, it offered broad proof of concept that equine-assisted interventions can benefit children and adolescents with autism. Promising outcomes support continued investigation focused on standardization, appropriateness, and efficacy.

Saunders, G. H., Biswas, K., Serpi, T., McGovern, S., Groer, S., Stock, E. M., Magruder, K. M., Storzbach, D., Skelton, K., Abrams, T., McCranie, M., Richerson, J., Dorn, P. A., Huang, G. D., and Fallon, M. T. Design and challenges for a randomized, multi-site clinical trial comparing the use of service dogs and emotional support dogs in Veterans with post-traumatic stress disorder (PTSD). Contemp.Clin.Trials. 8-26-2017; 62:105-113; PM: 28844986

ABSTRACT: Posttraumatic stress disorder (PTSD) is a leading cause of impairments in quality of life and functioning among Veterans. Service dogs have been promoted as an effective adjunctive intervention for PTSD, however published research is limited and design and implementation flaws in published studies limit validated conclusions. This paper describes the rationale for the study design, a detailed methodological description, and implementation challenges of a multisite randomized clinical trial examining the impact of service dogs on the on the functioning and quality of life of Veterans with PTSD. Trial design considerations prioritized participant and intervention (dog) safety, selection of an intervention comparison group that would optimize enrollment in all treatment arms, pragmatic methods to ensure healthy well-trained dogs, and the selection of outcomes for achieving scientific and clinical validity in a Veteran PTSD population. Since there is no blueprint for conducting a randomized clinical trial examining the impact of dogs on PTSD of this size and scope, it is our primary intent that the successful completion of this trial will set a benchmark for future trial design and scientific rigor, as well as guiding researchers aiming to better understand the role that dogs can have in the management of Veterans experiencing mental health conditions such as PTSD.

Vermohlen, V., Schiller, P., Schickendantz, S., Drache, M., Hussack, S., Gerber-Grote, A., and Pohlau, D. Hippotherapy for patients with multiple sclerosis: A multicenter randomized controlled trial (MS-HIPPO). Mult.Scler. 8-1-2017; 1352458517721354; PM: 28770664

ABSTRACT: ***BACKGROUND***: Evidence-based complementary treatment options for multiple sclerosis (MS) are limited. ***OBJECTIVE***: To investigate the effect of hippotherapy plus standard care versus standard care alone in MS patients. ***METHODS***: A total of 70 adults with MS were recruited in five German centers and randomly allocated to the intervention group (12 weeks of hippotherapy) or the control group. Primary outcome was the change in the Berg Balance Scale (BBS) after 12 weeks, and further outcome measures included fatigue, pain, quality of life, and spasticity. ***RESULTS***: Covariance analysis of the primary endpoint resulted in a mean difference in BBS change of 2.33 (95% confidence interval (CI): 0.03-4.63, p = 0.047) between intervention (n = 32) and control (n = 38) groups. Benefit on BBS was largest for the subgroup with an Expanded Disability Status Scale (EDSS) 5 (5.1, p = 0.001). Fatigue (-6.8, p = 0.02) and spasticity (-0.9, p = 0.03) improved in the intervention group. The mean difference in change between groups was 12.0 (p < 0.001) in physical health score and 14.4 (p < 0.001) in mental health score of Multiple Sclerosis Quality of Life-54 (MSQoL-54). ***CONCLUSION***: Hippotherapy plus standard care, while below the threshold of a minimal clinically important difference, significantly improved balance and also fatigue, spasticity, and quality of life in MS patients.

Vincent, C., Belleville, G., Gagnon, D. H., Dumont, F., Auger, E., Lavoie, V., Besemann, M., Champagne, N., and Lessart, G. Effectiveness of Service Dogs for Veterans with PTSD: Preliminary Outcomes. Stud.Health Technol.Inform. 2017; 242:130-136; PM: 28873789

ABSTRACT: Limited scientific evidence on the effectiveness of psychiatric service dogs used by Veterans with post-traumatic stress disorder (PTSD) is available. This study investigated their short-term effectiveness among 15 Canadian veterans who received a first psychiatric service dog. Preliminary results suggest potential beneficial effects at 3 months on the psychiatric symptoms.



F. Maggot Debridement Therapy

Flanderova, I. [Salvation of the diabetic foot through a comprehensive individualized treatment of the patient with type 2 diabetes: case study]. Vnitr.Lek. 2017; 63(5):343-347; PM: 28726434

ABSTRACT: This is a case of men with type 2 diabetes mellitus and diabetic foot. The patient was in danger of limb amputation. After improvement of diabetes, hypertension and dyslipidemia therapies a comprehensive treatment of diabetic foot including angioplasty, antibiotics and local maggot therapy was used for diabetic foot management. Therapy result was very satisfying for the patient. Despite of amputation of the 2nd digit due to advanced gangrene, the whole foot function was saved.Key words: diabetes foot - maggot therapies - type 2 diabetes mellitus.

Sherman, R. A. and Hetzler, M. R. Maggot Therapy for Wound Care in Austere Environments. J.Spec.Oper.Med. 2017; 17(2):154-162; PM: 28599051

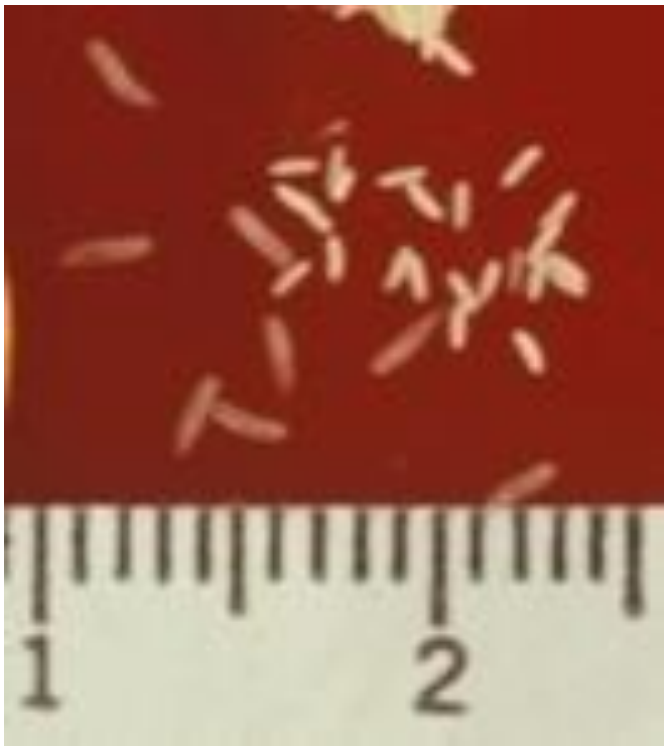
ABSTRACT: The past 25 years have seen an increase in use of maggot therapy for wound care. Maggot therapy is very effective in wound debridement; it is simple to apply and requires very little in the way of resources, costs, or skilled personnel. These characteristics make it well suited for use in austere environments. The use of medical-grade maggots makes maggot therapy nearly risk free, but medical grade maggots may not always be available, especially in the wilderness or in resource-limited communities. By understanding myiasis and fly biology, it should be possible even for the nonentomologist to obtain maggots from the wild and apply them therapeutically, with minimal risks.

Westby, M. J., Dumville, J. C., Soares, M. O., Stubbs, N., and Norman, G. Dressings and topical agents for treating pressure ulcers. Cochrane.Database.Syst.Rev. 6-22-2017; 6:CD011947; PM: 28639707

*ABSTRACT****: BACKGROUND***: Pressure ulcers, also known as bedsores, decubitus ulcers and pressure injuries, are localised areas of injury to the skin or the underlying tissue, or both. Dressings are widely used to treat pressure ulcers and promote healing, and there are many options to choose from including alginate, hydrocolloid and protease-modulating dressings. Topical agents have also been used as alternatives to dressings in order to promote healing.A clear and current overview of all the evidence is required to facilitate decision-making regarding the use of dressings or topical agents for the treatment of pressure ulcers. Such a review would ideally help people with pressure ulcers and health professionals assess the best treatment options. This review is a network meta-analysis (NMA) which assesses the probability of complete ulcer healing associated with alternative dressings and topical agents. ***OBJECTIVES***: To assess the effects of dressings and topical agents for healing pressure ulcers in any care setting. We aimed to examine this evidence base as a whole, determining probabilities that each treatment is the best, with full assessment of uncertainty and evidence quality. ***SEARCH METHODS***: In July 2016 we searched the Cochrane Wounds Specialised Register; the Cochrane Central Register of Controlled Trials (CENTRAL); Ovid MEDLINE; Ovid MEDLINE (In-Process & Other Non-Indexed Citations); Ovid Embase and EBSCO CINAHL Plus. We also searched clinical trials registries for ongoing and unpublished studies, and scanned reference lists of relevant included studies as well as reviews, meta-analyses, guidelines and health technology

reports to identify additional studies. There were no restrictions with respect to language, date of publication or study setting. ***SELECTION CRITERIA***: Published or unpublished randomised controlled trials (RCTs) comparing the effects of at least one of the following interventions with any other intervention in the treatment of pressure ulcers (Stage 2 or above): any dressing, or any topical agent applied directly to an open pressure ulcer and left in situ. We excluded from this review dressings attached to external devices such as negative pressure wound therapies, skin grafts, growth factor treatments, platelet gels and larval therapy. ***DATA COLLECTION AND ANALYSIS***: Two review authors independently performed study selection, risk of bias assessment and data extraction. We conducted network meta-analysis using frequentist mega-regression methods for the efficacy outcome, probability of complete healing. We modelled the relative effectiveness of any two treatments as a function of each treatment relative to the reference treatment (saline gauze). We assumed that treatment effects were similar within dressings classes (e.g. hydrocolloid, foam). We present estimates of effect with their 95% confidence intervals for individual treatments compared with every other, and we report ranking probabilities for each intervention (probability of being the best, second best, etc treatment). We assessed the certainty (quality) of the body of evidence using GRADE for each network comparison and for the network as whole. ***MAIN RESULTS***: We included 51 studies (2947 participants) in this review and carried out NMA in a network of linked interventions for the sole outcome of probability of complete healing. The network included 21 different interventions (13 dressings, 6 topical agents and 2 supplementary linking interventions) and was informed by 39 studies in 2127 participants, of whom 783 had completely healed wounds.We judged the network to be sparse: overall, there were relatively few participants, with few events, both for the number of interventions and the number of mixed treatment contrasts; most studies were small or very small. The consequence of this sparseness is high imprecision in the evidence, and this, coupled with the (mainly) high risk of bias in the studies informing the network, means that we judged the vast majority of the evidence to be of low or very low certainty. We have no confidence in the findings regarding the rank order of interventions in this review (very low-certainty evidence), but we report here a summary of results for some comparisons of interventions compared with saline gauze. We present here only the findings from evidence which we did not consider to be very low certainty, but these reported results should still be interpreted in the context of the very low certainty of the network as a whole.It is not clear whether regimens involving protease-modulating dressings increase the probability of pressure ulcer healing compared with saline gauze (risk ratio (RR) 1.65, 95% confidence interval (CI) 0.92 to 2.94) (moderate-certainty evidence: low risk of bias, downgraded for imprecision). This risk ratio of 1.65 corresponds to an absolute difference of 102 more people healed with protease modulating dressings per 1000 people treated than with saline gauze alone (95% CI 13 fewer to 302 more). It is unclear whether the following interventions increase the probability of healing compared with saline gauze (low-certainty evidence): collagenase ointment (RR 2.12, 95% CI 1.06 to 4.22); foam dressings (RR 1.52, 95% CI 1.03 to 2.26); basic wound contact dressings (RR 1.30, 95% CI 0.65 to 2.58) and polyvinylpyrrolidone plus zinc oxide (RR 1.31, 95% CI 0.37 to 4.62); the latter two interventions both had confidence intervals consistent with both a clinically important benefit and a clinically important harm, and the former two interventions each had high risk of bias as well as imprecision. ***AUTHORS' CONCLUSIONS***: A network meta-analysis (NMA) of data from 39 studies (evaluating 21 dressings and topical agents for pressure ulcers) is sparse and the evidence is of low or very low certainty (due mainly to risk of bias and imprecision). Consequently we are unable to determine which dressings or topical agents are the most likely to heal pressure ulcers, and it is generally unclear whether the treatments examined are more effective than saline gauze.More research is needed to determine whether particular dressings or topical agents improve the

probability of healing of pressure ulcers. The NMA is uninformative regarding which interventions might best be included in a large trial, and it may be that research is directed towards prevention, leaving clinicians to decide which treatment to use on the basis of wound symptoms, clinical experience, patient preference and cost.



Maggots near ruler, used with permission ©Monarch Labs

G. Olfactory Detection and Diagnosis

Reeve, C., Wentzell, P., Wielens, B., Jones, C., Stehouwer, K., and Gadbois, S. Assessing individual performance and maintaining breath sample integrity in biomedical detection dogs. Behav.Processes. 8-18-2017; PM: 28827118

ABSTRACT: In empirical tests of biomedical detection dogs, exhaled breath samples are often used because breath contains volatile organic compounds that can signal metabolic states, infection, or disease. However, in studies that present dogs with breath samples, results show a notable degree of variability both between and within studies. Differing protocols for the collection and storage of exhaled breath samples may contribute to this observed variability. The goal of the current study was therefore to test whether there was a difference in the detectability of breath samples collected using silicone-coated versus uncoated cotton balls. This was tested in two experiments. In the first experiment, breath samples were prepared using both silicone-coated and uncoated cotton balls, which were then left exposed to the surrounding air. Four dogs' detection of the samples was tested using a cued, three alternative forced choice (3AFC) procedure at regular intervals up to two hours after the samples were prepared. The results of Experiment 1 showed that the dogs' performance was above chance and there was no significant difference in the dogs' detection of the breath samples across conditions. In the second experiment, a series of breath samples were prepared and stored for one, two, three, and four week periods. The same four dogs' ability to detect the breath samples was tested each week using the same cued 3AFC procedure. The results of Experiment 2 showed that when silicone-coated cotton balls were used, all four dogs could detect the breath samples at above chance levels after the samples were stored for three weeks, and two dogs could detect the samples that were stored for four weeks. When the dogs were tested on their ability to detect the breath samples prepared using uncoated cotton, two dogs' performance fell to below chance levels at one week of storage time, while the other two dogs could detect the breath samples at above chance levels after the samples were stored for four weeks. Taken together, the results of the two experiments illustrate that silicone-coated cotton balls do not improve detectability of breath samples within two hours, but can greatly improve the detectability of breath samples stored over longer periods of time. Since the use of silicone-coated cotton balls only improved the detectability of the breath samples for two of the four dogs, these results highlight the importance of examining individual differences in dogs' performance. Furthermore, we argue that, given the inherent differences in olfactory ability across dogs, widespread use of silicone-coated cotton balls for the collection of breath samples would increase the pool of testable dogs for biomedical detection studies and would decrease the degree of variability both within and between studies.

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H. Phage Therapy

Abedon, S. T. Commentary: Communication between Viruses Guides Lysis-Lysogeny Decisions. Front Microbiol. 2017; 8:983; PM: 28620362

No Abstract Available.

Abedon, S. T. Bacteriophage Clinical Use as Antibacterial "Drugs": Utility and Precedent. Microbiol.Spectr. 2017; 5(4); PM: 28840811

ABSTRACT: For phage therapy-the treatment of bacterial infections using bacterial viruses-a key issue is the conflict between apparent ease of clinical application, on the one hand, and on the other hand, numerous difficulties that can be associated with undertaking preclinical development. These conflicts between achieving efficacy in the real world versus rigorously understanding that efficacy should not be surprising because equivalent conflicts have been observed in applied biology for millennia: exploiting the inherent, holistic tendencies of useful systems, e.g., of dairy cows, inevitably is easier than modeling those systems or maintaining effectiveness while reducing such systems to isolated parts. Trial and error alone, in other words, can be a powerful means toward technological development. Undertaking trial and error-based programs, especially in the clinic, nonetheless is highly dependent on those technologies possessing both inherent safety and intrinsic tendencies toward effectiveness, but in this modern era we tend to forget that ideally there would exist antibacterials which could be thus developed, that is, with tendencies toward both safety and effectiveness, and which are even relatively inexpensive. Consequently, we tend to demand rigor as well as expense of development even to the point of potentially squandering such utility, were it to exist. In this review I lay out evidence that in phage therapy such potential, in fact, does exist. Advancement of phage therapy unquestionably requires effective regulation as well as rigorous demonstration of efficacy, but after nearly 100 years of clinical practice, perhaps not as much emphasis on strictly laboratory-based proof of principle.

Abedon, S. T., Garcia, P., Mullany, P., and Aminov, R. Editorial: Phage Therapy: Past, Present and Future. Front Microbiol. 2017; 8:981; PM: 28663740

No Abstract Available.

Abramov, G., Shaharabani, R., Morag, O., Avinery, R., Haimovich, A., Oz, I., Beck, R., and Goldbourt, A. Structural Effects of Single Mutations in a Filamentous Viral Capsid Across Multiple Length Scales. Biomacromolecules. 8-14-2017; 18(8):2258-2266; PM: 28657731

ABSTRACT: Filamentous bacteriophage (phage) are single-stranded DNA viruses that infect bacteria. Single-site mutants of fd phage have been studied by magic-angle spinning nuclear magnetic resonance and by small-angle X-ray scattering. Detailed analysis has been performed that provides insight into structural variations on three length scales. The results, analyzed in conjunction with existing literature data, suggest that a single charge mutation on the capsid surface affects direct interviral interactions but not the structure of individual particles or the macroscale organization. On the other hand, a single hydrophobic mutation located at the hydrophobic interface that

stabilizes capsid assembly alters the atomic structure of the phage, mainly affecting intersubunit interactions, affects its macroscale organization, that is, the pitch of the cholesteric liquid crystal formed by the particles, but skips the nanoscale hence does not affect direct interparticle interactions. An X-ray scattering under osmotic pressure assay provides the effective linear charge density of the phage and we obtain values of 0.6 A-1 and 0.4 A-1 for fd and M13 phage, respectively. These values agree with a simple consideration of a single cylinder with protein and DNA charges spread according to the most recent atomic-resolution models of the phage.

Agirrezabala, X., Samatova, E., Klimova, M., Zamora, M., Gil-Carton, D., Rodnina, M. V., and Valle, M. Ribosome rearrangements at the onset of translational bypassing. Sci.Adv. 2017; 3(6):e1700147; PM: 28630923

ABSTRACT: Bypassing is a recoding event that leads to the translation of two distal open reading frames into a single polypeptide chain. We present the structure of a translating ribosome stalled at the bypassing take-off site of gene 60 of bacteriophage T4. The nascent peptide in the exit tunnel anchors the P-site peptidyl-tRNAGly to the ribosome and locks an inactive conformation of the peptidyl transferase center (PTC). The mRNA forms a short dynamic hairpin in the decoding site. The ribosomal subunits adopt a rolling conformation in which the rotation of the small subunit around its long axis causes the opening of the A-site region. Together, PTC conformation and mRNA structure safeguard against premature termination and read-through of the stop codon and reconfigure the ribosome to a state poised for take-off and sliding along the noncoding mRNA gap.

Ahiwale, S. S., Bankar, A. V., Tagunde, S., and Kapadnis, B. P. A Bacteriophage Mediated Gold Nanoparticles Synthesis and Their Anti-biofilm Activity. Indian J.Microbiol. 2017; 57(2):188-194; PM: 28611496

ABSTRACT: In the present study, gold nanoparticles (AuNPs) synthesis was carried out by using a rare bacteriophage which is morphologically similar to 7-11 phages of the C3 morphotype of tailed phage belonging to Podoviridae family as green route. Effect of various physiological parameters like pH, temperature and concentration of gold chloride salt on AuNPs synthesis was studied. The reaction mixtures have shown vivid colours at various physiological parameters. Phage inspired AuNPs were further characterized by using different techniques such as UV-Vis spectrophotometry, scanning electron microscopy (SEM), energy dispersive spectroscopy (EDS), X-ray diffraction (XRD) and dynamic light scattering (DLS). DLS study revealed synthesis of various sizes of AuNPs in the range of 20-100 nm. SEM studies revealed synthesis of varied shaped AuNPs, viz., spheres, hexagons, triangles, rhomboids and rectangular etc. The presence of Au in the nanostructures was confirmed by EDS. The XRD pattern reflects the crystalline nature and nano size of AuNPs. These phage inspired AuNPs showed anti-bacterial activity against different bacterial pathogens. Anti-biofilm activity of AuNPs was evaluated on a glass slide. It was noticed that at 0.2 mM concentration of these AuNPs about 80% of biofilm formation by Pseudomonas aeruginosa, a human pathogen was inhibited. Thus, the phage inspired AuNPs synthesis could be potential therapeutic agents against human pathogens.

Al-Fendi, A., Shueb, R. H., Foo, P. C., Ravichandran, M., and Yean, C. Y. Complete Genome Sequence of Lytic Bacteriophage VPUSM 8 against O1 El Tor Inaba Vibrio cholerae. Genome Announc. 5-25-2017; 5(21); PM: 28546472

ABSTRACT: The complete genome sequence of bacteriophage VPUSM 8 against O1 El Tor Inaba Vibrio cholerae is reported here. The isolated VPUSM 8 has potential use in future phage therapy or as a biocontrol agent for the prevention and treatment of cholera.

Alhmidi, H., John, A., Mana, T. C., Koganti, S., Cadnum, J. L., Shelton, M. B., and Donskey, C. J. Evaluation of Viral Surrogate Markers for Study of Pathogen Dissemination During Simulations of Patient Care. Open.Forum Infect.Dis. 2017; 4(3):ofx128; PM: 28752103

ABSTRACT: During patient care simulations, cauliflower mosaic virus DNA and bacteriophage MS2 performed similarly as surrogate markers of pathogen dissemination. These markers disseminated to the environment in a manner similar to Clostridium difficile spores but were more frequently detected on skin and clothing of personnel after personal protective equipment removal.

Alvarez, B. and Biosca, E. G. Bacteriophage-Based Bacterial Wilt Biocontrol for an Environmentally Sustainable Agriculture. Front Plant Sci. 2017; 8:1218; PM: 28769942

ABSTRACT: Bacterial wilt diseases caused by Ralstonia solanacearum, R. pseudosolanacearum, and R. syzygii subsp. indonesiensis (former R. solanacearum species complex) are among the most important plant diseases worldwide, severely affecting a high number of crops and ornamentals. Difficulties of bacterial wilt control by non-biological methods are related to effectiveness, bacterial resistance and environmental impact. Alternatively, a great many biocontrol strategies have been carried out, with the advantage of being environmentally friendly. Advances in bacterial wilt biocontrol include an increasing interest in bacteriophage-based treatments as a promising re-emerging strategy. Bacteriophages against the bacterial wilt pathogens have been described with either lytic or lysogenic effect but, they were proved to be active against strains belonging to R. pseudosolanacearum and/or R. syzygii subsp. indonesiensis, not to the present R. solanacearum species, and only two of them demonstrated successful biocontrol potential in planta. Despite the publication of three patents on the topic, until now no bacteriophage-based product is commercially available. Therefore, there is still much to be done to incorporate valid bacteriophages in an integrated management program to effectively fight bacterial wilt in the field.

Amarasiri, M., Kitajima, M., Nguyen, T. H., Okabe, S., and Sano, D. Bacteriophage removal efficiency as a validation and operational monitoring tool for virus reduction in wastewater reclamation: Review. Water Res. 9-15-2017; 121:258-269; PM: 28551509

ABSTRACT: The multiple-barrier concept is widely employed in international and domestic guidelines for wastewater reclamation and reuse for microbiological risk management, in which a wastewater reclamation system is designed to achieve guideline values of the performance target of microbe reduction. Enteric viruses are one of the pathogens for which the target reduction values are stipulated in guidelines, but frequent monitoring to validate human virus removal efficacy is challenging in a daily operation due to the

cumbersome procedures for virus quantification in wastewater. Bacteriophages have been the first choice surrogate for this task, because of the well-characterized nature of strains and the presence of established protocols for quantification. Here, we performed a meta-analysis to calculate the average log10 reduction values (LRVs) of somatic coliphages, F-specific phages, MS2 coliphage and T4 phage by membrane bioreactor, activated sludge, constructed wetlands, pond systems, microfiltration and ultrafiltration. The calculated LRVs of bacteriophages were then compared with reported human enteric virus LRVs. MS2 coliphage LRVs in MBR processes were shown to be lower than those of norovirus GII and enterovirus, suggesting it as a possible validation and operational monitoring tool. The other bacteriophages provided higher LRVs compared to human viruses. The data sets on LRVs of human viruses and bacteriophages are scarce except for MBR and conventional activated sludge processes, which highlights the necessity of investigating LRVs of human viruses and bacteriophages in multiple treatment unit processes.

Amarillas, L., Rubi-Rangel, L., Chaidez, C., Gonzalez-Robles, A., Lightbourn-Rojas, L., and Leon-Felix, J. Isolation and Characterization of phiLLS, a Novel Phage with Potential Biocontrol Agent against Multidrug-Resistant Escherichia coli. Front Microbiol. 2017; 8:1355; PM: 28785246

ABSTRACT: Foodborne diseases are a serious and growing problem, and the incidence and prevalence of antimicrobial resistance among foodborne pathogens is reported to have increased. The emergence of antibiotic-resistant bacterial strains demands novel strategies to counteract this epidemic. In this regard, lytic bacteriophages have reemerged as an alternative for the control of pathogenic bacteria. However, the effective use of phages relies on appropriate biological and genomic characterization. In this study, we present the isolation and characterization of a novel bacteriophage named phiLLS, which has shown strong lytic activity against generic and multidrug-resistant Escherichia coli strains. Transmission electron microscopy of phiLLS morphology revealed that it belongs to the Siphoviridae family. Furthermore, this phage exhibited a relatively large burst size of 176 plaque-forming units per infected cell. Phage phiLLS significantly reduced the growth of E. coli under laboratory conditions. Analyses of restriction profiles showed the presence of submolar fragments, confirming that phiLLS is a pac-type phage. Phylogenetic analysis based on the amino acid sequence of large terminase subunits confirmed that this phage uses a headful packaging strategy to package their genome. Genomic sequencing and bioinformatic analysis showed that phiLLS is a novel bacteriophage that is most closely related to T5-like phages. In silico analysis indicated that the phiLLS genome consists of 107,263 bp (39.0 % GC content) encoding 160 putative ORFs, 16 tRNAs, several potential promoters and transcriptional terminators. Genome analysis suggests that the phage phiLLS is strictly lytic without carrying genes associated with virulence factors and/or potential immunoreactive allergen proteins. The bacteriophage isolated in this study has shown promising results in the biocontrol of bacterial growth under in vitro conditions, suggesting that it may prove useful as an alternative agent for the control of foodborne pathogens. However, further oral toxicity testing is needed to ensure the safety of phage use.

Armstrong, A. M., Sobsey, M. D., and Casanova, L. M. Disinfection of bacteriophage MS2 by copper in water. Appl.Microbiol.Biotechnol. 7-30-2017; PM: 28756591

ABSTRACT: Households that lack piped water supply are often forced to meet water

needs by storing in the home, leaving water vulnerable to contamination by viruses. Storage in copper containers can potentially prevent this type of contamination, but the inactivation kinetics of viruses by copper need to be described to make appropriate storage recommendations. This work characterized inactivation kinetics of bacteriophage MS2 as a surrogate for enteric viruses by dissolved ionic copper in water. Reduction of MS2 increased with increasing doses of copper. At 0.3 mg/L, there was a 1.8-log10 reduction of MS2 within 6 h. At 1 and 3 mg/L, 2-2.5 log10 inactivation could be achieved between 6 and 24 h. Parameters for the Chick-Watson, Hom, and One Hit-Two Population models of inactivation were calculated and evaluated, all of which demonstrated strong goodness-of-fit and predictability at various contact times. Copper inactivates MS2 under controlled conditions at doses between 0.3 and 3 mg/L. Although requiring longer contact times than conventional disinfectants, it is a candidate for improving the safety of stored drinking water.

Baig, A., Colom, J., Barrow, P., Schouler, C., Moodley, A., Lavigne, R., and Atterbury, R. Biology and Genomics of an Historic Therapeutic Escherichia coli Bacteriophage Collection. Front Microbiol. 2017; 8:1652; PM: 28912765

ABSTRACT: We have performed microbiological and genomic characterization of an historic collection of nine bacteriophages, specifically infecting a K1 E. coli O18:K1:H7 ColV+ strain. These phages were isolated from sewage and tested for their efficacy in vivo for the treatment of systemic E. coli infection in a mouse infection model by Smith and Huggins (1982). The aim of the study was to identify common microbiological and genomic characteristics, which co-relate to the performance of these phages in in vivo study. These features will allow an informed selection of phages for use as therapeutic agents. Transmission electron microscopy showed that six of the nine phages were Podoviridae and the remaining three were Siphoviridae. The four best performing phages in vivo belonged to the Podoviridae family. In vitro, these phages exhibited very short latent and rise periods in our study. In agreement with their microbiological profiles, characterization by genome sequencing showed that all six podoviruses belong to the Autographivirinae subfamily. Of these, four were isolates of the same species (99% identity), whereas two had divergent genomes compared to other podoviruses. The Siphoviridae phages, which were moderate to poor performers in vivo, exhibited longer latent and rise periods in vitro. Two of the three siphoviruses were closely related to each other (99% identity), but all can be associated with the Guernseyvirinae subfamily. Genome sequence comparison of both types of phages showed that a gene encoding for DNA-dependent RNA polymerase was only present in phages with faster replication cycle, which may account for their better performance in vivo. These data define a combination of microbiological, genomic and in vivo characteristics which allow a more rational evaluation of the original in vivo data and pave the way for the selection of phages for future phage therapy trails.

Bakhshinejad, B. and Ghiasvand, S. Bacteriophages in the human gut: Our fellow travelers throughout life and potential biomarkers of heath or disease. Virus Res. 8-15-2017; 240:47-55; PM: 28743462

ABSTRACT: The gastrointestinal (GI) tract is populated by a huge variety of viruses. Bacterial viruses (bacteriophages) constitute the largest and the most unrecognized part of virome. The total bacteriophage community of the human gut is called phageome. Phages colonize the gut from the earliest moments of life and become our fellow travelers throughout life. Phageome seems to be unique to each individual and shows a

high degree of interpersonal variation. In the healthy gut, a vast majority of phages have a lysogenic lifestyle. These prophages serve as a major respository of mobile genetic elements in the gut and play key roles in the exchange of genetic material between bacterial species via horizontal gene transfer (HGT). But, imbalance in the gut microbial community during dysbiosis, caused by diseases or environmental stresses such as antibiotics, is accompanied by induction of prophages leading to a decreased ratio of symbionts to pathobionts. Based on this, a diseased gut is transformed from an environment predominantly occupied by prophages to an ecosystem mostly inhabited by lytic phages. A growing body of evidence has provided support for the notion that phageome structure and composition change dependent on the physiological or pathological status of the body. This has been demonstrated by pronounced quantitative and qualitative differences between the phageome of healthy individuals and patients. Although many aspects of the contribution made by phages to human biology remain to be understood, recent findings favor the suggestion that phageome might represent potential to serve as a biomarker of health or disease.

Bassetti, M., Poulakou, G., Ruppe, E., Bouza, E., Van Hal, S. J., and Brink, A. Antimicrobial resistance in the next 30 years, humankind, bugs and drugs: a visionary approach. Intensive Care Med. 7-21-2017; PM: 28733718

*ABSTRACT**: PURPOSE***: To describe the current standards of care and major recent advances with regard to antimicrobial resistance (AMR) and to give a prospective overview for the next 30 years in this field. ***METHODS***: Review of medical literature and expert opinion were used in the development of this review. ***RESULTS***: There is undoubtedly a large clinical and public health burden associated with AMR in ICU, but it is challenging to quantify the associated excess morbidity and mortality. In the last decade, antibiotic stewardship and infection prevention and control have been unable to prevent the rapid spread of resistant Gram-negative bacteria (GNB), in particular carbapenem-resistant Pseudomonas aeruginosa (and other non-fermenting GNB), extended-spectrum beta-lactamase (ESBL)-producing and carbapenem-resistant Enterobacteriaceae (CRE). The situation appears more optimistic currently for Gram-positive, where Staphylococcus aureus, and particularly methicillin-resistant S. aureus (MRSA), remains a cardinal cause of healthcare-associated infections worldwide. Recent advancements in laboratory techniques allow for a rapid identification of the infecting pathogen and antibiotic susceptibility testing. Their impact can be particularly relevant in settings with prevalence of MDR, since they may guide fine-tuning of empirically selected regimen, facilitate de-escalation of unnecessary antimicrobials, and support infection control decisions. Currently, antibiotics are the primary anti-infective solution for patients with known or suspected MDR bacteria in intensive care. Numerous incentives have been provided to encourage researchers to work on alternative strategies to reverse this trend and to provide a means to treat these pathogens. Although some promising antibiotics currently in phase 2 and 3 of development will soon be licensed and utilized in ICU, the continuous development of an alternative generation of compounds is extremely important. There are currently several promising avenues available to fight antibiotic resistance, such as faecal microbiota, and phage therapy.

Benesik, M., Novacek, J., Janda, L., Dopitova, R., Pernisova, M., Melkova, K., Tisakova, L., Doskar, J., Zidek, L., Hejatko, J., and Pantucek, R. Role of SH3b binding domain in a natural deletion mutant of Kayvirus endolysin LysF1 with a broad range of lytic activity. Virus Genes. 8-29-2017; PM: 28852930

ABSTRACT: The spontaneous host-range mutants 812F1 and K1/420 are derived from polyvalent phage 812 that is almost identical to phage K, belonging to family Myoviridae and genus Kayvirus. Phage K1/420 is used for the phage therapy of staphylococcal infections. Endolysin of these mutants designated LysF1, consisting of an N-terminal cysteine-histidine-dependent aminohydrolase/peptidase (CHAP) domain and C-terminal SH3b cell wall-binding domain, has deleted middle amidase domain compared to wild-type endolysin. In this work, LysF1 and both its domains were prepared as recombinant proteins and their function was analyzed. LysF1 had an antimicrobial effect on 31 Staphylococcus species of the 43 tested. SH3b domain influenced antimicrobial activity of LysF1, since the lytic activity of the truncated variant containing the CHAP domain alone was decreased. The results of a co-sedimentation assay of SH3b domain showed that it was able to bind to three types of purified staphylococcal peptidoglycan 11.2, 11.3, and 11.8 that differ in their peptide bridge, but also to the peptidoglycan type 11.5 of Streptococcus uberis, and this capability was verified in vivo using the fusion protein with GFP and fluorescence microscopy. Using several different approaches, including NMR, we have not confirmed the previously proposed interaction of the SH3b domain with the pentaglycine bridge in the bacterial cell wall. The new naturally raised deletion mutant endolysin LysF1 is smaller than LysK, has a broad lytic spectrum, and therefore is an appropriate enzyme for practical use. The binding spectrum of SH3b domain covering all known staphylococcal peptidoglycan types is a promising feature for creating new chimeolysins by combining it with more effective catalytic domains.

Bhardwaj, N., Bhardwaj, S. K., Mehta, J., Kim, K. H., and Deep, A. MOF-Bacteriophage Biosensor for Highly Sensitive and Specific Detection of S. aureus. ACS Appl.Mater.Interfaces. 9-11-2017; PM: 28891643

ABSTRACT: To produce a sensitive and specific biosensor for S. aureus, bacteriophages have been interfaced with a water-dispersible and environmentally stable metal organic framework, NH2-MIL-53 (Fe). The conjugation of the MOF with bacteriophages has been achieved through the use of glutaraldehyde as crosslinker. Highly sensitive detection of S. aureus in both synthetic and real samples was realized by the proposed MOF-bacteriophage biosensor based on the photoluminescence quenching phenomena: limit of detection (31 CFU/mL) and range of detection (40 to 4 x 108 CFU/mL). This is the first report exploiting the use of an MOF-bacteriophage complex for the biosensing of S. aureus. The results of our study highlight that the proposed biosensor is more sensitive than most of the previous methods while exhibiting some advanced features like specificity, regenerability, extended range of linear detection, and stability for long-term storage (even at the room temperature conditions).

Bille, E., Meyer, J., Jamet, A., Euphrasie, D., Barnier, J. P., Brissac, T., Larsen, A., Pelissier, P., and Nassif, X. A virulence-associated filamentous bacteriophage of Neisseria meningitidis increases host-cell colonisation. PLoS.Pathog. 2017; 13(7):e1006495; PM: 28704569

ABSTRACT: Neisseria meningitidis is a commensal of human nasopharynx. In some circumstances, this bacteria can invade the bloodstream and, after crossing the blood brain barrier, the meninges. A filamentous phage, designated MDAPhi for Meningococcal Disease Associated, has been associated with invasive disease. In this work we show that the prophage is not associated with a higher virulence during the bloodstream phase of the disease. However, looking at the interaction of N. meningitidis

with epithelial cells, a step essential for colonization of the nasopharynx, we demonstrate that the presence of the prophage, via the production of viruses, increases colonization of encapsulated meningococci onto monolayers of epithelial cells. The analysis of the biomass covering the epithelial cells revealed that meningococci are bound to the apical surface of host cells by few layers of heavily piliated bacteria, whereas, in the upper layers, bacteria are non-piliated but surrounded by phage particles which (i) form bundles of filaments, and/or (ii) are in some places associated with bacteria. The latter are likely to correspond to growing bacteriophages during their extrusion through the outer membrane. These data suggest that, as the biomass increases, the loss of piliation in the upper layers of the biomass does not allow type IV pilus bacterial aggregation, but is compensated by a large production of phage particles that promote bacterial aggregation via the formation of bundles of phage filaments linked to the bacterial cell walls. We propose that MDAPhi by increasing bacterial colonization in the mucosa at the site-of-entry, increase the occurrence of diseases.

Bock, D., Medeiros, J. M., Tsao, H. F., Penz, T., Weiss, G. L., Aistleitner, K., Horn, M., and Pilhofer, M. In situ architecture, function, and evolution of a contractile injection system. Science. 8-18-2017; 357(6352):713-717; PM: 28818949

ABSTRACT: Contractile injection systems mediate bacterial cell-cell interactions by a bacteriophage tail-like structure. In contrast to extracellular systems, the type 6 secretion system (T6SS) is defined by intracellular localization and attachment to the cytoplasmic membrane. Here we used cryo-focused ion beam milling, electron cryotomography, and functional assays to study a T6SS in Amoebophilus asiaticus The in situ architecture revealed three modules, including a contractile sheath-tube, a baseplate, and an anchor. All modules showed conformational changes upon firing. Lateral baseplate interactions coordinated T6SSs in hexagonal arrays. The system mediated interactions with host membranes and may participate in phagosome escape. Evolutionary sequence analyses predicted that T6SSs are more widespread than previously thought. Our insights form the basis for understanding T6SS key concepts and exploring T6SS diversity.

Bodier-Montagutelli, E., Morello, E., L'Hostis, G., Guillon, A., Dalloneau, E., Respaud, R., Pallaoro, N., Blois, H., Vecellio, L., Gabard, J., and Heuze-Vourc'h, N. Inhaled phage therapy: a promising and challenging approach to treat bacterial respiratory infections. Expert.Opin.Drug Deliv. 2017; 14(8):959-972; PM: 27776446

*ABSTRACT**: INTRODUCTION***: Bacterial respiratory tract infections (RTIs) are increasingly difficult to treat due to evolving antibiotic resistance. In this context, bacteriophages (or phages) are part of the foreseen alternatives or combination therapies. Delivering phages through the airways seems more relevant to accumulate these natural antibacterial viruses in proximity to their bacterial host, within the infectious site. ***Areas covered***: This review addresses the potential of phage therapy to treat RTIs and discusses preclinical and clinical results of phages administration in this context. Recent phage formulation and aerosolization attempts are also reviewed, raising technical challenges to achieve efficient pulmonary deposition via inhalation. Expert opinion: Overall, the inhalation of phages as antibacterial treatment seems both clinically relevant and technically feasible. Several crucial points still need to be investigated, such as phage product pharmacokinetics and immunogenicity. Furthermore, given phage-specific features, appropriate regulatory and manufacturing guidelines will need to be defined.

Finally, randomized controlled clinical trials should be carried out to establish phage therapy's clinical positioning in the antimicrobial arsenal against RTIs.

Boggione, D. M. G., Batalha, L. S., Gontijo, M. T. P., Lopez, M. E. S., Teixeira, A. V. N. C., Santos, I. J. B., and Mendonca, R. C. S. Evaluation of microencapsulation of the UFV-AREG1 bacteriophage in alginate-Ca microcapsules using microfluidic devices. Colloids Surf.B Biointerfaces. 6-28-2017; 158:182-189; PM: 28692873

ABSTRACT: The indiscriminate use of antibiotics and the emergence of resistant microorganisms have become a major challenge for the food industry. The purpose of this work was to microencapsulate the bacteriophage UFV-AREG1 in a calcium alginate matrix using microfluidic devices and to study the viability and efficiency of retention. The microcapsules were added to gel of propylene glycol for use as an antimicrobial in the food industry. The technique showed the number of the phage encapsulation, yielding drops with an average 100-250mum of diameter, 82.1+/-2% retention efficiency and stability in the gel matrix for 21days. The gel added to the microencapsulated phage showed efficiency (not detectable on the surface) in reducing bacterial contamination on the surface at a similar level to antimicrobial chemicals (alcohol 70%). Therefore, it was possible to microencapsulate bacteriophages in alginate-Ca and apply the microcapsules in gels for use as sanitizers in the food industry.

Borkotoky, S. and Murali, A. A computational assessment of pH-dependent differential interaction of T7 lysozyme with T7 RNA polymerase. BMC.Struct.Biol. 5-25-2017; 17(1):7; PM: 28545576

*ABSTRACT**: BACKGROUND***: T7 lysozyme (T7L), also known as N-acetylmuramoyl-L-alanine amidase, is a T7 bacteriophage gene product. It involves two functions: It can cut amide bonds in the bacterial cell wall and interacts with T7 RNA polymerase (T7RNAP) as a part of transcription inhibition. In this study, with the help of molecular dynamics (MD) calculations and computational interaction studies, we investigated the effect of varying pH conditions on conformational flexibilities of T7L and their influence on T7RNAP -T7L interactions. ***RESULTS***: From the MD studies of the T7L at three different pH strengths viz. 5, neutral and 7.9 it was observed that T7L structure at pH 5 exhibited less stable nature with more residue level fluctuations, decrease of secondary structural elements and less compactness as compared to its counterparts: neutral pH and pH 7.9. The T-pad analysis of the MD trajectories identified local fluctuations in few residues that influenced the conformational differences in three pH strengths. From the docking of the minimum energy representative structures of T7L at different pH strengths (obtained from the free energy landscape analysis) with T7RNAP structures at same pH strengths, we saw strong interaction patterns at pH 7.9 and pH 5. The MD analysis of these complexes also confirmed the observations of docking study. From the combined in silico studies, it was observed that there are conformational changes in N-terminal and near helix 1 of T7L at different pH strengths, which are involved in the T7RNAP interaction, thereby varying the interaction pattern. ***CONCLUSION***: Since T7L has been used for developing novel therapeutics and T7RNAP one of the most biologically useful protein in both in-vitro and in vivo experiments, this in silico study of pH dependent conformational differences in T7L and the differential interaction with T7RNAP at different pH can provide a significant insight into the structural investigations on T7L and T7RNAP in varying pH environments.

Born, Y., Fieseler, L., Thony, V., Leimer, N., Duffy, B., and Loessner, M. J. Engineering of Bacteriophages Y2::dpoL1-C and Y2::luxAB for Efficient Control and Rapid Detection of the Fire Blight Pathogen, Erwinia amylovora. Appl.Environ.Microbiol. 6-15-2017; 83(12); PM: 28389547

ABSTRACT: Erwinia amylovora is the causative agent of fire blight, a devastating plant disease affecting members of the Rosaceae Alternatives to antibiotics for control of fire blight symptoms and outbreaks are highly desirable, due to increasing drug resistance and tight regulatory restrictions. Moreover, the available diagnostic methods either lack sensitivity, lack speed, or are unable to discriminate between live and dead bacteria. Owing to their extreme biological specificity, bacteriophages are promising alternatives for both aims. In this study, the virulent broad-host-range E. amylovora virus Y2 was engineered to enhance its killing activity and for use as a luciferase reporter phage, respectively. Toward these aims, a depolymerase gene of E. amylovora virus L1 (dpoL1-C) or a bacterial luxAB fusion was introduced into the genome of Y2 by homologous recombination. The genes were placed downstream of the major capsid protein orf68, under the control of the native promoter. The modifications did not affect viability of infectivity of the recombinant viruses. Phage Y2::dpoL1-C demonstrated synergistic activity between the depolymerase degrading the exopolysaccharide capsule and phage infection, which greatly enhanced bacterial killing. It also significantly reduced the ability of E. amylovora to colonize the surface of detached flowers. The reporter phage Y2::luxAB transduced bacterial luciferase into host cells and induced synthesis of large amounts of a LuxAB luciferase fusion. After the addition of aldehyde substrate, bioluminescence could be readily monitored, and this enabled rapid and specific detection of low numbers of viable bacteria, without enrichment, both in vitro and in plant material. ***IMPORTANCE***: Fire blight, caused by Erwinia amylovora, is the major threat to global pome fruit production, with high economic losses every year. Bacteriophages represent promising alternatives to not only control the disease, but also for rapid diagnostics. To enhance biocontrol efficacy, we combined the desired properties of two phages, Y2 (broad host range) and L1 (depolymerase for capsule degradation) in a single recombinant phage. This phage showed enhanced biocontrol and could reduce E. amylovora on flowers. Phage Y2 was also genetically engineered into a luciferase reporter phage, which transduces bacterial bioluminescence into infected cells and allows detection of low numbers of viable target bacteria. The combination of speed, sensitivity, and specificity is superior to previously used diagnostic methods. In conclusion, genetic engineering could improve the properties of phage Y2 toward better killing efficacy and sensitive detection of E. amylovora cells.

Brady, T. M., Strauch, A. L., Almaguer, C. M., Niezgoda, G., Shaffer, R. E., Yorio, P. L., and Fisher, E. M. Transfer of Bacteriophage MS2 and Fluorescein from N95 Filtering Facepiece Respirators to Hands: Measuring Fomite Potential. J.Occup.Environ.Hyg. 6-26-2017; 0; PM: 28650715

ABSTRACT: Contact transmission of pathogens from personal protective equipment is a concern within the healthcare industry. During public health emergency outbreaks, resources become constrained and the reuse of personal protective equipment, such as N95 filtering facepiece respirators, may be needed. This study was designed to characterize the transfer of bacteriophage MS2 and fluorescein between filtering facepiece respirators and the wearer's hands during three simulated use scenarios. Filtering facepiece respirators were contaminated with MS2 and fluorescein in droplets or droplet nuclei. Thirteen test subjects performed filtering facepiece respirator use

scenarios including improper doffing, proper doffing and reuse, and improper doffing and reuse. Fluorescein and MS2 contamination transfer were quantified. The average MS2 transfer from filtering facepiece respirators to the subjects' hands ranged from 7.6-15.4% and 2.2-2.7% for droplet and droplet nuclei derived contamination, respectively. Handling filtering facepiece respirators contaminated with droplets resulted in higher levels of MS2 transfer compared to droplet nuclei for all use scenarios ($p = 0.007$). MS2 transfer from droplet contaminated filtering facepiece respirators during improper doffing and reuse was greater than transfer during improper doffing ($p = 0.008$) and proper doffing and reuse ($p = 0.042$). Droplet contamination resulted in higher levels of fluorescein transfer compared to droplet nuclei contaminated filtering facepiece respirators for all use scenarios ($p = 0.009$). Fluorescein transfer was greater for improper doffing and reuse ($p = 0.007$) from droplet contaminated masks compared to droplet nuclei contaminated filtering facepiece respirators and for improper doffing and reuse when compared improper doffing ($p = 0.017$) and proper doffing and reuse ($p = 0.018$) for droplet contaminated filtering facepiece respirators. For droplet nuclei contaminated filtering facepiece respirators, the difference in MS2 and fluorescein transfer did not reach statistical significance when comparing any of the use scenarios. The findings suggest that the results of fluorescein and MS2 transfer were consistent and highly correlated across the conditions of study. The data supports CDC recommendations for using proper doffing techniques and discarding filtering facepiece respirators that are directly contaminated with secretions from a cough or sneeze.

Brodel, A. K., Jaramillo, A., and Isalan, M. Intracellular directed evolution of proteins from combinatorial libraries based on conditional phage replication. Nat.Protoc. 2017; 12(9):1830-1843; PM: 28796233

ABSTRACT: Directed evolution is a powerful tool to improve the characteristics of biomolecules. Here we present a protocol for the intracellular evolution of proteins with distinct differences and advantages in comparison with established techniques. These include the ability to select for a particular function from a library of protein variants inside cells, minimizing undesired coevolution and propagation of nonfunctional library members, as well as allowing positive and negative selection logics using basally active promoters. A typical evolution experiment comprises the following stages: (i) preparation of a combinatorial M13 phagemid (PM) library expressing variants of the gene of interest (GOI) and preparation of the Escherichia coli host cells; (ii) multiple rounds of an intracellular selection process toward a desired activity; and (iii) the characterization of the evolved target proteins. The system has been developed for the selection of new orthogonal transcription factors (TFs) but is capable of evolving any gene-or gene circuit function-that can be linked to conditional M13 phage replication. Here we demonstrate our approach using as an example the directed evolution of the bacteriophage lambda cI TF against two synthetic bidirectional promoters. The evolved TF variants enable simultaneous activation and repression against their engineered promoters and do not cross-react with the wild-type promoter, thus ensuring orthogonality. This protocol requires no special equipment, allowing synthetic biologists and general users to evolve improved biomolecules within approximately 7 weeks.

Broeker, N. K. and Barbirz, S. Not a barrier but a key: How bacteriophages exploit host's O-antigen as an essential receptor to initiate infection. Mol.Microbiol. 2017; 105(3):353-357; PM: 28618013

ABSTRACT: Tailed bacteriophages specific for Gram-negative bacteria encounter lipopolysaccharide (LPS) during the first infection steps. Yet, it is not well understood how biochemistry of these initial interactions relates to subsequent events that orchestrate phage adsorption and tail rearrangements to initiate cell entry. For many phages, long O-antigen chains found on the LPS of smooth bacterial strains serve as essential receptor recognized by their tailspike proteins (TSP). Many TSP are depolymerases and O-antigen cleavage was described as necessary step for subsequent orientation towards a secondary receptor. However, O-antigen specific host attachment must not always come along with O-antigen degradation. In this issue of Molecular Microbiology Prokhorov et al. report that coliphage G7C carries a TSP that deacetylates O-antigen but does not degrade it, whereas rough strains or strains lacking O-antigen acetylation remain unaffected. Bacteriophage G7C specifically functionalizes its tail by attaching the deacetylase TSP directly to a second TSP that is nonfunctional on the host's O-antigen. This challenges the view that bacteriophages use their TSP only to clear their way to a secondary receptor. Rather, O-antigen specific phages may employ enzymatically active TSP as a tool for irreversible LPS membrane binding to initiate subsequent infection steps.

Brown, T. L., Petrovski, S., Hoyle, D., Chan, H. T., Lock, P., and Tucci, J. Characterization and formulation into solid dosage forms of a novel bacteriophage lytic against Klebsiella oxytoca. PLoS.One. 2017; 12(8):e0183510; PM: 28817689

ABSTRACT: ***AIM***: To isolate and characterize bacteriophage lytic for the opportunistic pathogen Klebsiella oxytoca and their formulation into a range of solid dosage forms for in-vitro testing. ***METHODS AND RESULTS***: We report the isolation, genomic and functional characterization of a novel bacteriophage lytic for Klebsiella oxytoca, which does not infect the closely related Klebsiella pneumoniae. This bacteriophage was formulated into suppositories and troches and shown to be released and lyse underlying Klebsiella oxytoca bacteria in an in-vitro model. These bacteriophage formulations were stable for at least 49 days at 4 degrees C. ***CONCLUSIONS***: The successful in-vitro assay of these formulations here suggests that they could potentially be tested in-vivo to determine whether such a therapeutic approach could modulate the gut microbiome, and control Klebsiella oxytoca overgrowth, during antibiotic therapy regimes. ***SIGNIFICANCE AND IMPACT OF THE STUDY***: This study reports a novel bacteriophage specific for Klebsiella oxytoca which can be formulated into solid dosage forms appropriate for potential delivery in testing as a therapy to modulate gut microbiome during antibiotic therapies.

Brussow, H. Phage therapy for the treatment of human intestinal bacterial infections: soon to be a reality? Expert.Rev.Gastroenterol.Hepatol. 2017; 11(9):785-788; PM: 28612636

No Abstract Available.

Cahill, J., Rajaure, M., Holt, A., Moreland, R., O'Leary, C., Kulkarni, A., Sloan, J., and Young, R. Suppressor Analysis of the Fusogenic Lambda Spanins. J.Virol. 7-15-2017; 91(14); PM: 28468876

ABSTRACT: The final step of lysis in phage lambda infections of Escherichia coli is mediated by the spanins Rz and Rz1. These proteins form a complex that bridges the cell

envelope and that has been proposed to cause fusion of the inner and outer membranes. Accordingly, mutations that block spanin function are found within coiled-coil domains and the proline-rich region, motifs essential in other fusion systems. To gain insight into spanin function, pseudorevertant alleles that restored plaque formation for lysis-defective mutants of Rz and Rz1 were selected. Most second-site suppressors clustered within a coiled-coil domain of Rz near the outer leaflet of the cytoplasmic membrane and were not allele specific. Suppressors largely encoded polar insertions within the hydrophobic core of the coiled-coil interface. Such suppressor changes resulted in decreased proteolytic stability of the Rz double mutants in vivo Unlike the wild type, in which lysis occurs while the cells retain a rod shape, revertant alleles with second-site suppressor mutations supported lysis events that were preceded by spherical cell formation. This suggests that destabilization of the membrane-proximal coiled coil restores function for defective spanin alleles by increasing the conformational freedom of the complex at the cost of its normal, all-or-nothing functionality. ***IMPORTANCE***: Caudovirales encode cell envelope-spanning proteins called spanins, which are thought to fuse the inner and outer membranes during phage lysis. Recent genetic analysis identified the functional domains of the lambda spanins, which are similar to class I viral fusion proteins. While the pre- and postfusion structures of model fusion systems have been well characterized, the intermediate structure(s) formed during the fusion reaction remains elusive. Genetic analysis would be expected to identify functional connections between intermediates. Since most membrane fusion systems are not genetically tractable, only few such investigations have been reported. Here, we report a suppressor analysis of lambda spanin function. To our knowledge this is the first suppression analysis of a class I-like complex and also the first such analysis of a prokaryote membrane fusion system.

Carding, S. R., Davis, N., and Hoyles, L. Review article: the human intestinal virome in health and disease. Aliment.Pharmacol.Ther. 9-4-2017; PM: 28869283

*ABSTRACT****: BACKGROUND***: The human virome consists of animal-cell viruses causing transient infections, bacteriophage (phage) predators of bacteria and archaea, endogenous retroviruses and viruses causing persistent and latent infections. High-throughput, inexpensive, sensitive sequencing methods and metagenomics now make it possible to study the contribution dsDNA, ssDNA and RNA virus-like particles make to the human virome, and in particular the intestinal virome. ***AIM***: To review and evaluate the pioneering studies that have attempted to characterise the human virome and generated an increased interest in understanding how the intestinal virome might contribute to maintaining health, and the pathogenesis of chronic diseases. ***METHODS***: Relevant virome-related articles were selected for review following extensive language- and date-unrestricted, electronic searches of the literature. ***RESULTS***: The human intestinal virome is personalised and stable, and dominated by phages. It develops soon after birth in parallel with prokaryotic communities of the microbiota, becoming established during the first few years of life. By infecting specific populations of bacteria, phages can alter microbiota structure by killing host cells or altering their phenotype, enabling phages to contribute to maintaining intestinal homeostasis or microbial imbalance (dysbiosis), and the development of chronic infectious and autoimmune diseases including HIV infection and Crohn's disease, respectively. ***CONCLUSIONS***: Our understanding of the intestinal virome is fragmented and requires standardised methods for virus isolation and sequencing to provide a more complete picture of the virome, which is key to explaining the basis of virome-disease associations, and how enteric viruses can contribute to disease aetiologies and be rationalised as targets for interventions.

Carrigy, N. B., Chang, R. Y., Leung, S. S. Y., Harrison, M., Petrova, Z., Pope, W. H., Hatfull, G. F., Britton, W. J., Chan, H. K., Sauvageau, D., Finlay, W. H., and Vehring, R. Anti-Tuberculosis Bacteriophage D29 Delivery with a Vibrating Mesh Nebulizer, Jet Nebulizer, and Soft Mist Inhaler. Pharm.Res. 6-23-2017; PM: 28646325

ABSTRACT: ***PURPOSE***: To compare titer reduction and delivery rate of active anti-tuberculosis bacteriophage (phage) D29 with three inhalation devices. ***METHODS***: Phage D29 lysate was amplified to a titer of 11.8 +/- 0.3 log10(pfu/mL) and diluted 1:100 in isotonic saline. Filters captured the aerosolized saline D29 preparation emitted from three types of inhalation devices: 1) vibrating mesh nebulizer; 2) jet nebulizer; 3) soft mist inhaler. Full-plate plaque assays, performed in triplicate at multiple dilution levels with the surrogate host Mycobacterium smegmatis, were used to quantify phage titer. ***RESULTS***: Respective titer reductions for the vibrating mesh nebulizer, jet nebulizer, and soft mist inhaler were 0.4 +/- 0.1, 3.7 +/- 0.1, and 0.6 +/- 0.3 log10(pfu/mL). Active phage delivery rate was significantly greater ($p < 0.01$) for the vibrating mesh nebulizer (3.3x108 +/- 0.8x108 pfu/min) than for the jet nebulizer (5.4x104 +/- 1.3x104 pfu/min). The soft mist inhaler delivered 4.6x106 +/- 2.0x106 pfu per 11.6 +/- 1.6 muL ex-actuator dose. ***CONCLUSIONS***: Delivering active phage requires a prudent choice of inhalation device. The jet nebulizer was not a good choice for aerosolizing phage D29 under the tested conditions, due to substantial titer reduction likely occurring during droplet production. The vibrating mesh nebulizer is recommended for animal inhalation studies requiring large amounts of D29 aerosol, whereas the soft mist inhaler may be useful for self-administration of D29 aerosol.

Carroll, M. and Zhou, X. Panacea in progress: CRISPR and the future of its biological research introduction. Microbiol.Res. 2017; 201:63-74; PM: 28602403

ABSTRACT: The elucidation of the CRISPR (clustered, regularly interspaced, short palindromic repeats) adaptive immune system endogenous to most microbial life has culminated in progress in a diversity of scientific disciplines. The concurrently promising and eccentric nature of its theoretically plausible applications has wrought enthusiasm in the research community globally, potentiating advancements in human and animal health, ecological stability, and economic wellbeing, that would hitherto be considered the unattainable fancies of a futurist. It may be supposed that the tomes of science fiction are the true books of prophecy. Here, we narrate the scientific dialogue regarding CRISPR/Cas biotechnologies, from the happenstantial initial observation of the locus to the litany of intriguing contemporary endeavors. We discuss the mechanistic underpinnings in detail, and the corpulent body of literature on CRISPR-based biotech is digested into a germane and informative review. CRISPR applications such as microbiome engineering in order to enhance the human immune system beyond the fortitude of the wild type, bacterial genome editing in industrial and medical aspects, conquering antibiotic resistance, the development of novel antimicrobial techniques, the harvesting of solventogenic microbes, the development of antifungal therapies, and investigation of the genetic properties of fungi, are here represented, and the authors posit unconventional, and at times gainfully tangential, thoughts and concepts in order to encourage a reflective disposition towards this sophisticated device of nature: a panacea in progress, such that the most impassive and technical writing still carries the ring of poetry.

Carvajal, G., Branch, A., Sisson, S. A., Roser, D. J., van den, Akker B., Monis, P., Reeve, P., Keegan, A., Regel, R., and Khan, S. J. Virus removal by ultrafiltration: Understanding long-term performance change by application of Bayesian analysis. Water Res. 10-1-2017; 122:269-279; PM: 28609730

ABSTRACT: Ultrafiltration is an effective barrier to waterborne pathogens including viruses. Challenge testing is commonly used to test the inherent reliability of such systems. Performance validation seeks to demonstrate the adequate reliability of the treatment system. Appropriate and rigorous data analysis is an essential aspect of validation testing. In this study we used Bayesian analysis to assess the performance of a full-scale ultrafiltration system which was validated and revalidated after five years of operation. A hierarchical Bayesian model was used to analyse a number of similar ultrafiltration membrane skids working in parallel during the two validation periods. This approach enhanced our ability to obtain accurate estimations of performance variability, especially when the sample size of some system skids was limited. This methodology enabled the quantitative estimation of uncertainty in the performance parameters and generation of predictive distributions incorporating those uncertainties. The results indicated that there was a decrease in the mean skid performance after five years of operation of approximately 1 log reduction value (LRV). Interestingly, variability in the LRV also reduced, with standard deviations from the revalidation data being decreased by a mean 0.37 LRV compared with the original validation data. The model was also useful in comparing the operating performance of the various parallel skids within the same year. Evidence of differences was obtained in 2015 for one of the membrane skids. A hierarchical Bayesian analysis of validation data provides robust estimations of performance and the incorporation of probabilistic analysis which is increasingly important for comprehensive quantitative risk assessment purposes.

Chaikeeratisak, V., Nguyen, K., Egan, M. E., Erb, M. L., Vavilina, A., and Pogliano, J. The Phage Nucleus and Tubulin Spindle Are Conserved among Large Pseudomonas Phages. Cell Rep. 8-15-2017; 20(7):1563-1571; PM: 28813669

ABSTRACT: We recently demonstrated that the large Pseudomonas chlororaphis bacteriophage 201phi2-1 assembles a nucleus-like structure that encloses phage DNA and segregates proteins according to function, with DNA processing proteins inside and metabolic enzymes and ribosomes outside the nucleus. Here, we investigate the replication pathway of the Pseudomonas aeruginosa bacteriophages phiKZ and phiPA3. Bacteriophages phiKZ and phiPA3 encode a proteinaceous shell that assembles a nucleus-like structure that compartmentalizes proteins and DNA during viral infection. We show that the tubulin-like protein PhuZ encoded by each phage assembles a bipolar spindle that displays dynamic instability and positions the nucleus at midcell. Our results suggest that the phage spindle and nucleus play the same functional role in all three phages, 201phi2-1, phiKZ, and phiPA3, demonstrating that these key structures are conserved among large Pseudomonas phages.

Chamakura, K. R., Tran, J. S., and Young, R. MS2 Lysis of Escherichia coli Depends on Host Chaperone DnaJ. J.Bacteriol. 6-15-2017; 199(12); PM: 28396351

ABSTRACT: The L protein of the single-stranded RNA phage MS2 causes lysis of Escherichia coli without inducing bacteriolytic activity or inhibiting net peptidoglycan (PG) synthesis. To find host genes required for L-mediated lysis, spontaneous lll (insensitivity to Llysis) mutants were selected as survivors of L expression and shown to have a missense

change of the highly conserved proline (P330Q) in the C-terminal domain of DnaJ. In the dnaJP330Q mutant host, L-mediated lysis is completely blocked at 30 degrees C without affecting the intracellular levels of L. At higher temperatures (37 degrees C and 42 degrees C), both lysis and L accumulation are delayed. The lysis block at 30 degrees C in the dnaJP330Q mutant was recessive and could be suppressed by Lovercomes dnaJ (Lodj) alleles selected for restoration of lysis. All three Lodj alleles lack the highly basic N-terminal half of the lysis protein and cause lysis approximately 20 min earlier than full-length L. DnaJ was found to form a complex with full-length L. This complex was abrogated by the P330Q mutation and was absent with the Lodj truncations. These results suggest that, in the absence of interaction with DnaJ, the N-terminal domain of L interferes with its ability to bind to its unknown target. The lysis retardation and DnaJ chaperone dependency conferred by the nonessential, highly basic N-terminal domain of L resembles the SlyD chaperone dependency conferred by the highly basic C-terminal domain of the E lysis protein of varphiX174, suggesting a common theme where single-gene lysis can be modulated by host factors influenced by physiological conditions.IMPORTANCE Small single-stranded nucleic acid lytic phages (Microviridae and Leviviridae) lyse their host by expressing a single "protein antibiotic." The protein antibiotics from two out of three prototypic small lytic viruses have been shown to inhibit two different steps in the conserved PG biosynthesis pathway. However, the molecular basis of lysis caused by L, the lysis protein of the third prototypic virus, MS2, is unknown. The significance of our research lies in the identification of DnaJ as a chaperone in the MS2 L lysis pathway and the identification of the minimal lytic domain of MS2 L. Additionally, our research highlights the importance of the highly conserved P330 residue in the C-terminal domain of DnaJ for specific protein interactions.

Chamakura, K. R., Sham, L. T., Davis, R. M., Min, L., Cho, H., Ruiz, N., Bernhardt, T. G., and Young, R. A viral protein antibiotic inhibits lipid II flippase activity. Nat.Microbiol. 9-11-2017; PM: 28894177

ABSTRACT: For bacteriophage infections, the cell walls of bacteria, consisting of a single highly polymeric molecule of peptidoglycan (PG), pose a major problem for the release of progeny virions. Phage lysis proteins that overcome this barrier can point the way to new antibacterial strategies 1 , especially small lytic single-stranded DNA (the microviruses) and RNA phages (the leviviruses) that effect host lysis using a single non-enzymatic protein 2 . Previously, the A2 protein of levivirus Qbeta and the E protein of the microvirus varphiX174 were shown to be 'protein antibiotics' that inhibit the MurA and MraY steps of the PG synthesis pathway 2-4 . Here, we investigated the mechanism of action of an unrelated lysis protein, LysM, of the Escherichia coli levivirus M 5 . We show that LysM inhibits the translocation of the final lipid-linked PG precursor called lipid II across the cytoplasmic membrane by interfering with the activity of MurJ. The finding that LysM inhibits a distinct step in the PG synthesis pathway from the A2 and E proteins indicates that small phages, particularly the single-stranded RNA (ssRNA) leviviruses, have a previously unappreciated capacity for evolving novel inhibitors of PG biogenesis despite their limited coding potential.LysM, the lysis protein of the Escherichia coli levivirus M, represents a new 'protein antibiotic' that interferes with the synthesis of peptidoglycan by inhibiting lipid II flipping.

Chang, R. Y., Wong, J., Mathai, A., Morales, S., Kutter, E., Britton, W., Li, J., and Chan, H. K. Production of highly stable spray dried phage formulations for treatment of Pseudomonas aeruginosa lung infection. Eur.J.Pharm.Biopharm. 9-7-2017; PM: 28890220

ABSTRACT: The potential of bacteriophage therapy for the treatment of pulmonary infections caused by antibiotic-resistant bacteria has been well recognised. The purpose of this study was to investigate the effect of excipients on stabilisation and aerosolisation of spray dried powders of morphologically different phages - PEV podovirus and PEV myovirus. Seven anti-pseudomonal phages were screened against 90 clinical strains of bacterial hosts and three of the phages were selected for formulation study based on the host range. Design of experiments was utilised to assess the effect of different excipients on the stabilisation and aerosolisation of spray dried phages. Both podovirus and myovirus phages were stable in spray dried formulations containing trehalose or lactose and leucine as excipients with less than 1-log10 titre reduction during spray drying, with lactose providing superior phage protection over trehalose. Furthermore, the spray dried phage formulations dispersed in an Osmohaler at 85 L/min produced a high fine particle fraction of over 50%. The results showed that the phages in this study can form respirable dry powder phage formulations using the same excipient composition. Spray dried various types of lytic phages hold significant potential for the treatment of pulmonary infections.

Chaudhary, K. BacteRiophage EXclusion (BREX): A novel anti-phage mechanism in the arsenal of bacterial defense system. J.Cell Physiol. 4-26-2017; PM: 28444888

ABSTRACT: The arm race between bacteria and phages leads to the development of many phage resistance mechanisms. Bacteria are perpetually changing their strategy to avert phage infection and killing. Recently, a study published that shed light on a novel bacterial defense system called bacteriophage exclusion (BREX). BREX system is a six-gene cassette in Bacillus cereus which provides complete phage resistance to a broad range of phages, including lytic and temperate ones. It is a novel defense strategy which involves DNA methylation of the host cell and block phage DNA replication.

Chechetkin, V. R. and Lobzin, V. V. Large-scale chromosome folding versus genomic DNA sequences: A discrete double Fourier transform technique. J.Theor.Biol. 8-7-2017; 426:162-179; PM: 28552553

ABSTRACT: Using state-of-the-art techniques combining imaging methods and high-throughput genomic mapping tools leaded to the significant progress in detailing chromosome architecture of various organisms. However, a gap still remains between the rapidly growing structural data on the chromosome folding and the large-scale genome organization. Could a part of information on the chromosome folding be obtained directly from underlying genomic DNA sequences abundantly stored in the databanks? To answer this question, we developed an original discrete double Fourier transform (DDFT). DDFT serves for the detection of large-scale genome regularities associated with domains/units at the different levels of hierarchical chromosome folding. The method is versatile and can be applied to both genomic DNA sequences and corresponding physico-chemical parameters such as base-pairing free energy. The latter characteristic is closely related to the replication and transcription and can also be used for the assessment of temperature or supercoiling effects on the chromosome folding. We tested the method on the genome of E. coli K-12 and found good correspondence with the annotated domains/units established experimentally. As a brief illustration of further abilities of DDFT, the study of large-scale genome organization for bacteriophage PHIX174 and bacterium Caulobacter crescentus was also added. The combined

experimental, modeling, and bioinformatic DDFT analysis should yield more complete knowledge on the chromosome architecture and genome organization.

Chen, B., Akusobi, C., Fang, X., and Salmond, G. P. C. Environmental T4-Family Bacteriophages Evolve to Escape Abortive Infection via Multiple Routes in a Bacterial Host Employing "Altruistic Suicide" through Type III Toxin-Antitoxin Systems. Front Microbiol. 2017; 8:1006; PM: 28620370

ABSTRACT: Abortive infection is an anti-phage mechanism employed by a bacterium to initiate its own death upon phage infection. This reduces, or eliminates, production of viral progeny and protects clonal siblings in the bacterial population by an act akin to an "altruistic suicide." Abortive infection can be mediated by a Type III toxin-antitoxin system called ToxINPa consisting of an endoribonuclease toxin and RNA antitoxin. ToxINPa is a heterohexameric quaternary complex in which pseudoknotted RNA inhibits the toxicity of the toxin until infection by certain phages causes destabilization of ToxINPa, leading to bacteriostasis and, eventually, lethality. However, it is still unknown why only certain phages are able to activate ToxINPa. To try to address this issue we first introduced ToxINPa into the Gram-negative enterobacterium, Serratia sp. ATCC 39006 (S 39006) and then isolated new environmental S 39006 phages that were scored for activation of ToxINPa and abortive infection capacity. We isolated three T4-like phages from a sewage treatment outflow point into the River Cam, each phage being isolated at least a year apart. These phages were susceptible to ToxINPa-mediated abortive infection but produced spontaneous "escape" mutants that were insensitive to ToxINPa. Analysis of these resistant mutants revealed three different routes of escaping ToxINPa, namely by mutating asiA (the product of which is a phage transcriptional co-activator); by mutating a conserved, yet functionally unknown, orf84; or by deleting a 6.5-10 kb region of the phage genome. Analysis of these evolved escape mutants may help uncover the nature of the corresponding phage product(s) involved in activation of ToxINPa.

Chen, J. and Gottesman, S. Hfq links translation repression to stress-induced mutagenesis in E. coli. Genes Dev. 8-9-2017; PM: 28794186

ABSTRACT: Mismatch repair (MMR) is a conserved mechanism exploited by cells to correct DNA replication errors both in growing cells and under nongrowing conditions. Hfq (host factor for RNA bacteriophage Qbeta replication), a bacterial Lsm family RNA-binding protein, chaperones RNA-RNA interactions between regulatory small RNAs (sRNAs) and target messenger RNAs (mRNAs), leading to alterations of mRNA translation and/or stability. Hfq has been reported to post-transcriptionally repress the DNA MMR gene mutS in stationary phase, possibly limiting MMR to allow increased mutagenesis. Here we report that Hfq deploys dual mechanisms to control mutS expression. First, Hfq binds directly to an (AAN)3 motif within the mutS 5' untranslated region (UTR), repressing translation in the absence of sRNA partners both in vivo and in vitro. Second, Hfq acts in a canonical pathway, promoting base-pairing of ArcZ sRNA with the mutS leader to inhibit translation. Most importantly, using pathway-specific mutS chromosomal alleles that specifically abrogate either regulatory pathway or both, we demonstrate that tight control of MutS levels in stationary phase contributes to stress-induced mutagenesis. By interacting with the mutS leader, Hfq serves as a critical switch that modulates bacteria from high-fidelity DNA replication to stress-induced mutagenesis.

Chen, X., Liu, Y., Fan, M., Wang, Z., Wu, W., and Wang, J. Thermal and chemical inactivation of Lactobacillus virulent bacteriophage. J.Dairy Sci. 2017; 100(9):7041-7050; PM: 28668532

ABSTRACT: The effect of thermal treatments and several biocides on the viability of Lactobacillus virulent phage P1 was evaluated. Times to achieve 99% inactivation (T99) of phage at different treatment conditions were calculated. The thermal treatments applied were 63, 72, and 90 degrees C in 3 suspension media (de Man, Rogosa, Sharpe broth, reconstituted skim milk, and Tris magnesium gelatin buffer). Phage P1 was completely inactivated in 5 and 10 min at 90 and 72 degrees C, respectively; however, reconstituted skim milk provided better thermal protection at 63 degrees C. When phage P1 was treated with various biocides, 800 mg/L of sodium hypochlorite was required for total inactivation (approximately 7.3 log reduction) within 60 min, whereas treatment with 100% ethanol resulted in only a approximately 4.7 log reduction, and 100% isopropanol resulted in a 5.2-log reduction. Peracetic acid (peroxyacetic acid) at the highest concentration used (0.45%) resulted in only a approximately 4.-log reduction of phage within 60 min. The results of this study provide additional information on effective treatments for the eradication of potential phage infections in dairy plants.

Chen, X., Kang, Y. M., and Fu, Y. X. Switches in a Genetic Regulatory System under Multiplicative Non-Gaussian Noise. J.Theor.Biol. 9-12-2017; PM: 28916451

ABSTRACT: The non-Gaussian noise is multiplicatively introduced to model the universal fluctuation in the gene regulation of the bacteriophage lambda. To investigate the key effect of non-Gaussian noise on the genetic on/off switch dynamics from the viewpoint of quantitative analysis, we employ the high-order perturbation expansion to deduce the stationary probability density of repressor concentration and the mean first passage time from low concentration to high concentration and vice versa. The occupation probability of different concentration states can be estimated from the height and shape of the peaks of the stationary probability density, which could be used to determine the overall expression level. A further concern is the mean first passage time, also referred to as the mean switching time, which can be adopted as an important measure to characterize the adaptability of gene expression to the environmental variation. Through our investigation, it is observed that the non-Gaussian heavy-tailed noise can better induce the switches between distinct genetic expression states and additionally, it accelerates the switching process more evidently compared to the Gaussian noise and the bounded noise.

Chen, Z., Sun, L., Zhang, Z., Fokine, A., Padilla-Sanchez, V., Hanein, D., Jiang, W., Rossmann, M. G., and Rao, V. B. Cryo-EM structure of the bacteriophage T4 isometric head at 3.3-A resolution and its relevance to the assembly of icosahedral viruses. Proc.Natl.Acad.Sci.U.S.A. 9-11-2017; PM: 28893988

ABSTRACT: The 3.3-A cryo-EM structure of the 860-A-diameter isometric mutant bacteriophage T4 capsid has been determined. WT T4 has a prolate capsid characterized by triangulation numbers (T numbers) Tend = 13 for end caps and Tmid = 20 for midsection. A mutation in the major capsid protein, gp23, produced T=13 icosahedral capsids. The capsid is stabilized by 660 copies of the outer capsid protein, Soc, which clamp adjacent gp23 hexamers. The occupancies of Soc molecules are proportional to the size of the angle between the planes of adjacent hexameric

capsomers. The angle between adjacent hexameric capsomers is greatest around the fivefold vertices, where there is the largest deviation from a planar hexagonal array. Thus, the Soc molecules reinforce the structure where there is the greatest strain in the gp23 hexagonal lattice. Mutations that change the angles between adjacent capsomers affect the positions of the pentameric vertices, resulting in different triangulation numbers in bacteriophage T4. The analysis of the T4 mutant head assembly gives guidance to how other icosahedral viruses reproducibly assemble into capsids with a predetermined T number, although the influence of scaffolding proteins is also important.

Cheng, M., Liang, J., Zhang, Y., Hu, L., Gong, P., Cai, R., Zhang, L., Zhang, H., Ge, J., Ji, Y., Guo, Z., Feng, X., Sun, C., Yang, Y., Lei, L., Han, W., and Gu, J. The Bacteriophage EF-P29 Efficiently Protects against Lethal Vancomycin-Resistant Enterococcus faecalis and Alleviates Gut Microbiota Imbalance in a Murine Bacteremia Model. Front Microbiol. 2017; 8:837; PM: 28536572

ABSTRACT: Enterococcus faecalis is becoming an increasingly important opportunistic pathogen worldwide, especially because it can cause life-threatening nosocomial infections. Treating E. faecalis infections has become increasingly difficult because of the prevalence of multidrug-resistant E. faecalis strains. Because bacteriophages show specificity for their bacterial hosts, there has been a growth in interest in using phage therapies to combat the rising incidence of multidrug-resistant bacterial infections. In this study, we isolated a new lytic phage, EF-P29, which showed high efficiency and a broad host range against E. faecalis strains, including vancomycin-resistant strains. The EF-P29 genome contains 58,984 bp (39.97% G+C), including 101 open reading frames, and lacks known putative virulence factors, integration-related proteins or antibiotic resistance determinants. In murine experiments, the administration of a single intraperitoneal injection of EF-P29 (4 x 105 PFU) at 1 h after challenge was sufficient to protect all mice against bacteremia caused by infection with a vancomycin-resistant E. faecalis strain (2 x 109 CFU/mouse). E. faecalis colony counts were more quickly eliminated in the blood of EF-P29-protected mice than in unprotected mice. We also found that exogenous E. faecalis challenge resulted in enrichment of members of the genus Enterococcus (family Enterococcaceae) in the guts of the mice, suggesting that it can enter the gut and colonize there. The phage EF-P29 reduced the number of colonies of genus Enterococcus and alleviated the gut microbiota imbalance that was caused by E. faecalis challenge. These data indicate that the phage EF-P29 shows great potential as a therapeutic treatment for systemic VREF infection. Thus, phage therapies that are aimed at treating opportunistic pathogens are also feasible. The dose of phage should be controlled and used at the appropriate level to avoid causing imbalance in the gut microbiota.

Chhibber, S., Shukla, A., and Kaur, S. Transfersomal phage cocktail: an effective treatment against methicillin resistant S.aureus (MRSA) mediated Skin and Soft tissue infections (SSTIs). Antimicrob.Agents Chemother. 7-24-2017; PM: 28739792

ABSTRACT: Emergence of drug resistance has rekindled the interest in phage therapy as an alternative treatment option. Its potency, safety and proven efficacy is worth noting. However, phage therapy still suffers from issues of poor stability, narrow spectrum and poor pharmacokinetic profile. It therefore becomes essential to look into the use of Drug Delivery Systems (DDS) for efficient delivery of lytic phages in vivo For the first time, the present study has evaluated the use of nano-structured lipid based carriers i.e.

Transfersomes as transdermal delivery systems for encapsulating MRSA phage cocktail. Further, therapeutic potential of the encapsulated phage cocktail has been studied in resolving experimental soft tissue infection in rats. Results from in vitro stability as well as in vivo phage titer experiments indicate that transfersome entrapped phage cocktail showed better persistence and stability than free phages. Besides this, rats administered with transfersome entrapped phage cocktail resolved the experimental thigh infection within a period of seven days, unlike the twenty-day time period required for untreated animals. The findings of the present study advocate the use of transferosme as delivery agents for enhancing the stability and in vivo persistence of the encapsulated phages. In addition, this study also highlights the advantage offered by transfersome encapsulated phages in providing better therapeutic option than free phage in treating skin and soft tissue infection. Transfersome entrapped phage cocktail was able to protect all test animals (with no mortality) even when administered at a delay of twelve-hour post infection unlike free phages, thus making this treatment option more suitable in clinical settings.

Chung, W. J., Cui, Y., Chen, C. S., Wei, W. H., Chang, R. S., Shu, W. Y., and Hsu, I. C. Freezing shortens the lifetime of DNA molecules under tension. J.Biol.Phys. 9-8-2017; PM: 28887655

ABSTRACT: DNA samples are commonly frozen for storage. However, freezing can compromise the integrity of DNA molecules. Considering the wide applications of DNA molecules in nanotechnology, changes to DNA integrity at the molecular level may cause undesirable outcomes. However, the effects of freezing on DNA integrity have not been fully explored. To investigate the impact of freezing on DNA integrity, samples of frozen and non-frozen bacteriophage lambda DNA were studied using optical tweezers. Tension (5-35 pN) was applied to DNA molecules to mimic mechanical interactions between DNA and other biomolecules. The integrity of the DNA molecules was evaluated by measuring the time taken for single DNA molecules to break under tension. Mean lifetimes were determined by maximum likelihood estimates and variances were obtained through bootstrapping simulations. Under 5 pN of force, the mean lifetime of frozen samples is 44.3 min with 95% confidence interval (CI) between 36.7 min and 53.6 min while the mean lifetime of non-frozen samples is 133.2 min (95% CI: 97.8-190.1 min). Under 15 pN of force, the mean lifetimes are 10.8 min (95% CI: 7.6-12.6 min) and 78.5 min (95% CI: 58.1-108.9 min). The lifetimes of frozen DNA molecules are significantly reduced, implying that freezing compromises DNA integrity. Moreover, we found that the reduced DNA structural integrity cannot be restored using regular ligation process. These results indicate that freezing can alter the structural integrity of the DNA molecules.

Cohen, J. E., Wang, R., Shen, R. F., Wu, W. W., and Keller, J. E. Comparative pathogenomics of Clostridium tetani. PLoS.One. 2017; 12(8):e0182909; PM: 28800585

ABSTRACT: Clostridium tetani and Clostridium botulinum produce two of the most potent neurotoxins known, tetanus neurotoxin and botulinum neurotoxin, respectively. Extensive biochemical and genetic investigation has been devoted to identifying and characterizing various C. botulinum strains. Less effort has been focused on studying C. tetani likely because recently sequenced strains of C. tetani show much less genetic diversity than C. botulinum strains and because widespread vaccination efforts have reduced the public health threat from tetanus. Our aim was to acquire genomic data on the U.S. vaccine strain of C. tetani to better understand its genetic relationship to previously published genomic data from European vaccine strains. We performed high

throughput genomic sequence analysis on two wild-type and two vaccine C. tetani strains. Comparative genomic analysis was performed using these and previously published genomic data for seven other C. tetani strains. Our analysis focused on single nucleotide polymorphisms (SNP) and four distinct constituents of the mobile genome (mobilome): a hypervariable flagellar glycosylation island region, five conserved bacteriophage insertion regions, variations in three CRISPR (clustered regularly interspaced short palindromic repeats)-Cas (CRISPR-associated) systems, and a single plasmid. Intact type IA and IB CRISPR/Cas systems were within 10 of 11 strains. A type IIIA CRISPR/Cas system was present in two strains. Phage infection histories derived from CRISPR-Cas sequences indicate C. tetani encounters phages common among commensal gut bacteria and soil-borne organisms consistent with C. tetani distribution in nature. All vaccine strains form a clade distinct from currently sequenced wild type strains when considering variations in these mobile elements. SNP, flagellar glycosylation island, prophage content and CRISPR/Cas phylogenic histories provide tentative evidence suggesting vaccine and wild type strains share a common ancestor.

Colavecchio, A., Cadieux, B., Lo, A., and Goodridge, L. D. Bacteriophages Contribute to the Spread of Antibiotic Resistance Genes among Foodborne Pathogens of the Enterobacteriaceae Family - A Review. Front Microbiol. 2017; 8:1108; PM: 28676794

ABSTRACT: Foodborne illnesses continue to have an economic impact on global health care systems. There is a growing concern regarding the increasing frequency of antibiotic resistance in foodborne bacterial pathogens and how such resistance may affect treatment outcomes. In an effort to better understand how to reduce the spread of resistance, many research studies have been conducted regarding the methods by which antibiotic resistance genes are mobilized and spread between bacteria. Transduction by bacteriophages (phages) is one of many horizontal gene transfer mechanisms, and recent findings have shown phage-mediated transduction to be a significant contributor to dissemination of antibiotic resistance genes. Here, we review the viability of transduction as a contributing factor to the dissemination of antibiotic resistance genes in foodborne pathogens of the Enterobacteriaceae family, including non-typhoidal Salmonella and Shiga toxin-producing Escherichia coli, as well as environmental factors that increase transduction of antibiotic resistance genes.

Colavecchio, A. and Goodridge, L. D. Phage Therapy Approaches to Reducing Pathogen Persistence and Transmission in Animal Production Environments: Opportunities and Challenges. Microbiol.Spectr. 2017; 5(3); PM: 28664828

ABSTRACT: The era of genomics has allowed for characterization of phages for use as antimicrobials to treat animal infections with a level of precision never before realized. As more research in phage therapy has been conducted, several advantages of phage therapy have been realized, including the ubiquitous nature, specificity, prevalence in the biosphere, and low inherent toxicity of phages, which makes them a safe and sustainable technology for control of animal diseases. These unique qualities of phages have led to several opportunities with respect to emerging trends in infectious disease treatment. However, the opportunities are tempered by several challenges to the successful implementation of phage therapy, such as the fact that an individual phage can only infect one or a few bacterial strains, meaning that large numbers of different phages will likely be needed to treat infections caused by multiple species of bacteria. In addition, phages are only effective if enough of them can reach the site of bacterial

colonization, but clearance by the immune system upon introduction to the animal is a reality that must be overcome. Finally, bacterial resistance to the phages may develop, resulting in treatment failure. Even a successful phage infection and lysis of its host has consequences, because large amounts of endotoxin are released upon lysis of Gram-negative bacteria, which can lead to local and systemic complications. Overcoming these challenges will require careful design and development of phage cocktails, including comprehensive characterization of phage host range and assessment of immunological risks associated with phage treatment.

Czajkowski, R., Smolarska, A., and Ozymko, Z. The viability of lytic bacteriophage PhiD5 in potato-associated environments and its effect on Dickeya solani in potato (Solanum tuberosum L.) plants. PLoS.One. 2017; 12(8):e0183200; PM: 28800363

ABSTRACT: Dickeya solani is one of the most important pectinolytic phytopathogens responsible for high losses in potato, especially in seed potato production in Europe. Lytic bacteriophages can affect the structure of the host population and may influence spread, survival and virulence of the pathogen and in consequence, infection of the plant. In this study, we aimed to acquire information on the viability of the broad host lytic bacteriophage PhiD5 on potato, as well as to apprehend the specific effect of this bacteriophage on its host D. solani type-strain in different settings, as a preliminary step to target co-adaptation of phages and host bacteria in plant environment. Viability of the PhiD5 phage in tuber extract, on tuber surface, in potting compost, in rainwater and on the leaf surface, as well as the effect of copper sulfate, were examined under laboratory conditions. Also, the interaction of PhiD5 with the target host D. solani in vitro and in compost-grown potato plants was evaluated. PhiD5 remained infectious in potato tuber extract and rain water for up to 72 h but was inactivated in solutions containing 50 mM of copper. The phage population was stable for up to 28 days on potato tuber surface and in potting compost. In both, tissue culture and compost-grown potato plants, PhiD5 reduced infection by D. solani by more than 50%. The implications of these findings are discussed.

D'Andrea, M. M., Marmo, P., Henrici De, Angelis L., Palmieri, M., Ciacci, N., Di, Lallo G., Dematte, E., Vannuccini, E., Lupetti, P., Rossolini, G. M., and Thaller, M. C. phiBO1E, a newly discovered lytic bacteriophage targeting carbapenemase-producing Klebsiella pneumoniae of the pandemic Clonal Group 258 clade II lineage. Sci.Rep. 6-1-2017; 7(1):2614; PM: 28572684

ABSTRACT: The pandemic dissemination of KPC carbapenemase-producing Klebsiella pneumoniae (KPC-KP) represents a major public health problem, given their extensive multidrug resistance profiles and primary role in causing healthcare-associated infections. This phenomenon has largely been contributed by strains of Clonal Group (CG) 258, mostly of clade II, which in some areas represent the majority of KPC-KP isolates. Here we have characterized a newly discovered lytic Podoviridae, named phiBO1E, targeting KPC-KP strains of clade II lineage of CG258. Genomic sequencing revealed that phiBO1E belongs to the Kp34virus genus (87% nucleotide identity to vB_KpnP_SU552A). PhiBO1E was stable over a broad pH and temperature range, exhibited strict specificity for K. pneumoniae strains of clade II of CG258, and was unable to establish lysogeny. In a Galleria mellonella infection model, phiBO1E was able to protect larvae from death following infection with KPC-KP strains of clade II of CG258, including one colistin resistant strain characterized by a hypermucoviscous phenotype.

To our best knowledge phiBO1E is the first characterized lytic phage targeting K. pneumoniae strains of this pandemic clonal lineage. As such, it could be of potential interest to develop new agents for treatment of KPC-KP infections and for decolonization of subjects chronically colonized by these resistant superbugs.

Damavandi, N., Raigani, M., Joudaki, A., Davami, F., and Zeinali, S. Rapid characterization of the CHO platform cell line and identification of pseudo attP sites for PhiC31 integrase. Protein Expr.Purif. 2017; 140:60-64; PM: 28802644

ABSTRACT: The Chinese Hamster Ovary (CHO) cell lines, applicable to post-translational modifications, are preferred systems for biopharmaceutical protein production. In this study, by using the Jump-In TI technology which employs PhiC31 and R4 bacteriophage recombinases, a platform CHO-K1 cell line containing a R4-attP site was generated. Here, a combination of Quantitative Fluorescent-Polymerase Chain Reaction (QF-PCR) and semi-random, two-step PCR (ST-PCR), was performed to feature the platform cell clones. Our results show that QF-PCR and ST-PCR, can be utilized for efficient and accelerated cell line characterization. By applying these approaches, we were able to accurately identify the copy number of integrated R4-attP sites and the genomic position of recombination of many clones. Three novel PhiC31 pseudo-attP sites were identified on chromosomes 1, 3 and 6, and their genomic features were analyzed. The characterized platform cell lines are stable, and because of single-copy, site-specific R4 recognition attP site, the cell lines could be retargeted for recombinant protein production and drug discovery applications.

Day, A., Ahn, J., Fang, X., and Salmond, G. P. C. Environmental Bacteriophages of the Emerging Enterobacterial Phytopathogen, Dickeya solani, Show Genomic Conservation and Capacity for Horizontal Gene Transfer between Their Bacterial Hosts. Front Microbiol. 2017; 8:1654; PM: 28912766

ABSTRACT: Dickeya solani is an economically important phytopathogen widespread in mainland Europe that can reduce potato crop yields by 25%. There are no effective environmentally-acceptable chemical systems available for diseases caused by Dickeya. Bacteriophages have been suggested for use in biocontrol of this pathogen in the field, and limited field trials have been conducted. To date only a small number of bacteriophages capable of infecting D. solani have been isolated and characterized, and so there is a need to expand the repertoire of phages that may have potential utility in phage therapy strategies. Here we describe 67 bacteriophages from environmental sources, the majority of which are members of the viral family Myoviridae. Full genomic sequencing of two isolates revealed a high degree of DNA identity with D. solani bacteriophages isolated in Europe in the past 5 years, suggesting a wide ecological distribution of this phage family. Transduction experiments showed that the majority of the new environmental bacteriophages are capable of facilitating efficient horizontal gene transfer. The possible risk of unintentional transfer of virulence or antibiotic resistance genes between hosts susceptible to transducing phages cautions against their environmental use for biocontrol, until specific phages are fully tested for transduction capabilities.

De, Smet J., Hendrix, H., Blasdel, B. G., nis-Wlodarczyk, K., and Lavigne, R. Pseudomonas predators: understanding and exploiting phage-host interactions. Nat.Rev.Microbiol. 2017; 15(9):517-530; PM: 28649138

ABSTRACT: Species in the genus Pseudomonas thrive in a diverse set of ecological niches and include crucial pathogens, such as the human pathogen Pseudomonas aeruginosa and the plant pathogen Pseudomonas syringae. The bacteriophages that infect Pseudomonas spp. mirror the widespread and diverse nature of their hosts. Therefore, Pseudomonas spp. and their phages are an ideal system to study the molecular mechanisms that govern virus-host interactions. Furthermore, phages are principal catalysts of host evolution and diversity, which directly affects the ecological roles of environmental and pathogenic Pseudomonas spp. Understanding these interactions not only provides novel insights into phage biology but also advances the development of phage therapy, phage-derived antimicrobial strategies and innovative biotechnological tools that may be derived from phage-bacteria interactions.

Deng, L., Roose, K., Job, E. R., De, Rycke R., Van, Hamme E., Goncalves, A., Parthoens, E., Cicchelero, L., Sanders, N., Fiers, W., and Saelens, X. Oral delivery of Escherichia coli persistently infected with M2e-displaying bacteriophages partially protects against influenza A virus. J.Control Release. 8-24-2017; 264:55-65; PM: 28842314

ABSTRACT: We describe a novel live oral vaccine type. Conceptually, this vaccine is based on a non-lytic, recombinant filamentous bacteriophage that displays an antigen of interest. To provide proof of concept we used the amino-terminal part of a conserved influenza A virus epitope, i.e. matrix protein 2 ectodomain (M2e) residues 2 to 16, as the antigen of interest. Rather than using the phages as purified virus-like particles as a vaccine, these phages were delivered to intestinal Peyer's patches as a live bacterium-phage combination that comprises Escherichia coli cells that conditionally express invasin derived from Yersinia pseudotuberculosis. Invasin-expressing E. coli cells were internalized by mammalian Hep-2 cells in vitro and adhered to mouse intestinal microfold (M) cells ex vivo. Invasin-expressing E. coli cells were permissive for recombinant filamentous bacteriophage f88 that displays M2e and became persistently infected. Oral administration of the live engineered E. coli-invasin-phage combination to mice induced M2e-specific serum IgG antibodies. Mice that had been immunized with invasin-expressing E. coli cells that carried M2e2-16 displaying fd phages seroconverted to M2e and showed partial protection against challenge with influenza A virus. Oral delivery of a live vaccine comprising a bacterial host that is targeted to Peyer's patches and is persistently infected with an antigen-displaying phage, can thus be exploited as an oral vaccine.

Dhungel, P., Cao, S., and Yang, Z. The 5'-poly(A) leader of poxvirus mRNA confers a translational advantage that can be achieved in cells with impaired cap-dependent translation. PLoS.Pathog. 2017; 13(8):e1006602; PM: 28854224

ABSTRACT: The poly(A) leader at the 5'-untranslated region (5'-UTR) is an unusually striking feature of all poxvirus mRNAs transcribed after viral DNA replication (post-replicative mRNAs). These poly(A) leaders are non-templated and of heterogeneous lengths; and their function during poxvirus infection remains a long-standing question. Here, we discovered that a 5'-poly(A) leader conferred a selective translational advantage to mRNA in poxvirus-infected cells. A constitutive and uninterrupted 5'-poly(A) leader with

12 residues was optimal. Because the most frequent lengths of the 5'-poly(A) leaders are 8-12 residues, the result suggests that the poly(A) leader has been evolutionarily optimized to boost poxvirus protein production. A 5'-poly(A) leader also could increase protein production in the bacteriophage T7 promoter-based expression system of vaccinia virus, the prototypic member of poxviruses. Interestingly, although vaccinia virus post-replicative mRNAs do have 5'- methylated guanosine caps and can use cap-dependent translation, in vaccinia virus-infected cells, mRNA with a 5'-poly(A) leader could also be efficiently translated in cells with impaired cap-dependent translation. However, the translation was not mediated through an internal ribosome entry site (IRES). These results point to a fundamental mechanism poxvirus uses to efficiently translate its post-replicative mRNAs.

Dong, X., Huang, C., Morsy, M. K., Li, Z., Zhou, Y., Willias, S. P., Abdelnabby, H. E., Liu, J., Feng, L., Wang, X., and Li, J. Complete Genome Sequence of Salmonella enterica Lytic Bacteriophage LPST10, Isolated in China. Genome Announc. 8-31-2017; 5(35); PM: 28860234

ABSTRACT: Bacteriophage LPST10 was isolated from Wuhan, China. Lytic activity was demonstrated against multiple Salmonella enterica serovars, including Salmonella enterica serovar Typhimurium strains. This bacteriophage has a 47,657-bp double-stranded DNA genome encoding 87 putative coding sequences.

Dorri, F., Pezeshk, H., and Sadeghi, M. Stochastic Cell Fate and Longevity of Offspring. Cell J. 2017; 19(3):343-351; PM: 28836397

*ABSTRACT**: OBJECTIVE***: Cellular decision-making is a key process in which cells with similar geneticand environmental background make dissimilar decisions. This stochastic process, which happens in prokaryotic and eukaryotic cells including stem cells, causes cellular diversity and phenotypic variation. In addition, fitness predicts and describes changes in the genetic composition of populations throughout the evolutionary history. Fitness may thus be defined as the ability to adapt and produce surviving offspring. Here, we present a mathematical model to predict the fitness of a cell and to address the fundamental issue of phenotypic variation. We study a basic decision-making scenario where a bacteriophage lambda reproduces in E. coli, using both the lytic and the lysogenic pathways. In the lytic pathway, the bacteriophage replicates itself within the host bacterium. This fast replication overcrowds and in turn destroys the host bacterium. In the lysogenic pathway, however, the bacteriophage inserts its DNA into the host genome, and is replicated simultaneously with the host genome. ***MATERIALS AND METHODS***: In this prospective study, a mathematical predictive model was developed to estimate fitness as an index of survived offspring. We then leverage experimental data to validate the predictive power of our proposed model. A mathematical model based on game theory was also generated to elucidate a rationale behind cell decision. ***RESULTS***: Our findings indicate that a rational decision that is aimed to maximize life expectancy of offspring is almost identical to bacteriophage behavior reported based on experimental data. The results also showed that stochastic decision on cell fate maximizes the expected number of survived offspring. ***CONCLUSION***: We present a mathematical framework for analyzing a basic phenotypic variation problem and explain how bacteriophages maximize offspring longevity based on this model. We also introduce a mathematical benchmark for other investigations of phenotypic variation that exists in eukaryotes including stem cell differentiation.

Doucet, M., El-Turabi, A., Zabel, F., Hunn, B. H. M., goa-Vergniory, N., Cioroch, M., Ramm, M., Smith, A. M., Gomes, A. C., Cabral de, Miranda G., Wade-Martins, R., and Bachmann, M. F. Preclinical development of a vaccine against oligomeric alpha-synuclein based on virus-like particles. PLoS.One. 2017; 12(8):e0181844; PM: 28797124

ABSTRACT: Parkinson's disease (PD) is a progressive and currently incurable neurological disorder characterised by the loss of midbrain dopaminergic neurons and the accumulation of aggregated alpha-synuclein (a-syn). Oligomeric a-syn is proposed to play a central role in spreading protein aggregation in the brain with associated cellular toxicity contributing to a progressive neurological decline. For this reason, a-syn oligomers have attracted interest as therapeutic targets for neurodegenerative conditions such as PD and other alpha-synucleinopathies. In addition to strategies using small molecules, neutralisation of the toxic oligomers by antibodies represents an attractive and highly specific strategy for reducing disease progression. Emerging active immunisation approaches using vaccines are already being trialled to induce such antibodies. Here we propose a novel vaccine based on the RNA bacteriophage (Qbeta) virus-like particle conjugated with short peptides of human a-syn. High titres of antibodies were successfully and safely generated in wild-type and human a-syn over-expressing (SNCA-OVX) transgenic mice following vaccination. Antibodies from vaccine candidates targeting the C-terminal regions of a-syn were able to recognise Lewy bodies, the hallmark aggregates in human PD brains. Furthermore, antibodies specifically targeted oligomeric and aggregated a-syn as they exhibited 100 times greater affinity for oligomeric species over monomer a-syn proteins in solution. In the SNCA-OVX transgenic mice used, vaccination was, however, unable to confer significant changes to oligomeric a-syn bioburden. Similarly, there was no discernible effect of vaccine treatment on behavioural phenotype as compared to control groups. Thus, antibodies specific for oligomeric a-syn induced by vaccination were unable to treat symptoms of PD in this particular mouse model.

du, Plessis J., Cloete, R., Burchell, L., Sarkar, P., Warren, R. M., Christoffels, A., Wigneshweraraj, S., and Sampson, S. L. Exploring the potential of T7 bacteriophage protein Gp2 as a novel inhibitor of mycobacterial RNA polymerase. Tuberculosis.(Edinb.). 2017; 106:82-90; PM: 28802409

ABSTRACT: Over the past six decades, there has been a decline in novel therapies to treat tuberculosis, while the causative agent of this disease has become increasingly resistant to current treatment regimens. Bacteriophages (phages) are able to kill bacterial cells and understanding this process could lead to novel insights for the treatment of mycobacterial infections. Phages inhibit bacterial gene transcription through phage-encoded proteins which bind to RNA polymerase (RNAP), thereby preventing bacterial transcription. Gp2, a T7 phage protein which binds to the beta prime (beta') subunit of RNAP in Escherichia coli, has been well characterized in this regard. Here, we aimed to determine whether Gp2 is able to inhibit RNAP in Mycobacterium tuberculosis as this may provide new possibilities for inhibiting the growth of this deadly pathogen. Results from an electrophoretic mobility shift assay and in vitro transcription assay revealed that Gp2 binds to mycobacterial RNAP and inhibits transcription; however to a much lesser degree than in E. coli. To further understand the molecular basis of these results, a series of in silico techniques were used to assess the interaction between mycobacterial RNAP and Gp2, providing valuable insight into the characteristics of this protein-protein interaction.

Dunkin, N., Weng, S., Jacangelo, J. G., and Schwab, K. J. Minimizing Bias in Virally Seeded Water Treatment Studies: Evaluation of Optimal Bacteriophage and Mammalian Virus Preparation Methodologies. Food Environ.Virol. 6-14-2017; PM: 28616834

ABSTRACT: One key assumption impacting data quality in viral inactivation studies is that reduction estimates are not altered by the virus seeding process. However, seeding viruses often involves the inadvertent addition of co-constituents such as cell culture components or additives used during preparation steps which can impact viral reduction estimates by inducing non-representative oxidant demand in disinfection studies and fouling in membrane assessments. The objective of this study was therefore to characterize a mammalian norovirus surrogate, murine norovirus (MNV), and bacteriophage MS2 at sequential stages of viral purification and to quantify their potential contribution to artificial oxidant demand and non-representative membrane fouling. Our results demonstrate that seeding solvent extracted and 0.1 micron filtered MNV to ~105 PFU/mL in an experimental water matrix will result in additional total organic carbon (TOC) and 30 min chlorine demand of 39.2 mg/L and 53.5 mg/L as Cl2, respectively. Performing sucrose cushion purification on the MNV stock prior to seeding reduces the impacts of TOC and chlorine demand to 1.6 and 0.15 mg/L as Cl2, respectively. The findings for MNV are likely relevant for other mammalian viruses propagated in serum-based media. Thus, advanced purification of mammalian virus stocks by sucrose cushion purification (or equivalent density-based separation approach) is warranted prior to seeding in water treatment assessments. Studies employing bacteriophage MS2 as a surrogate virus may not need virus purification, since seeding MS2 at a concentration of ~106 PFU/mL will introduce only ~1 mg/L of TOC and ~1 mg/L as Cl2 of chlorine demand to experimental water matrices.

Dunkin, N., Weng, S., Coulter, C. G., Jacangelo, J. G., and Schwab, K. Reduction of Human Norovirus GI, GII, and Surrogates by Peracetic Acid and Monochloramine in Municipal Secondary Wastewater Effluent. Environ.Sci.Technol. 9-14-2017; PM: 28910089

ABSTRACT: The objective of this study was to characterize human norovirus (hNoV) GI and GII reductions during disinfection by peracetic acid (PAA) and monochloramine in secondary wastewater (WW) and phosphate buffer (PB) as assessed by reverse transcription-qPCR (RT-qPCR). Infectivity and RT-qPCR reductions are also presented for surrogate viruses murine norovirus (MNV) and bacteriophage MS2 under identical experimental conditions to aid in interpretation of hNoV molecular data. In WW, RT-qPCR reductions were less than 0.5 log10 for all viruses at concentration-time (CT) values up to 450 mg-min/L except for hNoV GI, where 1 log10 reduction was observed at CT values of less than 50 mg-min/L for monochloramine and 200 mg-min/L for PAA. In PB, hNoV GI and MNV exhibited comparable resistance to PAA and monochloramine with CT values for 2 log10 RT-qPCR reduction between 300 to 360 mg-min/L. Less than 1 log10 reduction was observed for MS2 and hNoV GII in PB at CT values for both disinfectants up to 450 mg-min/L. Our results indicate that hNoVs exhibit genogroup dependent resistance and that disinfection practices targeting hNoV GII will result in equivalent or greater reductions for hNoV GI. These data provide valuable comparisons between hNoV and surrogate molecular signals that can begin the process of informing regulators and engineers on WW treatment plant design and operational practices necessary to inactivate hNoVs.

Dunkin, N., Weng, S. C., Jacangelo, J. G., and Schwab, K. J. Inactivation of Human Norovirus GI, GII, and Surrogates by Free Chlorine in Postharvest Leafy Green Wash Water. Appl.Environ.Microbiol. 9-8-2017; PM: 28887415

ABSTRACT: Human noroviruses (hNoVs) are a known public health concern associated with the consumption of leafy green vegetables. While a number of studies have investigated pathogen reduction on the surfaces of leafy greens during the postharvest washing process, there remains a paucity of data on the level of treatment needed to inactivate viruses in the wash water, which is critical for preventing cross-contamination. The objective of this study was to quantify the susceptibility of hNoV GI, hNoV GII, murine norovirus (MNV), and bacteriophage MS2 to free chlorine in whole leaf, chopped romaine, and shredded iceberg lettuce industrial leafy green wash waters, each sampled three times over a 4-month period. A suite of kinetic inactivation models was fit to the viral reduction data to aid in quantification of concentration x time (CT) values. Results indicate that 3 log10 infectivity reduction was achieved at CT values of less than 0.2 mg-min/L for MNV and 2.5 mg-min/L for MS2 in all wash water types. CT values for 2 log10 molecular reduction of hNoV GI in whole leaf and chopped romaine wash waters were 1.5 and 0.9 mg-min/L, respectively. For hNoV GII, CT values were 13.0 and 7.5 mg-min/L, respectively. In shredded iceberg wash water, 3 log10 molecular reduction was not observed for any virus over the time course of experiments. These findings demonstrate that noroviruses may exhibit genogroup dependent resistance to free chlorine and emphasize the importance of distinguishing between genogroups in hNoV persistence studies. Importance: Postharvest washing of millions of pounds of leafy greens is performed daily in industrial processing facilities with the intention of removing dirt, debris, and pathogenic microorganisms prior to packaging. Modest inactivation of pathogenic microorganisms (less than 1-2 log10) is known to occur on the surfaces of leafy greens during washing. Therefore, the primary purpose of the sanitizing agent is to maintain microbial quality of postharvest processing water in order to limit cross-contamination. This study modeled viral inactivation data and quantified the free chlorine CT values that processing facilities must meet in order to achieve the desired level of hNoV GI and GII reduction. Disinfection experiments were conducted in industrial leafy green wash water collected from a full-scale fresh produce processing facility in the U.S., and hNoV GI and GII results were compared with surrogate molecular and infectivity data.

El-Shibiny, A. and El-Sahhar, S. Bacteriophages: The possible solution to treat pathogenic bacteria. Can.J.Microbiol. 9-1-2017; PM: 28863269

ABSTRACT: Bacteriophages have been used to treat bacterial infections in animals and humans since their discovery in 1915, due to their unique ability to infect their specific bacterial hosts, without affecting other bacterial populations. The research carried out in this field throughout the twentieth century, largely in Georgia, part of USSR and Poland, led to the establishment of phage therapy protocols. However, the discovery of penicillin and sulphonamide antibiotics in the Western World during the 1930's was a setback in the advancement of phage therapy. The misuse of antibiotics reduced their efficacy in controlling pathogens and led to an increase in the number of antibiotic resistant bacteria. Bacteriophages have become a topic of interest as an alternative to antibiotics with the emergence of multidrug-resistant bacteria, which are a threat to public health. Recent studies have indicated that bacteriophages can be used indirectly to detect pathogenic bacteria or directly as biocontrol agents. Moreover, they can be

used to develop new molecules for clinical applications, vaccine production, drug design and in the nanomedicine field via phage display.

Erill, I. and Caruso, S. M. Bacillus cereus Group Bacteriophage Flapjack Genome Sequence. Genome Announc. 8-3-2017; 5(31); PM: 28774974

ABSTRACT: The Bacillus cereus group bacteriophage Flapjack, a double-stranded DNA (dsDNA) Myoviridae isolate collected from soil collected in Washington, DC, is a member of cluster C3 and encodes an intramolecular chaperone-containing tail fiber protein previously found in Podoviridae and Siphoviridae but not annotated in the Myoviridae.

Fatemi, F., Amini, S. M., Kharrazi, S., Rasaee, M. J., Mazlomi, M. A., sadi-Ghalehni, M., Rajabibazl, M., and Sadroddiny, E. Construction of genetically engineered M13K07 helper phage for simultaneous phage display of gold binding peptide 1 and nuclear matrix protein 22 ScFv antibody. Colloids Surf.B Biointerfaces. 8-24-2017; 159:770-780; PM: 28886513

ABSTRACT: The most common techniques of antibody phage display are based on the use of M13 filamentous bacteriophages. This study introduces a new genetically engineered M13K07 helper phage displaying multiple copies of a known gold binding peptide on p8 coat proteins. The recombinant helper phages were used to rescue a phagemid vector encoding the p3 coat protein fused to the nuclear matrix protein 22 (NMP22) ScFv antibody. Transmission electron microscopy (TEM), UV-vis absorbance spectroscopy, and field emission scanning electron microscopy (FE-SEM) with energy dispersive X-ray spectroscopy (EDX) analysis revealed that the expression of gold binding peptide 1 (GBP1) on major coat protein p8 significantly enhances the gold-binding affinity of M13 phages. The recombinant bacteriophages at concentrations above 5x104 pfu/ml red-shifted the UV-vis absorbance spectra of gold nanoparticles (AuNPs); however, the surface plasmon resonance of gold nanoparticles was not changed by the wild type bacteriophages at concentrations up to 1012 pfu/ml. The phage ELISA assay demonstrated the high affinity binding of bifunctional bacteriophages to NMP22 antigen at concentrations of 105 and 106 pfu/ml. Thus, the p3 end of the bifunctional bacteriophages would be able to bind to specific target antigen, while the AuNPs were assembled along the coat of virus for signal generation. Our results indicated that the complex of antigen-bacteriophages lead to UV-vis spectral changes of AuNPs and NMP22 antigen in concentration range of 10-80mug/ml can be detected by bifunctional bacteriophages at concentration of 104 pfu/ml. The ability of bifunctional bacteriophages to bind to antigen and generate signal at the same time, makes this approach applicable for identifying different antigens in immunoassay techniques.

Feng, Y., Chen, H. L., Chen, C. J., Chen, C. L., and Chiu, C. H. Genome comparisons of two Taiwanese community-associated methicillin-resistant Staphylococcus aureus ST59 clones support the multi-origin theory of CA-MRSA. Infect.Genet.Evol. 6-19-2017; 54:60-65; PM: 28642157

ABSTRACT: Sequence type (ST) 59 is an epidemic lineage of community-associated methicillin-resistant Staphylococcus aureus (CA-MRSA) in Asia. Two ST59 clones are prevalent in Taiwan: the Taiwan clone (TW) causes severe infections, whereas the Asian-Pacific clone (AP) is usually commensal. In this study, we sequenced the genome and transcriptome of the representative strains of these two clones and found their

differences to focus on three mobile genetic elements: TW carries SCCmec Type VT, Panton-Valentine leucocidin (PVL)-encoding prophage PhiSa2, whereas AP carries SCCmec Type IV and staphylokinase (SAK)-encoding prophage PhiSa3. The anti-virulent role of SAK was confirmed using murine skin and bloodstream infection models. PhiSa3 usually integrates into the hlb gene, but in AP was found to be integrated at the genomic island nuSabeta. The mutation of the attB site "TGTATCCAAACTGG" to "TGTATCCGAATTGG" led to a failure in the integration of PhiSa3 in hlb, prompting atypical integration at other sites. The sak gene possessed remarkably different patterns of distribution among the different STs of S. aureus. We conclude that the atypical integration of PhiSa3 may help S. aureus adapt to the human host habitat and that the subsequent loss of PhiSa3 contributes toward the development of a virulent CA-MRSA lineage for wider horizontal transmission.

Figueiredo, A. C. L. and Almeida, R. C. C. Antibacterial efficacy of nisin, bacteriophage P100 and sodium lactate against Listeria monocytogenes in ready-to-eat sliced pork ham. Braz.J.Microbiol. 6-3-2017; PM: 28641956

ABSTRACT: The effectiveness of bacteriophage P100, nisin and sodium lactate, individually and in combination, in inhibiting Listeria monocytogenes in ready-to-eat pork ham slices was assessed. The antimicrobials were applied to the surfaces of ready-to-eat pork ham slices, which were inoculated with a mixture of L. monocytogenes. Among the individual antimicrobial treatments, bacteriophage P100 was the most effective, decreasing L. monocytogenes to undetectable levels at zero and 72h post-infection. Sodium lactate was the least effective treatment. Treatment with nisin at zeroh significantly reduced initial cell density ($p<0.05$). However, this pattern was not observed at 72h of storage. A significant difference ($p<0.05$) existed between the results of separate bacteriophage and nisin treatments after refrigerated storage, but not immediately upon inoculation of the bacteria. The results showed that the use of bacteriophage P100 is the method of choice for the control of bacteria.

Fomenkov, A., Sun, Z., Dila, D. K., Anton, B. P., Roberts, R. J., and Raleigh, E. A. EcoBLMcrX, a classical modification-dependent restriction enzyme in Escherichia coli B: Characterization in vivo and in vitro with a new approach to cleavage site determination. PLoS.One. 2017; 12(6):e0179853; PM: 28654677

ABSTRACT: Here we characterize the modification-dependent restriction enzyme (MDE) EcoBLMcrX in vivo, in vitro and in its genomic environment. MDE cleavage of modified DNAs protects prokaryote populations from lethal infection by bacteriophage with highly modified DNA, and also stabilizes lineages by reducing gene import when sparse modification occurs in the wrong context. The function and distribution of MDE families are thus important. Here we describe the properties of EcoBLMcrX, an enzyme of the E. coli B lineage, in vivo and in vitro. Restriction in vivo and the genome location of its gene, ecoBLmcrX, were determined during construction and sequencing of a B/K-12 hybrid, ER2566. In classical restriction literature, this B system was named r6 or rglAB. Like many genome defense functions, ecoBLmcrX is found within a genomic island, where gene content is variable among natural E. coli isolates. In vitro, EcoBLMcrX was compared with two related enzymes, BceYI and NhoI. All three degrade fully cytosine-modified phage DNA, as expected for EcoBLMcrX from classical T4 genetic data. A new method of

characterizing MDE specificity was developed to better understand action on fully-modified targets such as the phage that provide major evolutionary pressure for MDE maintenance. These enzymes also cleave plasmids with m5C in particular motifs, consistent with a role in lineage-stabilization. The recognition sites were characterized using a site-ranking approach that allows visualization of preferred cleavage sites when fully-modified substrates are digested. A technical constraint on the method is that ligation of one-nucleotide 5' extensions favors G:C over A:T approximately five-fold. Taking this bias into account, we conclude that EcoBLMcrX can cleave 3' to the modified base in the motif Rm5C|. This is compatible with, but less specific than, the site reported by others. Highly-modified site contexts, such as those found in base-substituted virulent phages, are strongly preferred.

Forrest, D., James, K., Yuzenkova, Y., and Zenkin, N. Single-peptide DNA-dependent RNA polymerase homologous to multi-subunit RNA polymerase. Nat.Commun. 6-6-2017; 8:15774; PM: 28585540

ABSTRACT: Transcription in all living organisms is accomplished by multi-subunit RNA polymerases (msRNAPs). msRNAPs are highly conserved in evolution and invariably share a approximately 400 kDa five-subunit catalytic core. Here we characterize a hypothetical approximately 100 kDa single-chain protein, YonO, encoded by the SPbeta prophage of Bacillus subtilis. YonO shares very distant homology with msRNAPs, but no homology with single-subunit polymerases. We show that despite homology to only a few amino acids of msRNAP, and the absence of most of the conserved domains, YonO is a highly processive DNA-dependent RNA polymerase. We demonstrate that YonO is a bona fide RNAP of the SPbeta bacteriophage that specifically transcribes its late genes, and thus represents a novel type of bacteriophage RNAPs. YonO and related proteins present in various bacteria and bacteriophages have diverged from msRNAPs before the Last Universal Common Ancestor, and, thus, may resemble the single-subunit ancestor of all msRNAPs.

Fraga, H., Arnaud, C. A., Gauto, D. F., Audin, M., Kurauskas, V., Macek, P., Krichel, C., Guan, J. Y., Boisbouvier, J., Sprangers, R., Breyton, C., and Schanda, P. Solid-State NMR H-N-(C)-H and H-N-C-C 3D/4D Correlation Experiments for Resonance Assignment of Large Proteins. Chemphyschem. 8-9-2017; PM: 28792111

ABSTRACT: Solid-state NMR spectroscopy can provide insight into protein structure and dynamics at the atomic level without inherent protein size limitations. However, a major hurdle to studying large proteins by solid-state NMR spectroscopy is related to spectral complexity and resonance overlap, which increase with molecular weight and severely hamper the assignment process. Here the use of two sets of experiments is shown to expand the tool kit of 1 H-detected assignment approaches, which correlate a given amide pair either to the two adjacent CO-CA pairs (4D hCOCANH/hCOCAcoNH), or to the amide 1 H of the neighboring residue (3D HcocaNH/HcacoNH, which can be extended to 5D). The experiments are based on efficient coherence transfers between backbone atoms using INEPT transfers between carbons and cross-polarization for heteronuclear transfers. The utility of these experiments is exemplified with application to assemblies of deuterated, fully amide-protonated proteins from approximately 20 to 60 kDa monomer, at magic-angle spinning (MAS) frequencies from approximately 40 to 55 kHz. These experiments will also be applicable to protonated proteins at higher MAS frequencies. The resonance assignment of a domain within the 50.4 kDa bacteriophage

T5 tube protein pb6 is reported, and this is compared to NMR assignments of the isolated domain in solution. This comparison reveals contacts of this domain to the core of the polymeric tail tube assembly.

Gallandat, K. and Lantagne, D. Selection of a Biosafety Level 1 (BSL-1) surrogate to evaluate surface disinfection efficacy in Ebola outbreaks: Comparison of four bacteriophages. PLoS.One. 2017; 12(5):e0177943; PM: 28531182

ABSTRACT: The 2014 West African Ebola virus disease outbreak was the largest to date, and conflicting, chlorine-based surface disinfection protocols to interrupt disease transmission were recommended. We identified only one study documenting surface disinfection efficacy against the Ebola virus, showing a >6.6 log reduction after 5-minute exposure to 0.5% sodium hypochlorite (NaOCl) based on small-scale tests (Cook et al. (2015)). In preparation for future extensive, large-scale disinfection efficacy experiments, we replicated the Cook et al. experiment using four potential BSL-1 surrogates selected based on similarities to the Ebola virus: bacteriophages MS2, M13, Phi6, and PR772. Each bacteriophage was exposed to 0.1% and 0.5% NaOCl for 1, 5, and 10 minutes on stainless steel. MS2 and M13 were only reduced by 3.4 log and 3.5 log after a 10-minute exposure to 0.5% NaOCl, and would be overly conservative surrogates. Conversely, PR772 was too easily inactivated for surrogate use, as it was reduced by >4.8 log after only 1-minute exposure to 0.5% NaOCl. Phi6 was slightly more resistant than the Ebola virus, with 4.1 log reduction after a 5-minute exposure and not detected after a 10-minute exposure to 0.5% NaOCl. We therefore recommend Phi6 as a surrogate for evaluating the efficacy of chlorine-based surface disinfectants against the Ebola virus.

Galtier, M., De, Sordi L., Sivignon, A., de, Vallee A., Maura, D., Neut, C., Rahmouni, O., Wannerberger, K., rfeuille-Michaud, A., Desreumaux, P., Barnich, N., and Debarbieux, L. Bacteriophages Targeting Adherent Invasive Escherichia coli Strains as a Promising New Treatment for Crohn's Disease. J.Crohns.Colitis. 7-1-2017; 11(7):840-847. PM: 28130329

ABSTRACT: Background and Aims: Adherent invasive Escherichia coli [AIEC] are abnormally predominant on the ileal mucosa of Crohn's disease [CD] patients. They bind to the CEACAM6 receptor expressed on the surface of epithelial cells. We aimed to assess the potential of bacteriophages, viruses infecting bacteria, to decrease the levels of AIEC bacteria associated with the intestinal mucosa. Methods: We combined ex vivo and in vivo experiments with murine and human intestinal samples to quantify the ability of virulent bacteriophages to target the prototype AIEC strain LF82. Results: We found that three virulent bacteriophages were able to replicate in ileal, caecal and colonic sections and faeces homogenates from murine gut samples colonised with the prototype AIEC strain LF82. A single day of per os treatment with the three bacteriophages cocktail given to LF82-colonised CEABAC10 transgenic mice, expressing the human CEACAM6 receptor for AIEC, decreased significantly the number of AIEC in faeces and in the adherent flora of intestinal sections. In addition, a single dose of the cocktail reduced dextran sodium sulphate-induced colitis symptoms on conventional mice colonised with the strain LF82 over a 2-week period. The cocktail targeted also LF82 bacteria in homogenates of ileal biopsies taken from CD patients. Conclusions: These findings demonstrate that bacteriophages are a new treatment option for targeting AIEC in CD patients and represent a strong basis for a clinical trial evaluation.

Garcia, K. C. O. D., Correa, I. M. O., Pereira, L. Q., Silva, T. M., Mioni, M. S. R., Izidoro, A. C. M., Bastos, I. H. V., Goncalves, G. A. M., Okamoto, A. S., and ndreatti Filho, R. L. Bacteriophage use to control Salmonella biofilm on surfaces present in chicken slaughterhouses. Poult.Sci. 9-1-2017; 96(9):3392-3398; PM: 28595324

ABSTRACT: Foodborne diseases represent a major risk to public health worldwide. Pathogenic bacteria can live in the form of biofilm within the food industry, providing a permanent source of contamination. The aim of this study was to evaluate the influence of the types of adhesion surfaces on Salmonella biofilm formation at eight different times, and analyze the action time of a bacteriophage pool on established biofilms. Most of the samples used were classified as weak biofilm producers, with serovars Enteritidis and Heidelberg showing the highest frequency of biofilm formation. Glass and stainless steel surfaces significantly favored biofilm formation at 60 and 36 h of incubation respectively, but the polyvinyl chloride surface did not favor biofilm production, suggesting that the type of material may interfere with production. The bacteriophage pool action period focused on 3 h, but treatment of 9 h on glass surface biofilms was superior to other treatments because it affected the largest number of samples. These results suggests that some surface types and Salmonella serotypes may promote biofilm formation and indicate bacteriophages as an alternative to control biofilms. But further studies are required to prove the effectiveness and safety of bacteriophage therapy as an alternative in the antimicrobial control in the processing plants.

Gencay, Y. E., Sorensen, M. C. H., and Brondsted, L. Whole-Genome Sequence of the Bacteriophage-Sensitive Strain Campylobacter jejuni NCTC12662. Genome Announc. 5-25-2017; 5(21); PM: 28546493

ABSTRACT: Campylobacter jejuni NCTC12662 has been the choice bacteriophage isolation strain due to its susceptibility to C. jejuni bacteriophages. This trait makes it a good candidate for studying bacteriophage-host interactions. We report here the whole-genome sequence of NCTC12662, allowing future elucidation of the molecular mechanisms of phage-host interactions in C. jejuni.

Gotsbacher, M. P., Cho, S., Kwon, H. J., and Karuso, P. Daptomycin, a last-resort antibiotic, binds ribosomal protein S19 in humans. Proteome.Sci. 2016; 15:16; PM: 28680364

*ABSTRACT**: BACKGROUND***: Daptomycin is a recently introduced, last-resort antibiotic that displays a unique mode of action against Gram-positive bacteria that is not fully understood. Several bacterial targets have been proposed but no human binding partner is known. ***METHODS***: In the present study we tested daptomycin in cell viability and proliferation assays against six human cell lines, describe the synthesis of biotinylated and fluorescently labeled analogues of daptomycin. Biotinylated daptomycin was used as bait to isolate the human binding partner by the application of reverse chemical proteomics using T7 phage display of five human tumor cDNA libraries. The interaction between the rescued protein and daptomycin was validated via siRNA knockdown, DARTS assay and immunocytochemistry. ***RESULTS***: We have found that daptomycin possesses selective growth inhibition of some cancer cell lines, especially MCF7. The unbiased interrogation of human cDNA libraries, displayed on bacteriophage T7, revealed a single human target of daptomycin; ribosomal protein S19. Using a drug affinity responsive target stability (DARTS) assay in vitro, we show that daptomycin stabilizes RPS19 toward pronase. Fluorescently labeled daptomycin stained specific

structures in HeLa cells and co-localized with a RPS19 antibody. ***CONCLUSION***: This study provides, for the first time, a human protein target of daptomycin and identifies RPS19 as a possible anticancer drug target for the development of new pharmacological applications and research.

Granell, M., Namura, M., Alvira, S., Kanamaru, S., and van Raaij, M. J. Crystal Structure of the Carboxy-Terminal Region of the Bacteriophage T4 Proximal Long Tail Fiber Protein Gp34. Viruses. 6-30-2017; 9(7); PM: 28665339

ABSTRACT: Long tail fibers of bacteriophage T4 are formed by proteins gp34, gp35, gp36, and gp37, with gp34 located at the phage-proximal end and gp37 at the phage-distal, receptor-binding end. We have solved the structure of the carboxy-terminal region of gp34, consisting of amino acids 894-1289, by single-wavelength anomalous diffraction and extended the structure to amino acids 744-1289 using data collected from crystals containing longer gp34-fragments. The structure reveals three repeats of a mixed alpha-beta fibrous domain in residues 744 to 877. A triple-helical neck connects to an extended triple beta-helix domain (amino acids 900-1127) punctuated by two beta-prism domains. Next, a beta-prism domain decorated with short helices and extended beta-helices is present (residues 1146-1238), while the C-terminal end is capped with another short beta-helical region and three beta-hairpins. The structure provides insight into the stability of the fibrous gp34 protein.

Guo, J., Gao, S. H., Lu, J., Bond, P. L., Verstraete, W., and Yuan, Z. Copper Oxide Nanoparticles Induce Lysogenic Bacteriophage and Metal-Resistance Genes in Pseudomonas aeruginosa PAO1. ACS Appl.Mater.Interfaces. 7-12-2017; 9(27):22298-22307; PM: 28636321

ABSTRACT: The intensive use of metal-based nanoparticles results in their continuous release into the environment, leading to potential risks for human health and microbial ecosystems. Although previous studies have indicated that nanoparticles may be toxic to microorganisms, there is a scarcity of data available to assess the underlying molecular mechanisms of inhibitory and biocidal effects of nanoparticles on microorganisms. This study used physiological experiments, microscopy, live/dead staining, and the genome-wide RNA sequencing to investigate the multiple responses of Pseudomonas aeruginosa to the exposure of copper oxide nanoparticles (CuO NPs). The results for the first time show that CuO NPs induce lysogenic bacteriophage, which might render defective within a bacterial host. The presence of CuO NPs causes nitrite accumulation and great increases in N2O emissions. Respiration is likely inhibited as denitrification activity is depleted in terms of decreased transcript levels of most denitrification genes. Meanwhile, CuO NPs exposure significantly up-regulated gene expression for those coding for copper resistance, resistance-nodulation-division, P-type ATPase efflux, and cation diffusion facilitator transporters. Our findings offer insights into the interaction between environmental bacteria and CuO NPs at the transcriptional level and, thus, improve our understanding of potential risks of nanoparticles on microbial ecosystems and public health.

Guo, Z., Huang, J., Yan, G., Lei, L., Wang, S., Yu, L., Zhou, L., Gao, A., Feng, X., Han, W., Gu, J., and Yang, J. Identification and Characterization of Dpo42, a Novel Depolymerase Derived

from the Escherichia coli Phage vB_EcoM_ECOO78. Front Microbiol. 2017; 8:1460; PM: 28824588

ABSTRACT: Biofilm formation, one of the most important virulence factors of pathogenic bacteria, protects bacteria against desiccation, antibiotics, phages and host immune responses. However, phage-derived depolymerases show antibiofilm activity and demonstrate great potential to treat infections caused by biofilm-forming bacteria. In this study, the Escherichia coli phage vB_EcoM_ECOO78 was isolated and characterised, and we observed its ability to lyse five out of 34 tested E. coli clinical isolates. The highest phage titre was observed at a multiplicity of infection of 10-5 and a burst size of approximately 74 plaque forming units (PFU)/infection. Electron micrographs indicated that vB_EcoM_ECOO78 belongs to the family Myoviridae. The presence of increasing halos surrounding the lysis plaques formed by vB_EcoM_ECOO78 indicated that this phage may encode a depolymerase. Based on a sequencing analysis, the complete genome of vB_EcoM_ECOO78 was found to be 41,289 bp in size, with a GC content of 53.07%. Additionally, vB_EcoM_ECOO78 has 56 predicted open reading frames, 51 (91.07%) of which are assumed to be functional. A BLAST analysis indicated that ORF42 of vB_EcoM_ECOO78 (Dpo42) has low identity with other reported phage-associated depolymerases. Dpo42 was expressed and purified as a soluble protein using E. coli BL21. The biofilm formation ability of E. coli isolates and the antibiofilm activity of Dpo42 were tested by performing spot assays and using a 96-well micro-titre plate method. Dpo42 degraded the capsular polysaccharides surrounding E. coli and exhibited dose-dependent biofilm-formation prevention activity. Based on these results, Dpo42 appears to be a novel phage-derived depolymerase that represents a new potential strategy for preventing E. coli biofilm formation.

Gupta, K., Sharp, R., Yuan, J. B., Li, H., and Van Duyne, G. D. Coiled-coil interactions mediate serine integrase directionality. Nucleic Acids Res. 7-7-2017; 45(12):7339-7353; PM: 28549184

ABSTRACT: Serine integrases are bacteriophage enzymes that carry out site-specific integration and excision of their viral genomes. The integration reaction is highly directional; recombination between the phage attachment site attP and the host attachment site attB to form the hybrid sites attL and attR is essentially irreversible. In a recent model, extended coiled-coil (CC) domains in the integrase subunits are proposed to interact in a way that favors the attPxattB reaction but inhibits the attLxattR reaction. Here, we show for the Listeria innocua integrase (LI Int) system that the CC domain promotes self-interaction in isolated Int and when Int is bound to attachment sites. Three independent crystal structures of the CC domain reveal the molecular nature of the CC dimer interface. Alanine substitutions of key residues in the interface support the functional significance of the structural model and indicate that the same interaction is responsible for promoting integration and for inhibiting excision. An updated model of a LI Int*attL complex that incorporates the high resolution CC dimer structure provides insights that help to explain the unusual CC dimer structure and potential sources of stability in Int*attL and Int*attR complexes. Together, the data provide a molecular basis for understanding serine integrase directionality.

Gutierrez, D., Fernandez, L., Martinez, B., Ruas-Madiedo, P., Garcia, P., and Rodriguez, A. Real-Time Assessment of Staphylococcus aureus Biofilm Disruption by Phage-Derived Proteins. Front Microbiol. 2017; 8:1632; PM: 28883818

ABSTRACT: A current focus of research is the development of new tools for removing bacterial biofilms in industrial settings. Bacteriophage-encoded proteins, such as endolysins, virion-associated peptidoglycan hydrolases, and exopolysaccharide depolymerases, have been shown to be efficient against these structures. However, the current screening techniques for the identification of antibiofilm properties of phage-derived proteins have important shortcomings. The aim of this work was to use the rapid, reproducible and accurate technology "real-time cell analyzer" for screening and comparing the antibiofilm ability of four phage-derived compounds, three lytic proteins (LysH5, CHAP-SH3b, and HydH5-SH3b) and one exopolysaccharide depolymerase (Dpo7) against Staphylococcus aureus biofilms, which have been associated with recurrent contamination of food products. The data generated after biofilm treatment allowed for the calculation of different antibiofilm parameters: (1) the minimum biofilm eradicating concentration that removes 50% of the biofilm (ranging from 3.5 +/- 1.1 to 6.6 +/- 0.5 muM), (2) the lowest concentration needed to observe an antibiofilm effect (approximately 1.5 muM for all the proteins), and (3) the specific antibiofilm activity and the percentage of biofilm removal that revealed LysH5 as the best antibiofilm compound. Overall, this technology might be used to quickly assess and compare by standardized parameters the disaggregating activity of phage antibiofilm proteins.

Haaber, J., Penades, J. R., and Ingmer, H. Transfer of Antibiotic Resistance in Staphylococcus aureus. Trends Microbiol. 6-19-2017; PM: 28641931

ABSTRACT: Staphylococcus aureus is a serious human pathogen with remarkable adaptive powers. Antibiotic-resistant clones rapidly emerge mainly by acquisition of antibiotic-resistance genes from other S. aureus strains or even from other genera. Transfer is mediated by a diverse complement of mobile genetic elements and occurs primarily by conjugation or bacteriophage transduction, with the latter traditionally being perceived as the primary route. Recent work on conjugation and transduction suggests that transfer by these mechanisms may be more extensive than previously thought, in terms of the range of plasmids that can be transferred by conjugation and the efficiency with which transduction occurs. Here, we review the main routes of antibiotic resistance gene transfer in S. aureus in the context of its biology as a human commensal and a life-threatening pathogen.

Haddad, Kashani H., Fahimi, H., Dasteh, Goli Y., and Moniri, R. A Novel Chimeric Endolysin with Antibacterial Activity against Methicillin-Resistant Staphylococcus aureus. Front Cell Infect.Microbiol. 2017; 7:290; PM: 28713777

ABSTRACT: Cysteine/histidine-dependent amidohydrolase/peptidase (CHAP) and amidase are known as catalytic domains of the bacteriophage-derived endolysin LysK and were previously reported to show lytic activity against methicillin-resistant Staphylococcus aureus (MRSA). In the current study, the in silico design and analysis of chimeric CHAP-amidase model was applied to enhance the stability and solubility of protein, which was achieved through improving the properties of primary, secondary and tertiary structures. The coding gene sequence of the chimeric CHAP-amidase was synthesized and subcloned into the pET-22(+) expression vector, and the recombinant protein was expressed in E. coli BL21 (DE3) strain. Subsequent affinity-based purification yielded ~12 mg soluble protein per liter of E. coli culture. Statistical analysis indicated that concentrations of >/=1 mug/mL of the purified protein have significant antibacterial

activity against S. aureus MRSA252 cells. The engineered chimeric CHAP-amidase exhibited 3.2 log reduction of MRSA252 cell counts at the concentration of 10 mug/mL. A synergistic interaction between CHAP-amidase and vancomycin was detected by using checkerboard assay and calculating the fractional inhibitory concentration (FIC) index. This synergistic effect was shown by 8-fold reduction in the minimum inhibitory concentration of vancomycin. The chimeric CHAP-amidase displayed strong antibacterial activity against S. aureus, S. epidermidis, and enterococcus. However, it did not indicate any significant antibacterial activity against E. coli and Lactococcus lactis. Taken together, these findings suggest that our chimeric CHAP-amidase might represent potential to be used for the development of efficient antibacterial therapies targeting MRSA and certain Gram-positive bacteria.

Haque, F., Xu, C., Jasinski, D. L., Li, H., and Guo, P. Using Planar Phi29 pRNA Three-Way Junction to Control Size and Shape of RNA Nanoparticles for Biodistribution Profiling in Mice. Methods Mol.Biol. 2017; 1632:359-380; PM: 28730451

ABSTRACT: RNA is rapidly emerging as a versatile building block for nanoparticle assembly due to its simplicity in base pairing, while exhibiting diversity in function such as enzymatic activity similar to some proteins. Recent advances in RNA nanotechnology have generated significant interests in applying RNA nanoparticles for various applications in nanotechnology and nanomedicine. In particular, assessing the effect of size and shape on cell entry and intracellular trafficking as well as in vivo biodistribution of nanoparticles is challenging due to the lack of nanoparticles rich in structure while varying in size and shape. RNA nanotechnology exemplified by the packaging RNA (pRNA) of bacteriophage phi29 DNA packaging motor has provided a different prospect in nanoparticle designs. Of note, there is a robust three-way junction (3WJ) motif in pRNA which can serve as an adaptable scaffold to construct thermodynamically stable 2D planar and 3D globular RNA architectures with tunable shapes and sizes, and harboring various targeting, therapeutic, and imaging modules. This chapter focuses on the methods for constructing pRNA-3WJ based nanoparticles with controllable sizes and shapes, and assessment of their biodistribution profiles in cancer mouse models after systemic injection and ocular mouse models following subconjunctival injection.

Harrington, L. B., Doxzen, K. W., Ma, E., Liu, J. J., Knott, G. J., Edraki, A., Garcia, B., Amrani, N., Chen, J. S., Cofsky, J. C., Kranzusch, P. J., Sontheimer, E. J., Davidson, A. R., Maxwell, K. L., and Doudna, J. A. A Broad-Spectrum Inhibitor of CRISPR-Cas9. Cell. 9-7-2017; 170(6):1224-1233; PM: 28844692

ABSTRACT: CRISPR-Cas9 proteins function within bacterial immune systems to target and destroy invasive DNA and have been harnessed as a robust technology for genome editing. Small bacteriophage-encoded anti-CRISPR proteins (Acrs) can inactivate Cas9, providing an efficient off switch for Cas9-based applications. Here, we show that two Acrs, AcrIIC1 and AcrIIC3, inhibit Cas9 by distinct strategies. AcrIIC1 is a broad-spectrum Cas9 inhibitor that prevents DNA cutting by multiple divergent Cas9 orthologs through direct binding to the conserved HNH catalytic domain of Cas9. A crystal structure of an AcrIIC1-Cas9 HNH domain complex shows how AcrIIC1 traps Cas9 in a DNA-bound but catalytically inactive state. By contrast, AcrIIC3 blocks activity of a single Cas9 ortholog and induces Cas9 dimerization while preventing binding to the target DNA. These two

orthogonal mechanisms allow for separate control of Cas9 target binding and cleavage and suggest applications to allow DNA binding while preventing DNA cutting by Cas9.

Hasek, M. L., Maurer, J. B., Hendrix, R. W., and Duda, R. L. Flexible Connectors between Capsomer Subunits that Regulate Capsid Assembly. J.Mol.Biol. 8-4-2017; 429(16):2474-2489; PM: 28705762

ABSTRACT: Viruses build icosahedral capsids of specific size and shape by regulating the spatial arrangement of the hexameric and pentameric protein capsomers in the growing shell during assembly. In the T=7 capsids of Escherichia coli bacteriophage HK97 and other phages, 60 capsomers are hexons, while the rest are pentons that are correctly positioned during assembly. Assembly of the HK97 capsid to the correct size and shape has been shown to depend on specific ionic contacts between capsomers. We now describe additional ionic interactions within capsomers that also regulate assembly. Each is between the long hairpin, the "E-loop," that extends from one subunit to the adjacent subunit within the same capsomer. Glutamate E153 on the E-loop and arginine R210 on the adjacent subunit's backbone alpha-helix form salt bridges in hexamers and pentamers. Mutations that disrupt these salt bridges were lethal for virus production, because the mutant proteins assembled into tubes or sheets instead of capsids. X-ray structures show that the E153-R210 links are flexible and maintained during maturation despite radical changes in capsomer shape. The E153-R210 links appear to form early in assembly to enable capsomers to make programmed changes in their shape during assembly. The links also prevent flattening of capsomers and premature maturation. Mutant phenotypes and modeling support an assembly model in which flexible E153-R210 links mediate capsomer shape changes that control where pentons are placed to create normal-sized capsids. The E-loop may be conserved in other systems in order to play similar roles in regulating assembly.

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.

Herten, M., Idelevich, E. A., Sielker, S., Becker, K., Scherzinger, A. S., Osada, N., Torsello, G. B., and Bisdas, T. Vascular Graft Impregnation with Antibiotics: The Influence of High Concentrations of Rifampin, Vancomycin, Daptomycin, and Bacteriophage Endolysin HY-133 on Viability of Vascular Cells. Med.Sci.Monit.Basic Res. 6-27-2017; 23:250-257; PM: 28652563

*ABSTRACT**: BACKGROUND:*** Rifampin-soaked synthetic prosthetic grafts have been widely used for prevention or treatment of vascular graft infections (VGIs). This in vitro study investigated the effect of the antibiotics daptomycin and vancomycin and the new recombinant bacteriophage endolysin HY-133 on vascular cells, as potential alternatives compared to rifampin. ***MATERIAL AND METHODS***: Primary human ECs, vascular smooth muscle cells (vSMC), and fibroblasts were cultivated in 96-well plates and incubated with rifampin, daptomycin, vancomycin, and endolysin HY-133 for 24 h. Subsequently, after washing, cell viability was determined by measuring mitochondrial ATP concentration. Antibiotics were used in their corresponding minimum and maximum serum concentrations, in decimal multiples and in maximum soaking concentration. The experiments were performed in triplicate. ***RESULTS:*** The 10-fold max serum concentrations of rifampin, daptomycin, and vancomycin did not influence viability of EC and vSMC (100 microg/ml, $p>0.170$). Higher concentrations of rifampin (>1 mg/ml) significantly ($p<0.001$) reduced cell viability of all cell types. For the other antibiotics, high concentrations (close to maximum soaking concentration) were most cytotoxic for EC and vSMC and fibroblasts ($p<0.001$). Endolysin did not display any cytotoxicity towards vascular cells. ***CONCLUSIONS:*** Results of this in vitro study show the high cytotoxicity of rifampin against vascular cells, and may re-initiate the discussion about the benefit of prophylactic pre-soaking in high concentrations of rifampin. Further studies are necessary to determine the influence of rifampin on the restoration of vessel functionality versus its prophylactic effect against VGIs. Future use of recombinant phage endolysins for alternative prophylactic strategies needs further investigations.

Houot, L., Navarro, R., Nouailler, M., Duche, D., Guerlesquin, F., and Lloubes, R. Electrostatic interactions between the CTX phage minor coat protein and the bacterial host receptor TolA drive the pathogenic conversion of Vibrio cholerae. J.Biol.Chem. 8-18-2017; 292(33):13584-13598; PM: 28642371

ABSTRACT: Vibrio cholerae is a natural inhabitant of aquatic environments and converts to a pathogen upon infection by a filamentous phage, CTXPhi, that transmits the cholera toxin-encoding genes. This toxigenic conversion of V. cholerae has evident implication in both genome plasticity and epidemic risk, but the early stages of the infection have not been thoroughly studied. CTXPhi transit across the bacterial periplasm requires binding between the minor coat protein named pIII and a bacterial inner-membrane receptor, TolA, which is part of the conserved Tol-Pal molecular motor. To gain insight into the TolA-pIII complex, we developed a bacterial two-hybrid approach, named Oxi-BTH, suited for studying the interactions between disulfide bond-folded proteins in the bacterial cytoplasm of an Escherichia coli reporter strain. We found that two of the four disulfide bonds of pIII are required for its interaction with TolA. By combining Oxi-BTH assays, NMR, and genetic studies, we also demonstrate that two intermolecular salt bridges between TolA and pIII provide the driving forces of the complex interaction. Moreover, we show that TolA residue Arg-325 involved in one of the two salt bridges is critical for proper functioning of the Tol-Pal system. Our results imply that to prevent host evasion, CTXPhi

uses an infection strategy that targets a highly conserved protein of Gram-negative bacteria essential for the fitness of V. cholerae in its natural environment.

Jack, B. R., Boutz, D. R., Paff, M. L., Smith, B. L., Bull, J. J., and Wilke, C. O. Reduced Protein Expression in a Virus Attenuated by Codon Deoptimization. G3.(Bethesda.). 9-7-2017; 7(9):2957-2968; PM: 28698233

ABSTRACT: A general means of viral attenuation involves the extensive recoding of synonymous codons in the viral genome. The mechanistic underpinnings of this approach remain unclear, however. Using quantitative proteomics and RNA sequencing, we explore the molecular basis of attenuation in a strain of bacteriophage T7 whose major capsid gene was engineered to carry 182 suboptimal codons. We do not detect transcriptional effects from recoding. Proteomic observations reveal that translation is halved for the recoded major capsid gene, and a more modest reduction applies to several coexpressed downstream genes. We observe no changes in protein abundances of other coexpressed genes that are encoded upstream. Viral burst size, like capsid protein abundance, is also decreased by half. Together, these observations suggest that, in this virus, reduced translation of an essential polycistronic transcript and diminished virion assembly form the molecular basis of attenuation.

Jalasvuori, M. and Penttinen, R. What can evolutionary rescue tell us about the emergence of new resistant bacteria? Future.Microbiol. 2017; 12:731-733; PM: 28593799

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Jennes, S., Merabishvili, M., Soentjens, P., Pang, K. W., Rose, T., Keersebilck, E., Soete, O., Francois, P. M., Teodorescu, S., Verween, G., Verbeken, G., De, Vos D., and Pirnay, J. P. Use of bacteriophages in the treatment of colistin-only-sensitive Pseudomonas aeruginosa septicaemia in a patient with acute kidney injury-a case report. Crit Care. 6-4-2017; 21(1):129PM:28583189¶

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Johnson, M. C., Sena-Velez, M., Washburn, B. K., Platt, G. N., Lu, S., Brewer, T. E., Lynn, J. S., Stroupe, M. E., and Jones, K. M. Structure, proteome and genome of Sinorhizobium meliloti phage PhiM5: A virus with LUZ24-like morphology and a highly mosaic genome. J.Struct.Biol. 8-24-2017; PM: 28842338

ABSTRACT: Bacteriophages of nitrogen-fixing rhizobial bacteria are revealing a wealth of novel structures, diverse enzyme combinations and genomic features. Here we report the cryo-EM structure of the phage capsid at 4.9-5.7A-resolution, the phage particle proteome, and the genome of the Sinorhizobium meliloti-infecting Podovirus PhiM5. This is the first structure of a phage with a capsid and capsid-associated structural proteins related to those of the LUZ24-like viruses that infect Pseudomonas aeruginosa. Like many other Podoviruses, PhiM5 is a T=7 icosahedron with a smooth capsid and short, relatively featureless tail. Nonetheless, this group is phylogenetically quite distinct from Podoviruses of the well-characterized T7, P22, and epsilon 15 supergroups. Structurally, a distinct bridge of density that appears unique to PhiM5 reaches down the body of the coat

protein to the extended loop that interacts with the next monomer in a hexamer, perhaps stabilizing the mature capsid. Further, the predicted tail fibers of PhiM5 are quite different from those of enteric bacteria phages, but have domains in common with other rhizophages. Genomically, PhiM5 is highly mosaic. The PhiM5 genome is 44,005bp with 357bp direct terminal repeats (DTRs) and 58 unique ORFs. Surprisingly, the capsid structural module, the tail module, the DNA-packaging terminase, the DNA replication module and the integrase each appear to be from a different lineage. One of the most unusual features of PhiM5 is its terminase whose large subunit is quite different from previously-described short-DTR-generating packaging machines and does not fit into any of the established phylogenetic groups.

Johnson, S. A., Walsh, A., Brown, M. R., Lute, S. C., Roush, D. J., Burnham, M. S., and Brorson, K. A. The step-wise framework to design a chromatography-based hydrophobicity assay for viral particles. J.Chromatogr.B Analyt.Technol.Biomed.Life Sci. 9-1-2017; 1061-1062:430-437; PM: 28818800

ABSTRACT: A high-salt, hydrophobic interaction chromatography (HIC) method was developed to measure the relative hydrophobicity of a diverse set of solutes. Through the careful control of buffer pH and salt concentration, this assay was then used to ascertain for the first time the relative hydrophobicity values of three different bacteriophage, four mammalian viruses, and a range of biotech medicinal proteins as benchmarked to protein standards previously characterized for hydrophobicity.

Jonczyk-Matysiak, E., Weber-Dabrowska, B., Owczarek, B., Miedzybrodzki, R., Lusiak-Szelachowska, M., Lodej, N., and Gorski, A. Phage-Phagocyte Interactions and Their Implications for Phage Application as Therapeutics. Viruses. 6-14-2017; 9(6); PM: 28613272

ABSTRACT: Phagocytes are the main component of innate immunity. They remove pathogens and particles from organisms using their bactericidal tools in the form of both reactive oxygen species and degrading enzymes-contained in granules-that are potentially toxic proteins. Therefore, it is important to investigate the possible interactions between phages and immune cells and avoid any phage side effects on them. Recent progress in knowledge concerning the influence of phages on phagocytes is also important as such interactions may shape the immune response. In this review we have summarized the current knowledge on phage interactions with phagocytes described so far and their potential implications for phage therapy. The data suggesting that phage do not downregulate important phagocyte functions are especially relevant for the concept of phage therapy.

Joshi, H., Seniya, S. P., Venkatesan, S., Patidar, N. D., Singh, S. K., and Jain, V. Dissecting the Structure-function Relationship in Lysozyme Domain of Mycobacteriophage D29-encoded Peptidoglycan Hydrolase. FEBS Lett. 9-13-2017; PM: 28901529

ABSTRACT: Most bacteriophages rapidly infect and kill bacteria and, therefore, qualify as the next generation therapeutics for rapidly emerging drug-resistant bacteria such as Mycobacterium tuberculosis. We have previously characterized the mycobacteriophage D29-generated endolysin, Lysin A, for its activity against mycobacteria. Here, we present a detailed characterization of the lysozyme domain

(LD) of D29 Lysin A that hydrolyzes peptidoglycan of both Gram-positive and Gram-negative bacteria with high potency. By characterizing an exhaustive LD protein variant library, we have identified critical residues important for LD activity and stability. We further complement our in vitro experiments with detailed in silico investigations. We present LD as a potent candidate for developing phage-based broad spectrum therapeutics. This article is protected by copyright. All rights reserved.

Keller, N., Berndsen, Z. T., Jardine, P. J., and Smith, D. E. Experimental comparison of forces resisting viral DNA packaging and driving DNA ejection. Phys.Rev.E. 2017; 95(5-1):052408; PM: 28618627

ABSTRACT: We compare forces resisting DNA packaging and forces driving DNA ejection in bacteriophage phi29 with theoretical predictions. Ejection of DNA from prohead-motor complexes is triggered by heating complexes after in vitro packaging and force is inferred from the suppression of ejection by applied osmotic pressure. Ejection force from 0% to 80% filling is found to be in quantitative agreement with predictions of a continuum mechanics model that assumes a repulsive DNA-DNA interaction potential based on DNA condensation studies and predicts an inverse-spool conformation. Force resisting DNA packaging from approximately 80% to 100% filling inferred from optical tweezers studies is also consistent with the predictions of this model. The striking agreement with these two different measurements suggests that the overall energetics of DNA packaging is well described by the model. However, since electron microscopy studies of phi29 do not reveal a spool conformation, our findings suggest that the spool model overestimates the role of bending rigidity and underestimates the role of intrastrand repulsion. Below approximately 80% filling the inferred forces resisting packaging are unexpectedly lower than the inferred ejection forces, suggesting that in this filling range the forces are less accurately determined or strongly temperature dependent.

Khoa, H. V., Midorikawa, Y., Uchino, T., Nakai, T., Kato, G., Kondo, H., Hirono, I., Labaiden, M., Direkbusarakom, S., and Sano, M. Complete Genome Sequence of the Lytic Giant Bacteriophage pT24 Infecting Tenacibaculum spp., Isolated from a Shrimp Culture Pond. Genome Announc. 7-6-2017; 5(27); PM: 28684560

ABSTRACT: The lytic bacteriophage pT24, which infects Tenacibaculum spp., was isolated from the water of a whiteleg shrimp (Litopenaeus vannamei) culture pond in Thailand. This giant bacteriophage with myovirus morphology comprised 234,670 bp with 296 predicted genes.

Kick, B., Behler, K. L., Severin, T. S., and Weuster-Botz, D. Chemostat studies of bacteriophage M13 infected Escherichia coli JM109 for continuous ssDNA production. J.Biotechnol. 9-20-2017; 258:92-100; PM: 28645580

ABSTRACT: Steady state studies in a chemostat enable the control of microbial growth rate at defined reaction conditions. The effects of bacteriophage M13 infection on maximum growth rate of Escherichia coli JM109 were studied in parallel operated chemostats on a milliliter-scale to analyze the steady state kinetics of phage production. The bacteriophage infection led to a decrease in maximum specific growth rate of 15% from 0.74h-1 to 0.63h-1. Under steady state conditions, a constant cell specific ssDNA formation rate of 0.15+/-0.004 mgssDNA gCDW-1h-1 was observed, which was

independent of the growth rate. Using the estimated kinetic parameters for E. coli infected with bacteriophage M13, the ssDNA concentration in the steady state could be predicted as function of the dilution rate and the glucose concentration in the substrate. Scalability of milliliter-scale data was approved by steady state studies on a liter-scale at a selected dilution rate. An ssDNA space-time yield of 5.7mgL-1h-1 was achieved with increased glucose concentration in the feed at a dilution rate of 0.3h-1, which is comparable to established fed-batch fermentation with bacteriophage M13 for ssDNA production.

Kim, S. G., Jun, J. W., Giri, S. S., Yun, S., Kim, H. J., Chi, C., Kim, S. W., and Park, S. C. Complete Genome Sequence of Staphylococcus aureus Bacteriophage pSa-3. Genome Announc. 5-25-2017; 5(21); PM: 28546473

ABSTRACT: Staphylococcus aureus phage pSa-3, isolated in South Korea from a sewage sample, has a 137-kb genome with 29% G+C content. This phage was targeted to control the bacteria in clinical isolates (mainly from skin lesions) and can be used in the decolonization of S. aureus.

Kingsley, D. H., Chen, H., and Meade, G. K. Persistence of MS-2 Bacteriophage Within Eastern Oysters. Food Environ.Virol. 8-22-2017; PM: 28831665

ABSTRACT: Male-specific bacteriophages have been proposed as human enteric virus indicators for shellfish. In this study, Eastern oysters (Crassostrea virginica) were individually exposed to 5.6 x 1010 PFU of MS-2 for 48 h at 15 degrees C followed by collective maintenance in continuously UV-sterilized seawater for 0-6 weeks at either 7, 15, or 24 degrees C. Initial contamination levels of MS-2 were >6 log PFU. Assessment of weekly declines of viable MS-2 indicated that cooler temperatures dramatically enhanced the persistence of MS-2 within oyster tissues. At 3 weeks, the average log PFU reductions for MS-2 within oysters were 2.28, 2.90, and 4.57 for oysters held at 7, 15, and 24 degrees C, respectively. Fitting temporal survival data with linear and nonlinear Weibull models indicated that the Weibull model best fit the observed reductions. In total, these data can serve as a guideline for regulatory agencies regarding the influence of water temperature on indicator phage after episodic sewage exposure.

Kirk, J. A., Gebhart, D., Buckley, A. M., Lok, S., Scholl, D., Douce, G. R., Govoni, G. R., and Fagan, R. P. New class of precision antimicrobials redefines role of Clostridium difficile S-layer in virulence and viability. Sci.Transl.Med. 9-6-2017; 9(406); PM: 28878013

ABSTRACT: There is a medical need for antibacterial agents that do not damage the resident gut microbiota or promote the spread of antibiotic resistance. We recently described a prototypic precision bactericidal agent, Av-CD291.2, which selectively kills specific Clostridium difficile strains and prevents them from colonizing mice. We have since selected two Av-CD291.2-resistant mutants that have a surface (S)-layer-null phenotype due to distinct point mutations in the slpA gene. Using newly identified bacteriophage receptor binding proteins for targeting, we constructed a panel of Avidocin-CDs that kills diverse C. difficile isolates in an S-layer sequence-dependent manner. In addition to bacteriophage receptor recognition, characterization of the mutants also uncovered important roles for S-layer protein A (SlpA) in sporulation,

resistance to innate immunity effectors, and toxin production. Surprisingly, S-layer-null mutants were found to persist in the hamster gut despite a complete attenuation of virulence. These findings suggest antimicrobials targeting virulence factors dispensable for fitness in the host force pathogens to trade virulence for viability and would have clear clinical advantages should resistance emerge. Given their exquisite specificity for the pathogen, Avidocin-CDs have substantial therapeutic potential for the treatment and prevention of C. difficile infections.

Klyczek, K. K., Bonilla, J. A., Jacobs-Sera, D., Adair, T. L., Afram, P., Allen, K. G., Archambault, M. L., Aziz, R. M., Bagnasco, F. G., Ball, S. L., Barrett, N. A., Benjamin, R. C., Blasi, C. J., Borst, K., Braun, M. A., Broomell, H., Brown, C. B., Brynell, Z. S., Bue, A. B., Burke, S. O., Casazza, W., Cautela, J. A., Chen, K., Chimalakonda, N. S., Chudoff, D., Connor, J. A., Cross, T. S., Curtis, K. N., Dahlke, J. A., Deaton, B. M., Degroote, S. J., DeNigris, D. M., DeRuff, K. C., Dolan, M., Dunbar, D., Egan, M. S., Evans, D. R., Fahnestock, A. K., Farooq, A., Finn, G., Fratus, C. R., Gaffney, B. L., Garlena, R. A., Garrigan, K. E., Gibbon, B. C., Goedde, M. A., Guerrero Bustamante, C. A., Harrison, M., Hartwell, M. C., Heckman, E. L., Huang, J., Hughes, L. E., Hyduchak, K. M., Jacob, A. E., Kaku, M., Karstens, A. W., Kenna, M. A., Khetarpal, S., King, R. A., Kobokovich, A. L., Kolev, H., Konde, S. A., Kriese, E., Lamey, M. E., Lantz, C. N., Lapin, J. S., Lawson, T. O., Lee, I. Y., Lee, S. M., Lee-Soety, J. Y., Lehmann, E. M., London, S. C., Lopez, A. J., Lynch, K. C., Mageeney, C. M., Martynyuk, T., Mathew, K. J., Mavrich, T. N., McDaniel, C. M., McDonald, H., McManus, C. J., Medrano, J. E., Mele, F. E., Menninger, J. E., Miller, S. N., Minick, J. E., Nabua, C. T., Napoli, C. K., Nkangabwa, M., Oates, E. A., Ott, C. T., Pellerino, S. K., Pinamont, W. J., Pirnie, R. T., Pizzorno, M. C., Plautz, E. J., Pope, W. H., Pruett, K. M., Rickstrew, G., Rimple, P. A., Rinehart, C. A., Robinson, K. M., Rose, V. A., Russell, D. A., Schick, A. M., Schlossman, J., Schneider, V. M., Sells, C. A., Sieker, J. W., Silva, M. P., Silvi, M. M., Simon, S. E., Staples, A. K., Steed, I. L., Stowe, E. L., Stueven, N. A., Swartz, P. T., Sweet, E. A., Sweetman, A. T., Tender, C., Terry, K., Thomas, C., Thomas, D. S., Thompson, A. R., Vanderveen, L., Varma, R., Vaught, H. L., Vo, Q. D., Vonberg, Z. T., Ware, V. C., Warrad, Y. M., Wathen, K. E., Weinstein, J. L., Wyper, J. F., Yankauskas, J. R., Zhang, C., and Hatfull, G. F. Tales of diversity: Genomic and morphological characteristics of forty-six Arthrobacter phages. PLoS.One. 2017; 12(7):e0180517; PM: 28715480

ABSTRACT: The vast bacteriophage population harbors an immense reservoir of genetic information. Almost 2000 phage genomes have been sequenced from phages infecting hosts in the phylum Actinobacteria, and analysis of these genomes reveals substantial diversity, pervasive mosaicism, and novel mechanisms for phage replication and lysogeny. Here, we describe the isolation and genomic characterization of 46 phages from environmental samples at various geographic locations in the U.S. infecting a single Arthrobacter sp. strain. These phages include representatives of all three virion morphologies, and Jasmine is the first sequenced podovirus of an actinobacterial host. The phages also span considerable sequence diversity, and can be grouped into 10 clusters according to their nucleotide diversity, and two singletons each with no close relatives. However, the clusters/singletons appear to be genomically well separated from each other, and relatively few genes are shared between clusters. Genome size varies from among the smallest of siphoviral phages (15,319 bp) to over 70 kbp, and G+C contents range from 45-68%, compared to 63.4% for the host genome. Although temperate phages are common among other actinobacterial hosts, these Arthrobacter phages are primarily lytic, and only the singleton Galaxy is likely temperate.

Kolomeisky, A. B. How Viruses Enter Cells: A Story behind Bacteriophage T4. Biophys.J. 7-11-2017; 113(1):4-5; PM: 28700923

No Abstract Available.

Komisarova, E. V., Kislichkina, A. A., Krasilnikova, V. M., Bogun, A. G., Fursova, N. K., and Volozhantsev, N. V. Complete Nucleotide Sequence of Klebsiella pneumoniae Bacteriophage vB_KpnM_KpV477. Genome Announc. 9-14-2017; 5(37); PM: 28912306

ABSTRACT: The double-stranded DNA (dsDNA) bacteriophage vB_KpnM_KpV477, with a broad spectrum of lytic activity against Klebsiella pneumoniae, including strains of capsular serotypes K1, K2, and K57, was isolated from a clinical sample. The phage genome comprises 168,272 bp, with a G+C content of 39.3%, and it contains 275 putative coding sequences (CDSs) and 17 tRNAs.

Komor, A. C., Zhao, K. T., Packer, M. S., Gaudelli, N. M., Waterbury, A. L., Koblan, L. W., Kim, Y. B., Badran, A. H., and Liu, D. R. Improved base excision repair inhibition and bacteriophage Mu Gam protein yields C:G-to-T:A base editors with higher efficiency and product purity. Sci.Adv. 2017; 3(8):eaao4774; PM: 28875174

ABSTRACT: We recently developed base editing, the programmable conversion of target C:G base pairs to T:A without inducing double-stranded DNA breaks (DSBs) or requiring homology-directed repair using engineered fusions of Cas9 variants and cytidine deaminases. Over the past year, the third-generation base editor (BE3) and related technologies have been successfully used by many researchers in a wide range of organisms. The product distribution of base editing-the frequency with which the target C:G is converted to mixtures of undesired by-products, along with the desired T:A product-varies in a target site-dependent manner. We characterize determinants of base editing outcomes in human cells and establish that the formation of undesired products is dependent on uracil N-glycosylase (UNG) and is more likely to occur at target sites containing only a single C within the base editing activity window. We engineered CDA1-BE3 and AID-BE3, which use cytidine deaminase homologs that increase base editing efficiency for some sequences. On the basis of these observations, we engineered fourth-generation base editors (BE4 and SaBE4) that increase the efficiency of C:G to T:A base editing by approximately 50%, while halving the frequency of undesired by-products compared to BE3. Fusing BE3, BE4, SaBE3, or SaBE4 to Gam, a bacteriophage Mu protein that binds DSBs greatly reduces indel formation during base editing, in most cases to below 1.5%, and further improves product purity. BE4, SaBE4, BE4-Gam, and SaBE4-Gam represent the state of the art in C:G-to-T:A base editing, and we recommend their use in future efforts.

Koonin, E. V., Makarova, K. S., and Wolf, Y. I. Evolutionary Genomics of Defense Systems in Archaea and Bacteria. Annu.Rev.Microbiol. 9-8-2017; 71:233-261; PM: 28657885

ABSTRACT: Evolution of bacteria and archaea involves an incessant arms race against an enormous diversity of genetic parasites. Accordingly, a substantial fraction of the genes in most bacteria and archaea are dedicated to antiparasite defense. The functions of these defense systems follow several distinct strategies, including innate immunity; adaptive immunity; and dormancy induction, or programmed cell death.

Recent comparative genomic studies taking advantage of the expanding database of microbial genomes and metagenomes, combined with direct experiments, resulted in the discovery of several previously unknown defense systems, including innate immunity centered on Argonaute proteins, bacteriophage exclusion, and new types of CRISPR-Cas systems of adaptive immunity. Some general principles of function and evolution of defense systems are starting to crystallize, in particular, extensive gain and loss of defense genes during the evolution of prokaryotes; formation of genomic defense islands; evolutionary connections between mobile genetic elements and defense, whereby genes of mobile elements are repeatedly recruited for defense functions; the partially selfish and addictive behavior of the defense systems; and coupling between immunity and dormancy induction/programmed cell death.

Kopertekh, L. and Schiemann, J. Marker Removal in Transgenic Plants Using Cre Recombinase Delivered with Potato Virus X. Methods Mol.Biol. 2017; 1642:151-168; PM: 28815499

ABSTRACT: In this chapter we present an alternative method to develop marker-free transgenic plants. It makes use of the Cre/loxP recombination system from bacteriophage P1 and consists of two essential components. The first component is the transgenic plant containing a loxP-flanked marker gene. The second component is a cre transient expression vector based on potato virus X. The great benefit of this transient delivery method consists in the avoidance of stable integration of the cre recombinase gene into the plant genome. Upon infection of the loxP-target plant with PVX-Cre, the virus spreads systemically through the plant and causes the recombinase-mediated excision of the marker gene. Marker-free transgenic loci can be transmitted to the progeny by plant regeneration from PVX-Cre systemically infected leaves or self-pollination of virus-infected plants. The protocol covers generation of loxP-target transgenic plants, PVX-mediated delivery of Cre recombinase protein, phenotypic and molecular analysis of recombination events, and transmission of marker-free transgenic loci to the next generation. The transient expression system described in this chapter can be adapted for marker gene removal in other plant species that are amenable for virus infection.

Kosel, J., Gutierrez-Aguirre, I., Racki, N., Dreo, T., Ravnikar, M., and Dular, M. Efficient inactivation of MS-2 virus in water by hydrodynamic cavitation. Water Res. 7-31-2017; 124:465-471; PM: 28800517

ABSTRACT: The aim of this study was to accurately quantify the impact of hydrodynamic cavitation on the infectivity of bacteriophage MS2, a norovirus surrogate, and to develop a small scale reactor for testing the effect of hydrodynamic cavitation on human enteric viruses, which cannot be easily prepared in large quantities. For this purpose, 3 mL scale and 1 L scale reactors were constructed and tested. Both devices were efficient in generating hydrodynamic cavitation and in reducing the infectivity of MS2 virus. Furthermore, they reached more than 4 logs reductions of viral infectivity, thus confirming the scalability of hydrodynamic cavitation for this particular application. As for the mechanism of page inactivation, we suspect that cavitation generated OH-radicals formed an advanced oxidation process, which could have damaged the host's recognition receptors located on the surface of the bacteriophage. Additional damage could arise from the high shear forces inside the cavity. Moreover, the effectiveness of the cavitation was higher for suspensions containing low initial viral titers that are in similar concentration to the ones found in real water samples. According to this, cavitation

generators could prove to be a useful tool for treating virus-contaminated wastewaters in the future.

Kwon, J. H., Burnham, C. D., Reske, K. A., Liang, S. Y., Hink, T., Wallace, M. A., Shupe, A., Seiler, S., Cass, C., Fraser, V. J., and Dubberke, E. R. Assessment of Healthcare Worker Protocol Deviations and Self-Contamination During Personal Protective Equipment Donning and Doffing. Infect.Control Hosp.Epidemiol. 2017; 38(9):1077-1083; PM: 28606192

ABSTRACT: ***OBJECTIVE*** To evaluate healthcare worker (HCW) risk of self-contamination when donning and doffing personal protective equipment (PPE) using fluorescence and MS2 bacteriophage. ***DESIGN***: Prospective pilot study. ***SETTING***: Tertiary-care hospital. ***PARTICIPANTS***: A total of 36 HCWs were included in this study: 18 donned/doffed contact precaution (CP) PPE and 18 donned/doffed Ebola virus disease (EVD) PPE. ***INTERVENTIONS***: HCWs donned PPE according to standard protocols. Fluorescent liquid and MS2 bacteriophage were applied to HCWs. HCWs then doffed their PPE. After doffing, HCWs were scanned for fluorescence and swabbed for MS2. MS2 detection was performed using reverse transcriptase PCR. The donning and doffing processes were videotaped, and protocol deviations were recorded. ***RESULTS***: Overall, 27% of EVD PPE HCWs and 50% of CP PPE HCWs made >/=1 protocol deviation while donning, and 100% of EVD PPE HCWs and 67% of CP PPE HCWs made >/=1 protocol deviation while doffing (P=.02). The median number of doffing protocol deviations among EVD PPE HCWs was 4, versus 1 among CP PPE HCWs. Also, 15 EVD PPE protocol deviations were committed by doffing assistants and/or trained observers. Fluorescence was detected on 8 EVD PPE HCWs (44%) and 5 CP PPE HCWs (28%), most commonly on hands. MS2 was recovered from 2 EVD PPE HCWs (11%) and 3 CP PPE HCWs (17%). ***CONCLUSIONS***: Protocol deviations were common during both EVD and CP PPE doffing, and some deviations during EVD PPE doffing were committed by the HCW doffing assistant and/or the trained observer. Self-contamination was common. PPE donning/doffing are complex and deserve additional study. Infect Control Hosp Epidemiol 2017;38:1077-1083.

Laanto, E., Mantynen, S., De, Colibus L., Marjakangas, J., Gillum, A., Stuart, D. I., Ravantti, J. J., Huiskonen, J. T., and Sundberg, L. R. Virus found in a boreal lake links ssDNA and dsDNA viruses. Proc.Natl.Acad.Sci.U.S.A. 8-1-2017; 114(31):8378-8383; PM: 28716906

ABSTRACT: Viruses have impacted the biosphere in numerous ways since the dawn of life. However, the evolution, genetic, structural, and taxonomic diversity of viruses remain poorly understood, in part because sparse sampling of the virosphere has concentrated mostly on exploring the abundance and diversity of dsDNA viruses. Furthermore, viral genomes are highly diverse, and using only the current sequence-based methods for classifying viruses and studying their phylogeny is complicated. Here we describe a virus, FLiP (Flavobacterium-infecting, lipid-containing phage), with a circular ssDNA genome and an internal lipid membrane enclosed in the icosahedral capsid. The 9,174-nt-long genome showed limited sequence similarity to other known viruses. The genetic data imply that this virus might use replication mechanisms similar to those found in other ssDNA replicons. However, the structure of the viral major capsid protein, elucidated at near-atomic resolution using cryo-electron microscopy, is strikingly similar to that observed in dsDNA viruses of the PRD1-adenovirus lineage, characterized by a major capsid protein bearing two beta-barrels. The strong similarity between FLiP and another member of the structural lineage, bacteriophage PM2, extends to the capsid

organization (pseudo T = 21 dextro) despite the difference in the genetic material packaged and the lack of significant sequence similarity.

Lam, P. and Steinmetz, N. F. Plant viral and bacteriophage delivery of nucleic acid therapeutics. Wiley.Interdiscip.Rev.Nanomed.Nanobiotechnol. 7-18-2017; PM: 28719102

ABSTRACT: Nucleic acid therapeutics have emerged as a powerful method for treatment of many diseases. However, the challenge lies in safe and efficient delivery of nucleic acids to their target site, as they need to cross various extracellular and intracellular barriers. Mammalian viruses have initially been favored for delivery of nucleic acid therapeutics, but safety concerns regarding their immunogenicity and potential of integration have fueled the search for alternative delivery strategies. For example, chemistry and bioengineering have led to advances in the use of nonviral vectors composed of lipids and other polymers; nevertheless, the synthetic systems often do not match the efficiency achieved using the biological systems. More recently, researchers have turned toward the development of plant viruses and bacteriophages and virus-like particles as an alternative or complementary approach. These systems unite the properties of both the viral and nonviral systems and as such are a new exciting avenue toward nucleic acid delivery. This review highlights the benefits of plant viral and bacteriophage delivery of nucleic acids and provides a summary of the current progress in research in this field. For further resources related to this article, please visit the WIREs website.

Lang, A. S., Westbye, A. B., and Beatty, J. T. The Distribution, Evolution, and Roles of Gene Transfer Agents in Prokaryotic Genetic Exchange. Annu.Rev.Virol. 8-7-2017; PM: 28784044

ABSTRACT: Diverse prokaryotes produce gene transfer agents (GTAs), which are bacteriophage-like particles that exclusively package pieces of the producing cell's genome and transfer them to other cells. There are clear evolutionary connections between GTAs and phages, but GTAs have properties that lead us to suggest they are more than simply defective phages and instead provide a selective advantage for the producing organisms. The five types of currently known GTAs are genetically distinct, indicating multiple instances of convergent evolution. GTA production can be regulated by the producing organism and coordinated to coincide with development of the capability to receive DNA from GTAs. Recent discoveries of the genetic basis of GTA production in the bacterium Rhodobacter capsulatus and characterization of novel phages that possess homologs of this GTA's structural and regulatory genes have provided important new connections among these elements and highlight the tangled evolutionary relationships within the phageome. Expected final online publication date for the Annual Review of Virology Volume 4 is September 29, 2017. Please see http://www.annualreviews.org/page/journal/pubdates for revised estimates.

Laranjo, L. T., Gross, S. J., Zeiger, D. M., and Lovett, S. T. SSB recruitment of Exonuclease I aborts template-switching in Escherichia coli. DNA Repair (Amst). 2017; 57:12-16; PM: 28605670

ABSTRACT: Misalignment of a nascent strand and the use of an alternative template during DNA replication, a process termed "template-switching", can give rise to frequent mutations and genetic rearrangements. Mutational hotspots are frequently found associated with imperfect inverted repeats ("quasipalindromes" or "QPs") in many

organisms, including bacteriophage, bacteria, yeast and mammals. Evidence suggests that QPs mutate by a replication template-switch whereby one copy of the inverted repeat templates synthesis of the other. To study quasipalindrome-associated mutagenesis ("QPM") more systematically, we have engineered mutational reporters in the lacZ gene of Escherichia coli, that revert to Lac+ specifically by QPM. We and others have shown that QPM is more efficient during replication of the leading strand than it is on the lagging strand. We have previously shown that QPM is elevated and that the leading-strand bias is lost in mutants lacking the major 3' ssDNA exonucleases, ExoI and ExoVII. This suggests that one or both of these exonucleases more efficiently abort template-switches on the lagging strand. Here, we show that ExoI is primarily responsible for this bias and that its ability to be recruited by single-strand DNA binding protein plays a critical role in QPM avoidance and strand bias. In addition to these stand-alone exonucleases, loss of the 3' proofreading exonuclease activity of the replicative DNA polymerase III also greatly elevates QPM. This may be because template-switching is initiated by base misincorporation, leading to polymerase dissociation and subsequent nascent strand misalignment; alternatively or additionally, the proofreading exonuclease may scavenge displaced 3' DNA that would otherwise be free to misalign.

Latino, L., Caroff, M., and Pourcel, C. Fine structure analysis of lipopolysaccharides in bacteriophage-resistant Pseudomonas aeruginosa PAO1 mutants. Microbiology. 2017; 163(6):848-855; PM: 28682742

ABSTRACT: Pseudomonas aeruginosa lipopolysaccharides (LPS) serve as primary receptors for many bacteriophages and, consequently, their biosynthesis is frequently affected in phage-resistant mutants. We previously isolated phage-resistant PAO1 mutants using three different phages, and showed that they were affected in the synthesis of LPS. Here we have investigated in detail the effect of mutations in seven genes involved in different steps of the production of core and oligosaccharide chains. The band profile of purified LPS was analysed by PAGE, and we further characterized the O-chains and core structures by MALDI mass spectrometry (MS). Mild LPS extraction conditions and native LPS MS analyses helped unveil lipid A molecular species with three phosphate residues in the close vicinity of the already highly charged inner-core region. No other MS direct analysis has allowed this peculiarity to be demonstrated for native lipid A high-molecular-weight molecular species, in normal growth conditions and without involving separation techniques. The present results shed light on the possible interactions between the phages and the LPS structures in the early phase of infection.

Lee, H. K., Lee, Y., Kim, H., Lee, H. E., Chang, H., Nam, K. T., Jeong, D. H., and Chung, J. Screening of Pro-Asp Sequences Exposed on Bacteriophage M13 as an Ideal Anchor for Gold Nanocubes. ACS Synth.Biol. 9-15-2017; 6(9):1635-1641; PM: 28548828

ABSTRACT: Bacteriophages are thought to be ideal vehicles for linking antibodies to nanoparticles. Here, we define the sequence of peptides exposed as a fusion protein on M13 bacteriophages to yield optimal binding of gold nanocubes and efficient bacteriophage amplification. We generated five helper bacteriophage libraries using AE(X)2DP, AE(X)3DP, AE(X)4DP, AE(X)5DP, and AE(X)6DP as the exposed portion of pVIII, in which X was a randomized amino acid residue encoded by the nucleotide sequence NNK. Efficient phage amplification was achievable only in the AE(X)2DP, AE(X)3DP, and AE(X)4DP libraries. Through biopanning with gold nanocubes, we enriched the phage clones and selected the clone with the highest fold change after enrichment. This clone

displayed Pro-Asp on the surface of the bacteriophage and had amplification yields similar to those of the wild-type helper bacteriophage (VCSM13). The clone displayed even binding of gold nanocubes along its length and minimal aggregation after binding. We conclude that, for efficient amplification, the exposed pVIII amino acid length should be limited to six residues and Ala-Glu-Pro-Asp-Asp-Pro (AEPDDP) is the ideal fusion protein sequence for guaranteeing the optimal formation of a complex with gold nanocubes.

Lee, J. H., Warner, C. M., Jin, H. E., Barnes, E., Poda, A. R., Perkins, E. J., and Lee, S. W. Production of tunable nanomaterials using hierarchically assembled bacteriophages. Nat.Protoc. 2017; 12(9):1999-2013; PM: 28858289

ABSTRACT: Large-scale fabrication of precisely defined nanostructures with tunable functions is critical to the exploitation of nanoscience and nanotechnology for production of electronic devices, energy generators, biosensors, and bionanomedicines. Although self-assembly processes have been developed to exploit biological molecules for functional materials, the resulting nanostructures and functions are still very limited, and scalable synthesis is far from being realized. Recently, we have established a bacteriophage-based biomimetic process, called 'self-templating assembly'. We used bacteriophage as a nanofiber model system to exploit its liquid crystalline structure for the creation of diverse hierarchically organized structures. We have also demonstrated that genetic modification of functional peptides of bacteriophage results in structures that can be used as soft and hard tissue-regenerating materials, biosensors, and energy-generating materials. Here, we describe a comprehensive protocol to perform genetic engineering of phage, liter-scale amplification, purification, and self-templating assembly, and suggest approaches for characterizing hierarchical phage nanostructures using optical microscopy, atomic-force microscopy (AFM), and scanning electron microscopy (SEM). We also discuss sources of contamination, common mistakes during the fabrication process, and quality-control measures to ensure reproducible material production. The protocol takes approximately 8-10 d to complete.

Lekunberri, I., Villagrasa, M., Balcazar, J. L., and Borrego, C. M. Contribution of bacteriophage and plasmid DNA to the mobilization of antibiotic resistance genes in a river receiving treated wastewater discharges. Sci.Total Environ. 12-1-2017; 601-602:206-209; PM: 28551539

ABSTRACT: In this study, we quantified eleven antibiotic compounds and nine antibiotic resistance genes (ARGs) in water samples collected upstream and downstream of the discharge point from a municipal wastewater treatment plant (WWTP) into the Ter River. Antibiotics were analyzed by liquid chromatography coupled to mass spectrometry, whereas the concentration of ARGs in bacterial, phage and plasmid DNA fractions was determined by real-time PCR to explore their contribution to environmental antibiotic resistance. WWTP discharges resulted in higher concentrations of antibiotic residues as well as ARGs in water samples collected downstream the impact point. Specifically, genes conferring resistance to macrolides (ermB), fluoroquinolones (qnrS) and tetracyclines (tetW) showed significant differences ($p<0.05$) between upstream and downstream sites in the three DNA fractions (i.e. bacteria, plasmids and phages). Interestingly, genes conferring resistance to beta-lactams (blaTEM, blaNDM and blaKPC) and glycopeptides (vanA) only showed significant differences ($p<0.05$) between upstream and downstream sites in phage and plasmid DNA but not in the bacterial DNA fraction. Our results show for the first time the extent to which phages and plasmids

contribute to the mobilization of ARGs in an aquatic environment exposed to chronic antibiotic pollution via WWTP discharges. Accordingly, these mobile genetic elements should be included in further studies to get a global view of the spread of antibiotic resistance.

Leskinen, K., Tuomala, H., Wicklund, A., Horsma-Heikkinen, J., Kuusela, P., Skurnik, M., and Kiljunen, S. Characterization of vB_SauM-fRuSau02, a Twort-Like Bacteriophage Isolated from a Therapeutic Phage Cocktail. Viruses. 9-14-2017; 9(9); PM: 28906479

ABSTRACT: Staphylococcus aureus is a commensal and pathogenic bacterium that causes infections in humans and animals. It is a major cause of nosocomial infections worldwide. Due to increasing prevalence of multidrug resistance, alternative methods to eradicate the pathogen are necessary. In this respect, polyvalent staphylococcal myoviruses have been demonstrated to be excellent candidates for phage therapy. Here we present the characterization of the bacteriophage vB_SauM-fRuSau02 (fRuSau02) that was isolated from a commercial Staphylococcus bacteriophage cocktail produced by Microgen (Moscow, Russia). The genomic analysis revealed that fRuSau02 is very closely related to the phage MSA6, and possesses a large genome (148,464 bp), with typical modular organization and a low G+C (30.22%) content. It can therefore be classified as a new virus among the genus Twortlikevirus. The genome contains 236 predicted genes, 4 of which were interrupted by insertion sequences. Altogether, 78 different structural and virion-associated proteins were identified from purified phage particles by liquid chromatography-tandem mass spectrometry (LC-MS/MS). The host range of fRuSau02 was tested with 135 strains, including 51 and 54 Staphylococcus aureus isolates from humans and pigs, respectively, and 30 coagulase-negative Staphylococcus strains of human origin. All clinical S. aureus strains were at least moderately sensitive to the phage, while only 39% of the pig strains were infected. Also, some strains of Staphylococcus intermedius, Staphylococcus lugdunensis, Staphylococcus epidermidis, Staphylococcus haemolyticus, Staphylococcus saprophyticus and Staphylococcus pseudointer were sensitive. We conclude that fRuSau02, a phage therapy agent in Russia, can serve as an alternative to antibiotic therapy against S. aureus.

Leung, C. Y. J. and Weitz, J. S. Modeling the synergistic elimination of bacteria by phage and the innate immune system. J.Theor.Biol. 9-21-2017; 429:241-252; PM: 28668337

ABSTRACT: Phage therapy has been viewed as a potential treatment for bacterial infections for over a century. Yet, the year 2016 marks one of the first phase I/II human trials of a phage therapeutic - to treat burn wound patients in Europe. The slow progress in realizing clinical therapeutics is matched by a similar dearth in principled understanding of phage therapy. Theoretical models and in vitro experiments find that combining phage and bacteria often leads to coexistence of both phage and bacteria or phage elimination altogether. Both outcomes stand in contrast to the stated goals of phage therapy. A potential resolution to the gap between models, experiments, and therapeutic use of phage is the hypothesis that the combined effect of phage and host immune system can synergistically eliminate bacterial pathogens. Here, we propose a phage therapy model that considers the nonlinear dynamics arising from interactions between bacteria, phage and the host innate immune system. The model builds upon earlier efforts by incorporating a maximum capacity of the immune response and density-dependent immune evasion by bacteria. We analytically identify a synergistic

regime in this model in which phage and the innate immune response jointly contribute to the elimination of the target bacteria. Crucially, we find that in this synergistic regime, neither phage alone nor the innate immune system alone can eliminate the bacteria. We confirm these findings using numerical simulations in biologically plausible scenarios. We utilize our numerical simulations to explore the synergistic effect and its significance for guiding the use of phage therapy in clinically relevant applications.

Li, L., Shukla, S., Meilleur, F., Standaert, R. F., Pierce, J., Myles, D. A. A., and Cuneo, M. J. Neutron crystallographic studies of T4 lysozyme at cryogenic temperature. Protein Sci. 7-13-2017; PM: 28707382

ABSTRACT: Bacteriophage T4 lysozyme (T4L) has been used as a paradigm for seminal biophysical studies on protein structure, dynamics, and stability. Approximately 700 mutants of this protein and their respective complexes have been characterized by X-ray crystallography; however, despite the high resolution diffraction limits attained in several studies, no hydrogen atoms were reported being visualized in the electron density maps. To address this, a 2.2 A-resolution neutron data set was collected at 80 K from a crystal of perdeuterated T4L pseudo-wild type. We describe a near complete atomic structure of T4L, which includes the positions of 1737 hydrogen atoms determined by neutron crystallography. The cryogenic neutron model reveals explicit detail of the hydrogen bonding interactions in the protein, in addition to the protonation states of several important residues.

Lien, Y. W. and Lai, E. M. Type VI Secretion Effectors: Methodologies and Biology. Front Cell Infect.Microbiol. 2017; 7:254; PM: 28664151

ABSTRACT: The type VI secretion system (T6SS) is a nanomachine deployed by many Gram-negative bacteria as a weapon against eukaryotic hosts or prokaryotic competitors. It assembles into a bacteriophage tail-like structure that can transport effector proteins into the environment or target cells for competitive survival or pathogenesis. T6SS effectors have been identified by a variety of approaches, including knowledge/hypothesis-dependent and discovery-driven approaches. Here, we review and discuss the methods that have been used to identify T6SS effectors and the biological and biochemical functions of known effectors. On the basis of the nature and transport mechanisms of T6SS effectors, we further propose potential strategies that may be applicable to identify new T6SS effectors.

Lin, D. M., Koskella, B., and Lin, H. C. Phage therapy: An alternative to antibiotics in the age of multi-drug resistance. World J.Gastrointest.Pharmacol.Ther. 8-6-2017; 8(3):162-173; PM: 28828194

ABSTRACT: The practice of phage therapy, which uses bacterial viruses (phages) to treat bacterial infections, has been around for almost a century. The universal decline in the effectiveness of antibiotics has generated renewed interest in revisiting this practice. Conventionally, phage therapy relies on the use of naturally-occurring phages to infect and lyse bacteria at the site of infection. Biotechnological advances have further expanded the repertoire of potential phage therapeutics to include novel strategies using bioengineered phages and purified phage lytic proteins. Current research on the use of phages and their lytic proteins, specifically against multidrug-resistant bacterial infections, suggests phage therapy has the potential to be used as either an alternative

or a supplement to antibiotic treatments. Antibacterial therapies, whether phage- or antibiotic-based, each have relative advantages and disadvantages; accordingly, many considerations must be taken into account when designing novel therapeutic approaches for preventing and treating bacterial infections. Although much is still unknown about the interactions between phage, bacteria, and human host, the time to take phage therapy seriously seems to be rapidly approaching.

Liu, J., Yu, H., Huang, Y., Yu, Z., Fan, G., Jin, J., Liu, X., and Wang, G. Complete genome sequence of a novel bacteriophage infecting Bradyrhizobium diazoefficiens USDA110. Sci.China Life Sci. 7-27-2017; PM: 28755301

No Abstract Available.

Liu, W., Li, C., Qiu, Z. G., Jin, M., Wang, J. F., Yang, D., Xiao, Z. H., Yuan, Z. K., Li, J. W., Xu, Q. Y., and Shen, Z. Q. Development of a novel and highly efficient method of isolating bacteriophages from water. J.Microbiol.Methods. 2017; 139:143-149; PM: 28577899

ABSTRACT: Bacteriophages are widely used to the treatment of drug-resistant bacteria and the improvement of food safety through bacterial lysis. However, the limited investigations on bacteriophage restrict their further application. In this study, a novel and highly efficient method was developed for isolating bacteriophage from water based on the electropositive silica gel particles (ESPs) method. To optimize the ESPs method, we evaluated the eluent type, flow rate, pH, temperature, and inoculation concentration of bacteriophage using bacteriophage f2. The quantitative detection reported that the recovery of the ESPs method reached over 90%. The qualitative detection demonstrated that the ESPs method effectively isolated 70% of extremely low-concentration bacteriophage (100 PFU/100L). Based on the host bacteria composed of 33 standard strains and 10 isolated strains, the bacteriophages in 18 water samples collected from the three sites in the Tianjin Haihe River Basin were isolated by the ESPs and traditional methods. Results showed that the ESPs method was significantly superior to the traditional method. The ESPs method isolated 32 strains of bacteriophage, whereas the traditional method isolated 15 strains. The sample isolation efficiency and bacteriophage isolation efficiency of the ESPs method were 3.28 and 2.13 times higher than those of the traditional method. The developed ESPs method was characterized by high isolation efficiency, efficient handling of large water sample size and low requirement on water quality.

Maervoet, V. E. T. and Briers, Y. Synthetic biology of modular proteins. Bioengineered. 5-4-2017; 8(3):196-202; PM: 27645260

ABSTRACT: The evolution of natural modular proteins and domain swapping by protein engineers have shown the disruptive potential of non-homologous recombination to create proteins with novel functions or traits. Bacteriophage endolysins, cellulosomes and polyketide synthases are 3 examples of natural modular proteins with each module having a dedicated function. These modular architectures have been created by extensive duplication, shuffling of domains and insertion/deletion of new domains. Protein engineers mimic these natural processes in vitro to create chimeras with altered properties or novel functions by swapping modules between different parental genes. Most domain swapping efforts are realized with traditional restriction and ligation

techniques, which become particularly restrictive when either a large number of variants, or variants of proteins with multiple domains have to be constructed. Recent advances in homology-independent shuffling techniques increasingly address this need, but to realize the full potential of the synthetic biology of modular proteins a complete homology-independent method for both rational and random shuffling of modules from an unlimited number of parental genes is still needed.

Magare, B., Nair, A., and Khairnar, K. Isolation of bacteriophages from air using vacuum filtration technique: an improved and novel method. J.Appl.Microbiol. 8-2-2017; PM: 28766823

*ABSTRACT**: AIM***: Development of a simple and economical air sampler for isolation and enrichment of bacteriophages from air samples. ***METHODS AND RESULTS***: A vacuum filtration unit with simple modifications was used for isolation of bacteriophages from air sampled in the lavatory. Air was sampled at the rate of 62 l min-1 by bubbling into McIlvaine buffer for 30 min, which was used as bacteriophage solution for enrichment and plaque assessment against individual hosts. Alternatively, the aforementioned phage solution was enriched using a host consortium before plaque assessment. Phages were isolated in the range of 1-12 PFU per ml by the first method, whereas enrichment with host consortium gave phages around 10- to 1000-folds higher in number. Combining with established enrichment method, an improvement of about 10 times in phage isolation efficiency was attained. ***CONCLUSIONS***: The method is very useful for studying the natural bacteriophages of air, requiring only a basic microbiological laboratory setup making it simple and economical. ***SIGNIFICANCE AND IMPACT OF THE STUDY***: This study brings out a simple, economical air sampler for assessing air bacteriophages that can be employed by any microbial laboratory. Although various methods are available for studying bacteriophages in water and soil, very limited are available for air. To the best of our knowledge, the method developed in this study is unique in its design and concept for studying bacteriophages in air. The sampler is sterilizable by autoclaving and maintains a healthy rate of airflow provided by conventional vacuum pumps. The use of a nonspecific 'trapping solution' allows for the qualitative and quantitative study of air bacteriophages.

Maghsoodi, A., Chatterjee, A., Andricioaei, I., and Perkins, N. C. Dynamic Model Exposes the Energetics and Dynamics of the Injection Machinery for Bacteriophage T4. Biophys.J. 7-11-2017; 113(1):195-205; PM: 28700918

ABSTRACT: Bacteriophage T4 infects the bacterial host (Escherichia coli) using an efficient genomic delivery machine that is driven by elastic energy stored in a contractile tail sheath. Although the atomic structure of T4 is largely known, the dynamics of its fascinating injection machinery is not understood. This article contributes, to our knowledge, the first predictions of the energetics and dynamics of the T4 injection machinery using a novel dynamic model. The model employs an atomistic (molecular dynamics) representation of a fraction of the sheath structure to generate a continuum model of the entire sheath that also couples to a model of the viral capsid and tail tube. The resulting model of the entire injection machine reveals estimates for the energetics, timescale, and pathway of the T4 injection process as well as the force available for cell rupture. It also reveals the large and highly nonlinear conformational changes of the sheath whose elastic energy drives the injection process.

Mahalakshmi, R., Maurya, S. R., Burdak, B., Surti, P., Patel, M. S., and Jain, V. Structural plasticity of T4 transcription co-activator gp33 revealed by a protease-resistant unfolded state. Biochem.Biophys.Res.Commun. 10-7-2017; 492(1):61-66; PM: 28807826

ABSTRACT: Gene 33 protein (gp33) is a transcriptional coactivator for late genes of the T4 bacteriophage. gp33 possesses a 5-helix bundle core, with unstructured N- and C-terminal regions that account for >50% of the protein sequence. It plays a unique role of interacting with host RNA polymerase, couples transcription with DNA replication, and plays the dual function as repressor and co-activator in phage transcription. Here, we identify protein structural plasticity as the molecular basis of the dual nature in gp33. We find that gp33 has the peculiar property of remaining protease insensitive in its urea-unfolded state. Using NMR studies with spectroscopic measurements, we propose that intra-protein interactions are replaced by protein-urea interactions in gp33. This process not only unfolds gp33 but also renders it protease-resistant. Our studies shed new light on the unique structural malleability of gp33 that might be important in its transition from a repressor to a late transcription co-activator.

Mahony, J., Cambillau, C., and van, Sinderen D. Host recognition by lactic acid bacterial phages. FEMS Microbiol.Rev. 8-1-2017; 41(Supp_1):S16-S26; PM: 28830088

ABSTRACT: Bacteriophage infection of lactic acid bacteria (LAB) is one of the most significant causes of inconsistencies in the manufacture of fermented foods, affecting production schedules and organoleptic properties of the final product. Consequently, LAB phages, and particularly those infecting Lactococcus lactis, have been the focus of intensive research efforts. During the past decade, multidisciplinary scientific approaches have uncovered molecular details on the exquisite process of how a lactococcal phage recognises and binds to its host. Such approaches have incorporated genomic/molecular analyses and their partnership with phage structural analysis and host cell wall biochemical studies are discussed in this review, which will also provide our views on future directions of this research field.

Malik, D. J., Sokolov, I. J., Vinner, G. K., Mancuso, F., Cinquerrui, S., Vladisavljevic, G. T., Clokie, M. R. J., Garton, N. J., Stapley, A. G. F., and Kirpichnikova, A. Formulation, stabilisation and encapsulation of bacteriophage for phage therapy. Adv.Colloid Interface Sci. 5-14-2017; PM: 28688779

ABSTRACT: Against a backdrop of global antibiotic resistance and increasing awareness of the importance of the human microbiota, there has been resurgent interest in the potential use of bacteriophages for therapeutic purposes, known as phage therapy. A number of phage therapy phase I and II clinical trials have concluded, and shown phages don't present significant adverse safety concerns. These clinical trials used simple phage suspensions without any formulation and phage stability was of secondary concern. Phages have a limited stability in solution, and undergo a significant drop in phage titre during processing and storage which is unacceptable if phages are to become regulated pharmaceuticals, where stable dosage and well defined pharmacokinetics and pharmacodynamics are de rigueur. Animal studies have shown that the efficacy of phage therapy outcomes depend on the phage concentration (i.e. the dose) delivered at the site of infection, and their ability to target and kill bacteria, arresting bacterial growth and clearing the infection. In addition, in vitro and animal studies have shown the importance of using phage cocktails rather than single phage preparations to achieve better therapy outcomes. The in vivo reduction of phage

concentration due to interactions with host antibodies or other clearance mechanisms may necessitate repeated dosing of phages, or sustained release approaches. Modelling of phage-bacterium population dynamics reinforces these points. Surprisingly little attention has been devoted to the effect of formulation on phage therapy outcomes, given the need for phage cocktails, where each phage within a cocktail may require significantly different formulation to retain a high enough infective dose. This review firstly looks at the clinical needs and challenges (informed through a review of key animal studies evaluating phage therapy) associated with treatment of acute and chronic infections and the drivers for phage encapsulation. An important driver for formulation and encapsulation is shelf life and storage of phage to ensure reproducible dosages. Other drivers include formulation of phage for encapsulation in micro- and nanoparticles for effective delivery, encapsulation in stimuli responsive systems for triggered controlled or sustained release at the targeted site of infection. Encapsulation of phage (e.g. in liposomes) may also be used to increase the circulation time of phage for treating systemic infections, for prophylactic treatment or to treat intracellular infections. We then proceed to document approaches used in the published literature on the formulation and stabilisation of phage for storage and encapsulation of bacteriophage in micro- and nanostructured materials using freeze drying (lyophilization), spray drying, in emulsions e.g. ointments, polymeric microparticles, nanoparticles and liposomes. As phage therapy moves forward towards Phase III clinical trials, the review concludes by looking at promising new approaches for micro- and nanoencapsulation of phages and how these may address gaps in the field.

Manor, M. and Qimron, U. Selection of Genetically Modified Bacteriophages Using the CRISPR-Cas System. Bio Protoc. 8-5-2017; 7(15); PM:28804739

ABSTRACT: We present a CRISPR-Cas based technique for deleting genes from the T7 bacteriophage genome. A DNA fragment encoding homologous arms to the target gene to be deleted is first cloned into a plasmid. The T7 phage is then propagated in Escherichia coli harboring this plasmid. During this propagation, some phage genomes undergo homologous recombination with the plasmid, thus deleting the targeted gene. To select for these genomes, the CRISPR-Cas system is used to cleave non-edited genomes, enabling isolation of the desired recombinant phages. This protocol allows seamless deletion of desired genes in a T7 phage, and can be expanded to other phages and other types of genetic manipulations as well.

Marakasova, E. S., Eisenhaber, B., Maurer-Stroh, S., Eisenhaber, F., and Baranova, A. Prenylation of viral proteins by enzymes of the host: Virus-driven rationale for therapy with statins and FT/GGT1 inhibitors. Bioessays. 9-8-2017; PM: 28885709

ABSTRACT: Intracellular bacteria were recently shown to employ eukaryotic prenylation system for modifying activity and ensuring proper intracellular localization of their own proteins. Following the same logic, the proteins of viruses may also serve as prenylation substrates. Using extensively validated high-confidence prenylation predictions by PrePS with a cut-off for experimentally confirmed farnesylation of hepatitis delta virus antigen, we compiled in silico evidence for several new prenylation candidates, including IRL9 (CMV) and few other proteins encoded by Herpesviridae, Nef (HIV-1), E1A (human adenovirus 1), NS5A (HCV), PB2 (influenza), HN (human parainfluenza virus 3), L83L (African swine fever), MC155R (molluscum contagiosum virus), other Poxviridae proteins, and some bacteriophages of human associated bacteria. If confirmed experimentally, these findings may aid in dissection of molecular functions of uncharacterized viral

proteins and provide a novel rationale for statin and FT/GGT1-based inhibition of viral infections. Prenylation of bacteriophage proteins may aid in moderation of microbial infections.

Mavrich, T. N. and Hatfull, G. F. Bacteriophage evolution differs by host, lifestyle and genome. Nat.Microbiol. 7-10-2017; 2:17112; PM: 28692019

ABSTRACT: Bacteriophages play key roles in microbial evolution1,2, marine nutrient cycling3 and human disease4. Phages are genetically diverse, and their genome architectures are characteristically mosaic, driven by horizontal gene transfer with other phages and host genomes5. As a consequence, phage evolution is complex and their genomes are composed of genes with distinct and varied evolutionary histories6,7. However, there are conflicting perspectives on the roles of mosaicism and the extent to which it generates a spectrum of genome diversity8 or genetically discrete populations9,10. Here, we show that bacteriophages evolve within two general evolutionary modes that differ in the extent of horizontal gene transfer by an order of magnitude. Temperate phages distribute into high and low gene flux modes, whereas lytic phages share only the lower gene flux mode. The evolutionary modes are also a function of the bacterial host and different proportions of temperate and lytic phages are distributed in either mode depending on the host phylum. Groups of genetically related phages fall into either the high or low gene flux modes, suggesting there are genetic as well as ecological drivers of horizontal gene transfer rates. Consequently, genome mosaicism varies depending on the host, lifestyle and genetic constitution of phages.

Meneghini, L. M., Tripathi, S., Woodworth, M. A., Majumdar, S., Poulos, T. L., and Weiss, G. A. Dissecting binding of a beta-barrel membrane protein by phage display. Mol.Biosyst. 7-25-2017; 13(8):1438-1447; PM: 28627567

ABSTRACT: Membrane proteins (MPs) constitute a third of all proteomes, and contribute to a myriad of cellular functions including intercellular communication, nutrient transport and energy generation. For example, TonB-dependent transporters (TBDTs) in the outer membrane of Gram-negative bacteria play an essential role transporting iron and other nutrients into the bacterial cell. The inherently hydrophobic surfaces of MPs complicates protein expression, purification, and characterization. Thus, dissecting the functional contributions of individual amino acids or structural features through mutagenesis can be a challenging ordeal. Here, we apply a new approach for the expedited protein characterization of the TBDT ShuA from Shigella dysenteriae, and elucidate the protein's initial steps during heme-uptake. ShuA variants were displayed on the surface of an M13 bacteriophage as fusions to the P8 coat protein. Each ShuA variant was analyzed for its ability to display on the bacteriophage surface, and functionally bind to hemoglobin. This technique streamlines isolation of stable MP variants for rapid characterization of binding to various ligands. Site-directed mutagenesis studies targeting each extracellular loop region of ShuA demonstrate no specific extracellular loop is required for hemoglobin binding. Instead two residues, His420 and His86 mediate this interaction. The results identify a loop susceptible to antibody binding, and also a small molecule motif capable of disrupting ShuA from S. dysenteriae. The approach is generalizable to the dissection of other phage-displayed TBDTs and MPs.

Michniewski, S., Redgwell, T., Scanlan, D. J., and Millard, A. D. Draft Genome Sequence of Bacteriophage vB_Eco_swan01. Genome Announc. 7-13-2017; 5(28); PM: 28705961

ABSTRACT: Bacteriophage vB_Eco_swan01 was isolated from an ornamental pool using Escherichia coli MG1655 as the host. Bacteriophage vB_Eco_swan01 has limited similarity with other known phages at the nucleotide level and likely represents a new bacteriophage species within the Tunavirinae.

Mills, S., Ross, R. P., and Hill, C. Bacteriocins and bacteriophage; a narrow-minded approach to food and gut microbiology. FEMS Microbiol.Rev. 8-1-2017; 41(Supp_1):S129-S153; PM: 28830091

ABSTRACT: Bacteriocins and bacteriophage (phage) are biological tools which exhibit targeted microbial killing, a phenomenon which until recently was seen as a major drawback for their use as antimicrobial agents. However, in an age when the deleterious consequences of broad-spectrum antibiotics on human health have become apparent, there is an urgent need to develop narrow-spectrum substitutes. Indeed, disruption of the microbial communities which exist on and in our bodies can generate immediate and long-term negative effects and this is particularly borne out in the gut microbiota community whose disruption has been linked to a number of disorders reaching as far as the brain. Moreover, the antibiotic resistance crisis has resulted in our inability to treat many bacterial infections and has triggered the search for damage-limiting alternatives. As bacteriocins and phage are natural entities they are relatively easy to isolate and characterise and are also ideal candidates for improving food safety and quality, forfeiting the need for largely unpopular chemical preservatives. This review highlights the efficacy of both antimicrobial agents in terms of gut health and food safety and explores the body of scientific evidence supporting their effectiveness in both environments.

Milrot, E., Shimoni, E., Dadosh, T., Rechav, K., Unger, T., Van Etten, J. L., and Minsky, A. Structural studies demonstrating a bacteriophage-like replication cycle of the eukaryote-infecting Paramecium bursaria chlorella virus-1. PLoS.Pathog. 2017; 13(8):e1006562; PM: 28850602

ABSTRACT: A fundamental stage in viral infection is the internalization of viral genomes in host cells. Although extensively studied, the mechanisms and factors responsible for the genome internalization process remain poorly understood. Here we report our observations, derived from diverse imaging methods on genome internalization of the large dsDNA Paramecium bursaria chlorella virus-1 (PBCV-1). Our studies reveal that early infection stages of this eukaryotic-infecting virus occurs by a bacteriophage-like pathway, whereby PBCV-1 generates a hole in the host cell wall and ejects its dsDNA genome in a linear, base-pair-by-base-pair process, through a membrane tunnel generated by the fusion of the virus internal membrane with the host membrane. Furthermore, our results imply that PBCV-1 DNA condensation that occurs shortly after infection probably plays a role in genome internalization, as hypothesized for the infection of some bacteriophages. The subsequent perforation of the host photosynthetic membranes presumably enables trafficking of viral genomes towards host nuclei. Previous studies established that at late infection stages PBCV-1 generates cytoplasmic organelles, termed viral factories, where viral assembly takes place, a feature characteristic of many large dsDNA viruses that infect eukaryotic organisms. PBCV-1 thus appears to combine a bacteriophage-like mechanism during early infection stages with a eukaryotic-like infection pathway in its late replication cycle.

Moon, J. S., Kim, W. G., Shin, D. M., Lee, S. Y., Kim, C., Lee, Y., Han, J., Kim, K., Yoo, S. Y., and Oh, J. W. Bioinspired M-13 bacteriophage-based photonic nose for differential cell recognition. Chem.Sci. 2-1-2017; 8(2):921-927; PM: 28572902

ABSTRACT: A bioinspired M-13 bacteriophage-based photonic nose was developed for differential cell recognition. The M-13 bacteriophage-based photonic nose exhibits characteristic color patterns when phage bundle nanostructures, which were genetically modified to selectively capture vapor phase molecules, are structurally deformed. We characterized the color patterns of the phage bundle nanostructure in response to cell proliferation via several biomarkers differentially produced by cells, including hydrazine, o-xylene, ethylbenzene, ethanol and toluene. A specific color enables the successful identification of different types of molecular and cellular species. Our sensing technique utilized the versatile M-13 bacteriophage as a building block for fabricating bioinspired photonic crystals, which enables ease of fabrication and tunable selectivity through genetic engineering. Our simple and versatile bioinspired photonic nose could have possible applications in sensors for human health and national security, food discrimination, environmental monitoring, and portable and wearable sensors.

Motwani, T., Lokareddy, R. K., Dunbar, C. A., Cortines, J. R., Jarrold, M. F., Cingolani, G., and Teschke, C. M. A viral scaffolding protein triggers portal ring oligomerization and incorporation during procapsid assembly. Sci.Adv. 2017; 3(7):e1700423; PM: 28782023

ABSTRACT: Most double-stranded DNA viruses package genetic material into empty precursor capsids (or procapsids) through a dodecameric portal protein complex that occupies 1 of the 12 vertices of the icosahedral lattice. Inhibiting incorporation of the portal complex prevents the formation of infectious virions, making this step an excellent target for antiviral drugs. The mechanism by which a sole portal assembly is selectively incorporated at the special vertex is unclear. We recently showed that, as part of the DNA packaging process for bacteriophage P22, the dodecameric procapsid portal changes conformation to a mature virion state. We report that preformed dodecameric rings of P22 portal protein, as opposed to portal monomers, incorporate into nascent procapsids, with preference for the procapsid portal conformation. Finally, a novel role for P22 scaffolding protein in triggering portal ring formation from portal monomers is elucidated and validated by incorporating de novo assembled portal rings into procapsids.

Nakaminami, H., Ito, T., Han, X., Ito, A., Matsuo, M., Uehara, Y., Baba, T., Hiramatsu, K., and Noguchi, N. First report of sasX-positive methicillin-resistant Staphylococcus aureus in Japan. FEMS Microbiol.Lett. 9-1-2017; 364(16); PM: 28873947

ABSTRACT: SasX is a known virulence factor of Staphylococcus aureus involved in colonisation and immune evasion of the bacterium. The sasX gene, which is located on the varphiSPbeta prophage, is frequently found in the sequence type (ST) 239 S. aureus lineage, which is the predominant healthcare-associated clone in Asian countries. In Japan, ST239 clones have rarely been identified, and sasX-positive strains have not been reported to date. Here, we report the first identification of 18 sasX-positive methicillin-resistant S. aureus (MRSA) strains in Japanese hospitals between 2009 and 2011. All sasX-positive isolates belonged to an ST239-staphylococcal cassette chromosome mec type III (ST239-III) lineage. However, we were unable to identify additional sasX-positive MRSA

strains from 2012 to 2016, indicating that the small epidemic of sasX-positive isolates observed in this study was temporary. The sequence surrounding sasX in the strain TOHH628 lacked 51 genes that encode phage packaging and structural proteins, and no bacteriophage was induced by mitomycin C. Additionally, in the TOHH628 strain, the region (64.6 kb) containing sasX showed high identity to the varphiSPbeta-like element (71.3 kb) of the Taiwanese MRSA strain Z172. The data strongly suggest that the present sasX-positive isolates found in Japanese hospitals were transmitted incidentally from other countries.

Naveca, F. G., Nascimento, V. A. D., Souza, V. C., Nunes, B. T. D., Rodrigues, D. S. G., and Vasconcelos, P. F. D. C. Multiplexed reverse transcription real-time polymerase chain reaction for simultaneous detection of Mayaro, Oropouche, and Oropouche-like viruses. Mem.Inst.Oswaldo Cruz. 2017; 112(7):510-513; PM: 28591313

ABSTRACT: We describe a sensitive method for simultaneous detection of Oropouche and Oropouche-like viruses carrying the Oropouche S segment, as well as the Mayaro virus, using a multiplexed one-step reverse transcription real-time polymerase chain reaction (RT-qPCR). A chimeric plasmid containing both Mayaro and Oropouche targets was designed and evaluated for the in vitro production of transcribed RNA, which could be easily used as a non-infectious external control. To track false-negative results due to PCR inhibition or equipment malfunction, the MS2 bacteriophage was also included in the multiplex assay as an internal positive control. The specificity of the multiplex assay was evaluated by Primer-Blast analysis against the entire GenBank database, and further against a panel of 17 RNA arboviruses. The results indicated an accurate and highly sensitive assay with amplification efficiency greater than 98% for both targets, and a limit of detection between two and 20 copies per reaction. We believe that the assay described here will provide a tool for Mayaro and Oropouche virus detection, especially in areas where differential diagnosis of Dengue, Zika and Chikungunya viruses should be performed.

Nguyen, V. S., Logger, L., Spinelli, S., Legrand, P., Huyen Pham, T. T., Nhung Trinh, T. T., Cherrak, Y., Zoued, A., Desmyter, A., Durand, E., Roussel, A., Kellenberger, C., Cascales, E., and Cambillau, C. Type VI secretion TssK baseplate protein exhibits structural similarity with phage receptor-binding proteins and evolved to bind the membrane complex. Nat.Microbiol. 6-26-2017; 2:17103; PM: 28650463

ABSTRACT: The type VI secretion system (T6SS) is a multiprotein machine widespread in Gram-negative bacteria that delivers toxins into both eukaryotic and prokaryotic cells. The mechanism of action of the T6SS is comparable to that of contractile myophages. The T6SS builds a tail-like structure made of an inner tube wrapped by a sheath, assembled under an extended conformation. Contraction of the sheath propels the inner tube towards the target cell. The T6SS tail is assembled on a platform-the baseplate-which is functionally similar to bacteriophage baseplates. In addition, the baseplate docks the tail to a trans-envelope membrane complex that orients the tail towards the target. Here, we report the crystal structure of TssK, a central component of the T6SS baseplate. We show that TssK is composed of three domains, and establish the contribution of each domain to the interaction with TssK partners. Importantly, this study reveals that the N-terminal domain of TssK is structurally homologous to the shoulder domain of phage receptor-binding proteins, and the C-terminal domain binds the membrane complex. We propose that TssK has conserved the domain of attachment to

the virion particle but has evolved the reception domain to use the T6SS membrane complex as receptor.

Nikkhahi, F., Soltan Dallal, M. M., Alimohammadi, M., Rahimi, Foroushani A., Rajabi, Z., Fardsanei, F., Imeni, S. M., and Torabi, Bonab P. Phage therapy: assessment of the efficacy of a bacteriophage isolated in the treatment of salmonellosis induced by Salmonella enteritidis in mice. Gastroenterol.Hepatol.Bed.Bench. 2017; 10(2):131-136; PM: 28702137

ABSTRACT: ***AIM***: This work aims to isolate and perform comparative studies of a phages active against a Salmonella enteritidis strain from Iran. Also, suitable phage candidates for therapy of mice will be selected. ***BACKGROUND***: Bacteriophage is of particular interest as a biocontrol agent in the prevention of food-borne illnesses. In recent years tend to use bacteriophages to control pathogenic bacteria has increased. A bacteriophage is considered to be a potent antibiotic alternative for treating bacterial infections. ***METHODS***: the specific phages against Salmonella Enteritidis was isolated and candidates for therapy of mice will be selected. Mouses divided into the six specific groups. Groups of mice were as follows: A: Bacteri (control) B: Bacteri+ bacteriophage (Simultaneous), C: Bacteri + bacteriophage Four days later, D: Bacteriophage + bacteri four days later E: Bacteri+ Ciprofloxacin (Simultaneous) F: Bacteri+ ciprofloxacin+ bacteriophage (Simultaneous). ***RESULTS***: In this study, a lytic bacteriophage is isolated and it shows that phage has a head size of 46 nm and without a tail, by using an electron microscope. Oral administration of a single dose of 2 x 109 PFU/mouse bacteriophage enable to protect mouse against salmonellosis and it causes treatment of salmonellosis in mice. ***CONCLUSION***: The use of this phage compared to ciprofloxacin shows that in addition of the treatment of mouse, it also prevents weight loss.

Nogueira, F., Karumidze, N., Kusradze, I., Goderdzishvili, M., Teixeira, P., and Gouveia, I. C. Immobilization of bacteriophage in wound-dressing nanostructure. Nanomedicine. 8-25-2017; PM: 28842374

ABSTRACT: Opportunistic bacteria that cause life-threatening infections are still a central problem associated with a healthcare setting. Bacteriophage capsid immobilization on nanostructured polymers maximizes its tail exposure and looks promising in applications toward skin-infections as alternative to antibiotics standardly used. The main goal of this work was to investigate the covalent immobilization of vB_Pae_Kakheti25 bacteriophage capsid on polycaprolactone (PCL) nanofibers (non-woven textile), as a potential effective antimicrobial, laundry resistant and non-toxic dressing for biomedical use. Surface analyses showed that the immobilization of vB_Pae_Kakheti25 bacteriophage capsid on PCL nanofibres oriented bacteriophage tails to interact with bacteria. Furthermore, antimicrobial assays showed a very effective 6 log bacterial reduction, which was equivalent to 99.9999%, after immediate and 2 hours of contact, even following 25 washing cycles (due to covalent bond). The activity of PCL-vB_Pae_Kakheti25 against P. aeruginosa was immediate and its reduction was complete.

Nonis, J., Premaratne, A., Billington, C., and Varsani, A. Genome Sequence of a Podovirus (AAPEc6) Isolated from Wastewater in New Zealand That Infects Escherichia coli O45:H10. Genome Announc. 8-3-2017; 5(31); PM: 28774967

ABSTRACT: Bacteriophages are ideal candidates for pathogen biocontrol to mitigate

outbreaks of prevalent foodborne pathogens, such as Escherichia coli We identified a bacteriophage (AAPEc6) from wastewater that infects E. coli O45:H10. The AAPEc6 genome sequence shares 93% identity (with 92% coverage) to enterobacterial phage K1E (Sp6likevirus) in the Autographivirinae subfamily (Podoviridae).

Nyambe, S., Burgess, C., Whyte, P., and Bolton, D. An investigation of vtx2 bacteriophage transduction to different Escherichia coli patho-groups in food matrices and nutrient broth. Food Microbiol. 2017; 68:1-6; PM: 28800816

ABSTRACT: This study investigated bacteriophage (phage) mediated transfer of the vtx2 gene from a donor Escherichia coli (C600phi3538(Deltavtx2::cat)) to enteropathogenic (EPEC), enterotoxigenic (ETEC), enteroaggregative (EAEC), enteroinvasive (EIEC) and diffusely adherent (DAEC) E. coli strains in LB broth, milk, ground beef and lettuce. Two bacterial concentrations for both the E. coli donor and recipient strains, 3 and 5 log10 CFU/ml (LB broth and milk)/g (beef) or/cm2 (lettuce), were used. When transductants were obtained, the location of insertion of the phage (insertion sites wrbA, yehA, sbcB, yecE and/or Z2577) in the E. coli chromosome was investigated by PCR. The vtx2 gene was readily transferred to EAEC O104:H4 (E99518) in all matrices and inserted into the chromosome at the sbcB locus. At higher cell concentrations, transductants were also obtained with ETEC E4683, ETEC E8057 (insertion site unknown) and DAEC O75:H- E66438 (insertion site unknown) in LB broth and milk. It was concluded that the vtx2 gene may be transferred by bacteriophage to different E. coli pathotypes in laboratory and food matrices, resulting in the spread of the vtx2 gene and the emergence of novel foodborne pathogens.

Olorunniji, F. J., McPherson, A. L., Rosser, S. J., Smith, M. C. M., Colloms, S. D., and Stark, W. M. Control of serine integrase recombination directionality by fusion with the directionality factor. Nucleic Acids Res. 8-21-2017; 45(14):8635-8645; PM: 28666339

ABSTRACT: Bacteriophage serine integrases are extensively used in biotechnology and synthetic biology for assembly and rearrangement of DNA sequences. Serine integrases promote recombination between two different DNA sites, attP and attB, to form recombinant attL and attR sites. The 'reverse' reaction requires another phage-encoded protein called the recombination directionality factor (RDF) in addition to integrase; RDF activates attL x attR recombination and inhibits attP x attB recombination. We show here that serine integrases can be fused to their cognate RDFs to create single proteins that catalyse efficient attL x attR recombination in vivo and in vitro, whereas attP x attB recombination efficiency is reduced. We provide evidence that activation of attL x attR recombination involves intra-subunit contacts between the integrase and RDF moieties of the fusion protein. Minor changes in the length and sequence of the integrase-RDF linker peptide did not affect fusion protein recombination activity. The efficiency and single-protein convenience of integrase-RDF fusion proteins make them potentially very advantageous for biotechnology/synthetic biology applications. Here, we demonstrate efficient gene cassette replacement in a synthetic metabolic pathway gene array as a proof of principle.

Olorunniji, F. J., Merrick, C., Rosser, S. J., Smith, M. C. M., Stark, W. M., and Colloms, S. D. Multipart DNA Assembly Using Site-Specific Recombinases from the Large Serine Integrase Family. Methods Mol.Biol. 2017; 1642:303-323; PM: 28815508

ABSTRACT: Assembling multiple DNA fragments into functional plasmids is an important and often rate-limiting step in engineering new functions in living systems. Bacteriophage integrases are enzymes that carry out efficient recombination reactions between short, defined DNA sequences known as att sites. These DNA splicing reactions can be used to assemble large numbers of DNA fragments into a functional circular plasmid in a method termed serine integrase recombinational assembly (SIRA). The resulting DNA assemblies can easily be modified by further recombination reactions catalyzed by the same integrase in the presence of its recombination directionality factor (RDF). Here we present a set of protocols for the overexpression and purification of bacteriophage varphiC31 and Bxb1 integrase and RDF proteins, their use in DNA assembly reactions, and subsequent modification of the resulting DNA assemblies.

Ostapchuk, P., Suomalainen, M., Zheng, Y., Boucke, K., Greber, U. F., and Hearing, P. The adenovirus major core protein VII is dispensable for virion assembly but is essential for lytic infection. PLoS.Pathog. 2017; 13(6):e1006455; PM: 28628648

ABSTRACT: The Adenovirus (Ad) genome within the capsid is tightly associated with a virus-encoded, histone-like core protein-protein VII. Two other Ad core proteins, V and X/mu, also are located within the virion and are loosely associated with viral DNA. Core protein VII remains associated with the Ad genome during the early phase of infection. It is not known if naked Ad DNA is packaged into the capsid, as with dsDNA bacteriophage and herpesviruses, followed by the encapsidation of viral core proteins, or if a unique packaging mechanism exists with Ad where a DNA-protein complex is simultaneously packaged into the virion. The latter model would require an entirely new molecular mechanism for packaging compared to known viral packaging motors. We characterized a virus with a conditional knockout of core protein VII. Remarkably, virus particles were assembled efficiently in the absence of protein VII. No changes in protein composition were evident with VII-virus particles, including the abundance of core protein V, but changes in the proteolytic processing of some capsid proteins were evident. Virus particles that lack protein VII enter the cell, but incoming virions did not escape efficiently from endosomes. This greatly diminished all subsequent aspects of the infectious cycle. These results reveal that the Ad major core protein VII is not required to condense viral DNA within the capsid, but rather plays an unexpected role during virus maturation and the early stages of infection. These results establish a new paradigm pertaining to the Ad assembly mechanism and reveal a new and important role of protein VII in early stages of infection.

Pallavali, R. R., Degati, V. L., Lomada, D., Reddy, M. C., and Durbaka, V. R. P. Isolation and in vitro evaluation of bacteriophages against MDR-bacterial isolates from septic wound infections. PLoS.One. 2017; 12(7):e0179245; PM: 28719657

ABSTRACT: Multi-drug resistance has become a major problem for the treatment of pathogenic bacterial infections. The use of bacteriophages is an attractive approach to overcome the problem of drug resistance in several pathogens that cause fatal diseases. Our study aimed to isolate multi drug resistant bacteria from patients with septic wounds and then isolate and apply bacteriophages in vitro as alternative therapeutic agents. Pus samples were aseptically collected from Rajiv Gandhi Institute of Medical Science (RIMS), Kadapa, A.P., and samples were analyzed by gram staining, evaluating morphological characteristics, and biochemical methods. MDR-bacterial strains were

collected using the Kirby-Bauer disk diffusion method against a variety of antibiotics. Bacteriophages were collected and tested in vitro for lytic activity against MDR-bacterial isolates. Analysis of the pus swab samples revealed that the most of the isolates detected had Pseudomonas aeruginosa as the predominant bacterium, followed by Staphylococcus aureus, Klebsiella pneumoniae and Escherichia coli. Our results suggested that gram-negative bacteria were more predominant than gram-positive bacteria in septic wounds; most of these isolates were resistant to ampicillin, amoxicillin, penicillin, vancomycin and tetracycline. All the gram-positive isolates (100%) were multi-drug resistant, whereas 86% of the gram-negative isolates had a drug resistant nature. Further bacteriophages isolated from sewage demonstrated perfect lytic activity against the multi-drug resistant bacteria causing septic wounds. In vitro analysis of the isolated bacteriophages demonstrated perfect lysis against the corresponding MDR-bacteria, and these isolated phages may be promising as a first choice for prophylaxis against wound sepsis, Moreover, phage therapy does not enhance multi-drug resistance in bacteria and could work simultaneously on a wide variety of MDR-bacteria when used in a bacteriophage cocktail. Hence, our results suggest that these bacteriophages could be potential therapeutic options for treating septic wounds caused by P. aeruginosa, S. aureus, K. pneumoniae and E. coli.

Pan, D., Nolan, J., Williams, K. H., Robbins, M. J., and Weber, K. A. Abundance and Distribution of Microbial Cells and Viruses in an Alluvial Aquifer. Front Microbiol. 2017; 8:1199; PM: 28744257

ABSTRACT: Viruses are the most abundant biological entity on Earth and their interactions with microbial communities are recognized to influence microbial ecology and impact biogeochemical cycling in various ecosystems. While the factors that control the distribution of viruses in surface aquatic environments are well-characterized, the abundance and distribution of continental subsurface viruses with respect to microbial abundance and biogeochemical parameters have not yet been established. In order to begin to understand the factors governing virus distribution in subsurface environments, we assessed microbial cell and virus abundance in groundwater concurrent with groundwater chemistry in a uranium impacted alluvial aquifer adjoining the Colorado River near Rifle, CO. Virus abundance ranged from 8.0 x 104 to 1.0 x 106 mL-1 and exceeded cell abundance in all samples (cell abundance ranged from 5.8 x 104 to 6.1 x 105 mL-1). The virus to microbial cell ratio ranged from 1.1 to 8.1 and averaged 3.0 +/- 1.6 with virus abundance most strongly correlated to cell abundance (Spearman's rho = 0.73, $p < 0.001$). Both viruses and cells were positively correlated to dissolved organic carbon (DOC) with cells having a slightly stronger correlation (Spearman's rho = 0.46, $p < 0.05$ and rho = 0.54, $p < 0.05$; respectively). Groundwater uranium was also strongly correlated with DOC and virus and cell abundance (Spearman's rho = 0.62, $p < 0.05$; rho = 0.46, $p < 0.05$; and rho = 0.50, $p < 0.05$; respectively). Together the data indicate that microbial cell and virus abundance are correlated to the geochemical conditions in the aquifer. As such local geochemical conditions likely control microbial host cell abundance which in turn controls viral abundance. Given the potential impacts of viral-mediated cell lysis such as liberation of labile organic matter from lysed cells and changes in microbial community structure, viral interactions with the microbiota should be considered in an effort to understand subsurface biogeochemical cycling and contaminant mobility.

Parajuli, P., Adamski, M., and Verma, N. K. Bacteriophages are the major drivers of Shigella flexneri serotype 1c genome plasticity: a complete genome analysis. BMC.Genomics. 9-12-2017; 18(1):722; PM: 28899344

*ABSTRACT**: BACKGROUND***: Shigella flexneri is the primary cause of bacillary dysentery in the developing countries. S. flexneri serotype 1c is a novel serotype, which is found to be endemic in many developing countries, but little is known about its genomic architecture and virulence signatures. We have sequenced for the first time, the complete genome of S. flexneri serotype 1c strain Y394, to provide insights into its diversity and evolution. ***RESULTS***: We generated a high-quality reference genome of S. flexneri serotype 1c using the hybrid methods of long-read single-molecule real-time (SMRT) sequencing technology and short-read MiSeq (Illumina) sequencing technology. The Y394 chromosome is 4.58 Mb in size and shares the basic genomic features with other S. flexneri complete genomes. However, it possesses unique and highly modified O-antigen structure comprising of three distinct O-antigen modifying gene clusters that potentially came from three different bacteriophages. It also possesses a large number of hypothetical unique genes compared to other S. flexneri genomes. ***CONCLUSIONS***: Despite a high level of structural and functional similarities of Y394 genome with other S. flexneri genomes, there are marked differences in the pathogenic islands. The diversity in the pathogenic islands suggests that these bacterial pathogens are well adapted to respond to the selection pressures during their evolution, which might contribute to the differences in their virulence potential.

Patterson, D., Schwarz, B., Avera, J., Western, B., Hicks, M., Krugler, P., Terra, M., Uchida, M., McCoy, K., and Douglas, T. Sortase-Mediated Ligation as a Modular Approach for the Covalent Attachment of Proteins to the Exterior of the Bacteriophage P22 Virus-like Particle. Bioconjug.Chem. 8-16-2017; 28(8):2114-2124; PM: 28612603

ABSTRACT: Virus-like particles are unique platforms well suited for the construction of nanomaterials with broad-range applications. The research presented here describes the development of a modular approach for the covalent attachment of protein domains to the exterior of the versatile bacteriophage P22 virus-like particle (VLP) via a sortase-mediated ligation strategy. The bacteriophage P22 coat protein was genetically engineered to incorporate an LPETG amino acid sequence on the C-terminus, providing the peptide recognition sequence utilized by the sortase enzyme to catalyze peptide bond formation between the LPETG-tagged protein and a protein containing a polyglycine sequence on the N-terminus. Here we evaluate attachment of green fluorescent protein (GFP) and the head domain of the influenza hemagglutinin (HA) protein by genetically producing polyglycine tagged proteins. Attachment of both proteins to the exterior of the P22 VLP was found to be highly efficient as judged by SDS-PAGE densitometry. These results enlarge the tool kit for modifying the P22 VLP system and provide new insights for other VLPs that have an externally displayed C-terminus that can use the described strategy for the modular modification of their external surface for various applications.

Peabody, J., Muttil, P., Chackerian, B., and Tumban, E. Characterization of a spray-dried candidate HPV L2-VLP vaccine stored for multiple years at room temperature. Papillomavirus.Res. 2017; 3:116-120; PM: 28720444

ABSTRACT: HPV infections are associated with human cancers. Although three

prophylactic vaccines have been approved to protect against HPV infections, the vaccines require cold-chain storage and may not be suitable for third world countries with less developed refrigeration facilities. We previously developed a bacteriophage L2 virus-like particle (VLP)-based candidate vaccine, which elicited broadly protective antibodies against diverse HPV types. Spray-drying of MS2-16L2 VLPs into a dry powder enhanced the stability of these VLPs. Building on these studies, we assessed the long-term stability and immunogenicity of the spray-dried VLPs. Mice immunized with a single dose of spray-dried MS2-16L2 VLPs, which had been stored for 14 months at room temperature (RT), were partially protected from challenge with a high dose of HPV16, one year after immunization. However, immunization with two doses of MS2-16L2 VLPs stored at RT for 34 months elicited high titer anti-HPV antibodies. More importantly, this group of mice showed significant protection from HPV16, 4 months after immunization. These results suggest that spray-dried MS2-16L2 VLPs retain their effectiveness after long-term storage at RT, and may be suitable in third world countries with less developed refrigeration facilities.

Peng, S. Y., You, R. I., Lai, M. J., Lin, N. T., Chen, L. K., and Chang, K. C. Highly potent antimicrobial modified peptides derived from the Acinetobacter baumannii phage endolysin LysAB2. Sci.Rep. 9-13-2017; 7(1):11477; PM: 28904355

ABSTRACT: The increase in the prevalence of multidrug-resistant Acinetobacter baumannii (MDRAB) strains is a serious public health concern. Antimicrobial peptides (AMPs) are a possible solution to this problem. In this study, we examined whether AMPs could be derived from phage endolysins. We synthesized four AMPs based on an amphipathic helical region in the C-terminus of endolysin LysAB2 encoded by the A. baumannii phage PhiAB2. These peptides showed potent antibacterial activity against A. baumannii (minimum inhibitory concentration, 4-64 muM), including some MDR and colistin-resistant A. baumannii. Of the four peptides, LysAB2 P3, with modifications that increased its net positive charge and decreased its hydrophobicity, showed high antibacterial activity against A. baumannii but little haemolytic and no cytotoxic activity against normal eukaryotic cells. The results of electron microscopy experiments and a fluorescein isothiocyanate staining assay indicated that this peptide killed A. baumannii through membrane permeabilization. Moreover, in a mouse intraperitoneal infection model, at 4 h after the bacterial injection, LysAB2 P3 decreased the bacterial load by 13-fold in ascites and 27-fold in blood. Additionally, LysAB2 P3 rescued sixty percent of mice heavily infected with A. baumannii from lethal bacteremia. Our results confirmed that bacteriophage endolysins are a promising resource for developing effective AMPs.

Philippe, C., Jaomanjaka, F., Claisse, O., Laforgue, R., Maupeu, J., Petrel, M., and Le, Marrec C. A survey of oenophages during wine making reveals a novel group with unusual genomic characteristics. Int.J.Food Microbiol. 9-18-2017; 257:138-147; PM: 28651079

ABSTRACT: Oenophages have so far been mostly isolated from red wines under malolactic fermentation (MLF), and correspond to temperate or ex-temperate phages of Oenococcus oeni. Their genomes are clustered into 4 integrase gene sequence groups, which are also related to the chromosomal integration site. Our aims were to survey the occurrence of oenophages in a broader and more diverse collection of samples than those previously explored. Active phages were isolated from 33 out of 166 samples, which mostly originated from must and MLF. Seventy one phage lysates were produced and 30% were assigned to a novel group with unusual genomic

characteristics, called unk. All unk members produced similar RAPD and DNA restriction patterns, were negative by PCR for the signature sequences previously identified in the integrase and endolysin genes of oenophages, and lacked any BamHI restriction site in their genome. The data support that development of additional and novel signature genes for assessing oenophage diversity is now required.

Pomerantsev, A. P., McCall, R. M., Chahoud, M., Hepler, N. K., Fattah, R., and Leppla, S. H. Genome engineering in Bacillus anthracis using tyrosine site-specific recombinases. PLoS.One. 2017; 12(8):e0183346; PM: 28829806

ABSTRACT: Tyrosine site-specific recombinases (T-SSR) are polynucleotidyltransferases that catalyze cutting and joining reactions between short specific DNA sequences. We developed three systems for performing genetic modifications in Bacillus anthracis that use T-SSR and their cognate target sequences, namely Escherichia coli bacteriophage P1 Cre-loxP, Saccharomyces cerevisiae Flp-FRT, and a newly discovered IntXO-PSL system from B. anthracis plasmid pXO1. All three tyrosine recombinase systems were used for creation of a B. anthracis sporulation-deficient, plasmid-free strain deleted for ten proteases which had been identified by proteomic analysis as being present in the B. anthracis secretome. This strain was used successfully for production of various recombinant proteins, including several that are candidates for inclusion in improved anthrax vaccines. These genetic tools developed for DNA manipulation in B. anthracis were also used for construction of strains having chromosomal insertions of 1, 2, or 3 adjacent atxA genes. AtxA is a B. anthracis global transcriptional regulator required for the response of B. anthracis virulence factor genes to bicarbonate. We found a positive correlation between the atxA copy number and the expression level of the pagA gene encoding B. anthracis protective antigen, when strains were grown in a carbon dioxide atmosphere. These results demonstrate that the three T-SSR systems described here provide effective tools for B. anthracis genome editing. These T-SSR systems may also be applicable to other prokaryotes and to eukaryotes.

Pope, W. H., Mavrich, T. N., Garlena, R. A., Guerrero-Bustamante, C. A., Jacobs-Sera, D., Montgomery, M. T., Russell, D. A., Warner, M. H., and Hatfull, G. F. Bacteriophages of Gordonia spp. Display a Spectrum of Diversity and Genetic Relationships. MBio. 8-15-2017; 8(4); PM: 28811342

ABSTRACT: The global bacteriophage population is large, dynamic, old, and highly diverse genetically. Many phages are tailed and contain double-stranded DNA, but these remain poorly characterized genomically. A collection of over 1,000 phages infecting Mycobacterium smegmatis reveals the diversity of phages of a common bacterial host, but their relationships to phages of phylogenetically proximal hosts are not known. Comparative sequence analysis of 79 phages isolated on Gordonia shows these also to be diverse and that the phages can be grouped into 14 clusters of related genomes, with an additional 14 phages that are "singletons" with no closely related genomes. One group of six phages is closely related to Cluster A mycobacteriophages, but the other Gordonia phages are distant relatives and share only 10% of their genes with the mycobacteriophages. The Gordonia phage genomes vary in genome length (17.1 to 103.4 kb), percentage of GC content (47 to 68.8%), and genome architecture and contain a variety of features not seen in other phage genomes. Like the mycobacteriophages, the highly mosaic Gordonia phages demonstrate a spectrum of genetic relationships. We show this is a general property of bacteriophages and suggest

that any barriers to genetic exchange are soft and readily violable.IMPORTANCE Despite the numerical dominance of bacteriophages in the biosphere, there is a dearth of complete genomic sequences. Current genomic information reveals that phages are highly diverse genomically and have mosaic architectures formed by extensive horizontal genetic exchange. Comparative analysis of 79 phages of Gordonia shows them to not only be highly diverse, but to present a spectrum of relatedness. Most are distantly related to phages of the phylogenetically proximal host Mycobacterium smegmatis, although one group of Gordonia phages is more closely related to mycobacteriophages than to the other Gordonia phages. Phage genome sequence space remains largely unexplored, but further isolation and genomic comparison of phages targeted at related groups of hosts promise to reveal pathways of bacteriophage evolution.

Popova, A. V., Lavysh, D. G., Klimuk, E. I., Edelstein, M. V., Bogun, A. G., Shneider, M. M., Goncharov, A. E., Leonov, S. V., and Severinov, K. V. Novel Fri1-like Viruses Infecting Acinetobacter baumannii-vB_AbaP_AS11 and vB_AbaP_AS12-Characterization, Comparative Genomic Analysis, and Host-Recognition Strategy. Viruses. 7-17-2017; 9(7); PM: 28714913

ABSTRACT: Acinetobacter baumannii is a gram-negative, non-fermenting aerobic bacterium which is often associated with hospital-acquired infections and known for its ability to develop resistance to antibiotics, form biofilms, and survive for long periods in hospital environments. In this study, we present two novel viruses, vB_AbaP_AS11 and vB_AbaP_AS12, specifically infecting and lysing distinct multidrug-resistant clinical A. baumannii strains with K19 and K27 capsular polysaccharide structures, respectively. Both phages demonstrate rapid adsorption, short latent periods, and high burst sizes in one-step growth experiments. The AS11 and AS12 linear double-stranded DNA genomes of 41,642 base pairs (bp) and 41,402 bp share 86.3% nucleotide sequence identity with the most variable regions falling in host receptor-recognition genes. These genes encode tail spikes possessing depolymerizing activities towards corresponding capsular polysaccharides which are the primary bacterial receptors. We described AS11 and AS12 genome organization and discuss the possible regulation of transcription. The overall genomic architecture and gene homology analyses showed that the phages are new representatives of the recently designated Fri1virus genus of the Autographivirinae subfamily within the Podoviridae family.

Poudel, L., Twarock, R., Steinmetz, N. F., Podgornik, R., and Ching, W. Y. Impact of Hydrogen Bonding in the Binding Site between Capsid Protein and MS2 Bacteriophage ssRNA. J.Phys.Chem.B. 7-6-2017; 121(26):6321-6330; PM: 28581757

ABSTRACT: MS2 presents a well-studied example of a single-stranded RNA virus for which the genomic RNA plays a pivotal role in the virus assembly process based on the packaging signal-mediated mechanism. Packaging signals (PSs) are multiple dispersed RNA sequence/structure motifs varying around a central recognition motif that interact in a specific way with the capsid protein in the assembly process. Although the discovery and identification of these PSs was based on bioinformatics and geometric approaches, in tandem with sophisticated experimental protocols, we approach this problem using large-scale ab initio computation centered on critical aspects of the consensus protein-RNA interactions recognition motif. DFT calculations are carried out on two nucleoprotein complexes: wild-type and mutated (PDB IDs: 1ZDH and 5MSF). The calculated partial charge distribution of residues and the strength of hydrogen bonding (HB) between them

enabled us to locate the exact binding sites with the strongest HBs, identified to be LYS43-A-4, ARG49-C-13, TYR85-C-5, and LYS61-C-5, due to the change in the sequence of the mutated RNA.

Pyenson, N. C., Gayvert, K., Varble, A., Elemento, O., and Marraffini, L. A. Broad Targeting Specificity during Bacterial Type III CRISPR-Cas Immunity Constrains Viral Escape. Cell Host.Microbe. 9-13-2017; 22(3):343-353; PM: 28826839

ABSTRACT: CRISPR loci are a cluster of repeats separated by short "spacer" sequences derived from prokaryotic viruses and plasmids that determine the targets of the host's CRISPR-Cas immune response against its invaders. For type I and II CRISPR-Cas systems, single-nucleotide mutations in the seed or protospacer adjacent motif (PAM) of the target sequence cause immune failure and allow viral escape. This is overcome by the acquisition of multiple spacers that target the same invader. Here we show that targeting by the Staphylococcus epidermidis type III-A CRISPR-Cas system does not require PAM or seed sequences, and thus prevents viral escape via single-nucleotide substitutions. Instead, viral escapers can only arise through complete target deletion. Our work shows that, as opposed to type I and II systems, the relaxed specificity of type III CRISPR-Cas targeting provides robust immune responses that can lead to viral extinction with a single spacer targeting an essential phage sequence.

Pyra, A., Brzozowska, E., Pawlik, K., Gamian, A., Dauter, M., and Dauter, Z. Tail tubular protein A: a dual-function tail protein of Klebsiella pneumoniae bacteriophage KP32. Sci.Rep. 5-22-2017; 7(1):2223; PM: 28533535

ABSTRACT: Tail tubular protein A (TTPA) is a structural tail protein of Klebsiella pneumoniae bacteriophage KP32, and is responsible for adhering the bacteriophage to host cells. For the first time, we found that TTPA also exhibits lytic activity towards capsular exopolysaccharide (EPS) of the multiresistant clinical strain of Klebsiella pneumoniae, PCM2713, and thus should be regarded as a dual-function macromolecule that exhibits both structural and enzymatic actions. Here, we present our crystallographic and enzymatic studies of TTPA. TTPA was crystallized and X-ray diffraction data were collected to a resolution of 1.9 A. In the crystal, TTPA molecules were found to adopt a tetrameric structure with alpha-helical domains on one side and beta-strands and loops on the other. The novel crystal structure of TTPA resembles those of the bacteriophage T7 tail protein gp11 and gp4 of bacteriophage P22, but TTPA contains an additional antiparallel beta-sheet carrying a lectin-like domain that could be responsible for EPS binding. The enzymatic activity of TTPA may reflect the presence of a peptidoglycan hydrolase domain in the alpha-helical region (amino acid residues 126 to 173). These novel results provide new insights into the enzymatic mechanism through which TTPA acts on polysaccharides.

Qian, J., Bu, Z., Lang, X., Yan, G., Yang, Y., Wang, X., and Wang, X. A safe and molecular-tagged Brucella canis ghosts confers protection against virulent challenge in mice. Vet.Microbiol. 2017; 204:121-128; PM: 28532790

ABSTRACT: Canine brucellosis, caused by Brucella canis, is a persistent infectious reproductive disease in dogs. The absence of effective treatment to the intracellular

pathogen and the irreversible consequence of infection makes the need of a specific vaccine urgent. Bacterial ghosts (BGs) are the empty envelopes of bacteria with no genome content inside, which emerge as a proper vaccine candidate due to its intact outer antigen. It is generally derived from a genetically engineered strain, through the expression of Bacteriophage phiX174 lysis E gene upon induction. In this study, we combined the homologous recombination (HR) and bacterial ghost technologies, generating a genetically stable B. canis ghost strain which bears no drug resistance gene. When the ghost strain grows to OD600 of 0.6, 100% inactivation can be achieved under 42 degrees C in 60h. The resultant BGs showed guaranteed safety and comparable immunogenicity to a live vaccine. The bacterial B0419 protein was depleted during HR process, which is subsequently proved to work as a molecular tag in distinguishing natural infection and BGs immunization through ELISA. Additionally, the BGs also conferred protection against B. canis RM6/66 and B. melitensis 16M. Therefore, the application of current BGs as a vaccine candidate and the corresponding serological diagnostic approach may provide better B. canis prevention strategy.

quino de, Carvalho N., Stachler, E. N., Cimabue, N., and Bibby, K. Evaluation of Phi6 Persistence and Suitability as an Enveloped Virus Surrogate. Environ.Sci.Technol. 8-1-2017; 51(15):8692-8700; PM: 28657725

ABSTRACT: Recent outbreaks involving enveloped viruses, such as Ebola virus, have raised questions regarding the persistence of enveloped viruses in the water environment. Efforts have been made to find enveloped virus surrogates due to challenges investigating viruses that require biosafety-level 3 or 4 handling. In this study, the enveloped bacteriophage Phi6 was evaluated as a surrogate for enveloped waterborne viruses. The persistence of Phi6 was tested in aqueous conditions chosen based on previously published viral persistence studies. Our results demonstrated that the predicted T90 (time for 90% inactivation) of Phi6 under the 12 evaluated conditions varied from 24 min to 117 days depending on temperature, biological activity, and aqueous media composition. Phi6 persistence was then compared with persistence values from other enveloped viruses reported in the literature. The apparent suitability of Phi6 as an enveloped virus surrogate was dependent on the temperature and composition of the media tested. Of evaluated viruses, 33%, including all conditions considered, had T90 values greater than the 95% confidence interval for Phi6. Ultimately, these results highlight the variability of enveloped virus persistence in the environment and the value of working with the virus of interest for environmental persistence studies.

Radford, D., Guild, B., Strange, P., Ahmed, R., Lim, L. T., and Balamurugan, S. Characterization of antimicrobial properties of Salmonella phage Felix O1 and Listeria phage A511 embedded in xanthan coatings on Poly(lactic acid) films. Food Microbiol. 2017; 66:117-128; PM: 28576360

ABSTRACT: Beyond simply providing a barrier between food and external contaminants, active packaging technologies aim to inhibit pathogen survival and growth within the packaged environment. Bacteriophages have a proven track record as targeted antimicrobials but have yet to be successfully integrated in active packaging without serious loss of activity. We have developed two bacteriophage based xanthan coatings on poly(lactic acid) (PLA) film which significantly inhibits Salmonella Typhimurium and Listeria monocytogenes growth in culture ($P < 0.01$), and significantly reduces survival and growth of diverse cocktails of Salmonella sp. and L. monocytogenes respectively on precooked sliced turkey breast over 30 days of anaerobic packaging at 4 or 10 degrees

C ($P < 0.05$). Specifically reductions of 0.832 log at 4 degrees C and 1.30 log at 10 degrees C for Salmonella sp., and 6.31 log at 4 degrees C and 1.52 log at 10 degrees C for L. monocytogenes were observed. The coating containing Listeria phage A511 also significantly inhibited growth of L. monocytogenes over 14 days in aerobic packaging (3.79 log at 4 degrees C, 2.17 log at 10 degrees C, $P < 0.05$). These coatings showed 99.99% phage release within 30 min for both phages. Similar approaches could be used to develop packaging inhibitory to other significant foodborne pathogens such as Campylobacter, and Escherichia coli, as well as spoilage bacteria.

Ramphul, C., Casareto, B. E., Dohra, H., Suzuki, T., Yoshimatsu, K., Yoshinaga, K., and Suzuki, Y. Genome analysis of three novel lytic Vibrio coralliilyticus phages isolated from seawater, Okinawa, Japan. Mar.Genomics. 7-6-2017; PM: 28689690

ABSTRACT: Three novel Vibrio phages were isolated from seawater in Okinawa. The Vibrio phage RYC infected Vibrio coralliilyticus SWA 07, while Vibrio phages CKB-S1 and CKB-S2 infected the coral pathogen V. coralliilyticus P1 (LMG 23696). The Vibrio phages CKB-S1 and CKB-S2 displayed head-tail structures whereas the Vibrio phage RYC showed a tailless non-enveloped capsid. All these Vibrio phages contained linear and double-stranded DNA. The whole genome sequencing revealed that Vibrio phage RYC has a larger genome size compared to Vibrio phages CKB-S1 and CKB-S2, and six tRNAs genes were found only in Vibrio phage RYC. Genome-wide comparison showed that Vibrio phage CKB-S1 was closely related, but was not identical, to Vibrio parahaemolyticus phages VP16T and VP16C. Meanwhile, the Vibrio phages RYC and CKB-S2 did not show high genome-wide similarity to any phages. These results suggest that the Vibrio phages CKB-S1, CKB-S2 and RYC are novel phages, which need further exploration, especially for their potential applications in phage therapy.

Rastogi, V., Yadav, P., Verma, A., and Pandit, J. K. Ex vivo and in vivo evaluation of microemulsion based transdermal delivery of E. coli specific T4 bacteriophage: A rationale approach to treat bacterial infection. Eur.J.Pharm.Sci. 9-30-2017; 107:168-182; PM: 28711712

ABSTRACT: This study is focused on the development and evaluation of transdermal delivery of E. coli-specific T4 bacteriophages both ex-vivo and in-vivo using microemulsion as delivery carrier in eradicating the infection caused by E. coli. Microemulsions were prepared by mixing selected oil, surfactants and aqueous phase containing bacteriophages. The formulations were subjected to physicochemical characterization, ex-vivo and in-vivo permeation, stability studies, histological and immunofluorescence examination. The colloidal system exhibits a uniform size distribution, of finite size (150-320nm). Transmission electron microscopy revealed the encapsulation of bacteriophage in the aqueous globule. Ex-vivo permeation across skin was successfully achieved as 6x106PFU/mL and 6.7x106PFU/mL of T4 permeated from ME 6% and 10%, respectively. ME 6% was found to be thermodynamically stable and in-vivo permeation resulted in 5.49x105PFU/mL of bacteriophages in the blood of the E. coli challenged rats, while 2.48x105PFU/mL was detected in germ free rats, at the end of the study. Infected rats that were treated with bacteriophage were survived while significant mortality was observed in others. Histological and IL-6 immunofluorescence examination of the tissues revealed the efficacy/safety of the therapy. The microemulsion-based transdermal delivery of bacteriophage could be a promising approach to treat the infections caused by antibiotic-resistant bacteria.

Reeve, P. J. and Fallowfield, H. J. The toxicity of cationic surfactant HDTMA-Br, desorbed from surfactant modified zeolite, towards faecal indicator and environmental microorganisms. J.Hazard.Mater. 10-5-2017; 339:208-215; PM: 28651198

ABSTRACT: Surfactant Modified Zeolite (SMZ) represents a versatile, cost-effective permeable reactive material, capable of treating multiple classes of contaminants. The potential for HDTMA-Br, a cationic surfactant commonly used to modify zeolite, to desorb from the zeolite surface has been identified as a potential issue for the ongoing use of SMZ in water remediation contexts. This paper investigates the toxicity of HDTMA-Br towards enteric virus surrogates, F-RNA bacteriophage MS2 and E. coli, Bacillus subtilis, and soil microflora. The concentration of surfactant desorbing from SMZ was quantified through a bioassay using E. coli. Results showed HDTMA-Br concentrations of >/=10-5M were toxic to MS2, >/=10-4M were toxic to E. coli and >/=10-6M were toxic to B. subtilis. No toxic relationship was established between HDTMA-Br and soil microflora. Desorption of >/=10-4M of HDTMA-Br was shown for the two SMZ samples under the mixing conditions used. Effects of this surfactant on total soil microflora were ambiguous since no toxic relationship could be established, however, HDTMA-Br, at concentrations desorbing from SMZ, were shown to impact the soil bacterium B. subtilis. Further research is required to determine the effect of this surfactant on microbial populations and species diversity in soils.

Rippa, M., Castagna, R., Pannico, M., Musto, P., Borriello, G., Paradiso, R., Galiero, G., Bolletti, Censi S., Zhou, J., Zyss, J., and Petti, L. Octupolar Metastructures for a Highly Sensitive, Rapid, and Reproducible Phage-Based Detection of Bacterial Pathogens by Surface-Enhanced Raman Scattering. ACS Sens. 7-28-2017; 2(7):947-954; PM: 28750539

ABSTRACT: The development of fast and ultrasensitive methods to detect bacterial pathogens at low concentrations is of high relevance for human and animal health care and diagnostics. In this context, surface-enhanced Raman scattering (SERS) offers the promise of a simplified, rapid, and high-sensitive detection of biomolecular interactions with several advantages over previous assay methodologies. In this work, we have conceived reproducible SERS nanosensors based on tailored multilayer octupolar nanostructures which can combine high enhancement factor and remarkable molecular selectivity. We show that coating novel multilayer octupolar metastructures with proper self-assembled monolayer (SAM) and immobilized phages can provide label-free analysis of pathogenic bacteria via SERS leading to a giant increase in SERS enhancement. The strong relative intensity changes of about 2100% at the maximum scattered SERS wavelength, induced by the Brucella bacterium captured, demonstrate the performance advantages of the bacteriophage sensing scheme. We performed measurements at the single-cell level thus allowing fast identification in less than an hour without any demanding sample preparation process. Our results based on designing well-controlled octupolar coupling platforms open up new opportunities toward the use of bacteriophages as recognition elements for the creation of SERS-based multifunctional biochips for rapid culture and label-free detection of bacteria.

Roach, D. R., Leung, C. Y., Henry, M., Morello, E., Singh, D., Di Santo, J. P., Weitz, J. S., and Debarbieux, L. Synergy between the Host Immune System and Bacteriophage Is Essential for Successful Phage Therapy against an Acute Respiratory Pathogen. Cell Host.Microbe. 7-12-2017; 22(1):38-47; PM: 28704651

ABSTRACT: The rise of multi-drug-resistant (MDR) bacteria has spurred renewed interest in the use of bacteriophages in therapy. However, mechanisms contributing to phage-mediated bacterial clearance in an animal host remain unclear. We investigated the effects of host immunity on the efficacy of phage therapy for acute pneumonia caused by MDR Pseudomonas aeruginosa in a mouse model. Comparing efficacies of phage-curative and prophylactic treatments in healthy immunocompetent, MyD88-deficient, lymphocyte-deficient, and neutrophil-depleted murine hosts revealed that neutrophil-phage synergy is essential for the resolution of pneumonia. Population modeling of in vivo results further showed that neutrophils are required to control both phage-sensitive and emergent phage-resistant variants to clear infection. This "immunophage synergy" contrasts with the paradigm that phage therapy success is largely due to bacterial permissiveness to phage killing. Lastly, therapeutic phages were not cleared by pulmonary immune effector cells and were immunologically well tolerated by lung tissues.

Sadekuzzaman, M., Yang, S., Mizan, M. F. R., and Ha, S. D. Reduction of Escherichia coli O157:H7 in Biofilms Using Bacteriophage BPECO 19. J.Food Sci. 2017; 82(6):1433-1442; PM: 28542913

ABSTRACT: Biofilm formation is a growing concern in the food industry. Escherichia coli O157:H7 is one of the most important foodborne pathogens that can persists in food and food-related environments and subsequently produce biofilms. The efficacy of bacteriophage BPECO 19 was evaluated against three E. coli O157:H7 strains in biofilms. Biofilms of the three E. coli O157:H7 strains were grown on abiotic (stainless steel, rubber, and minimum biofilm eradication concentration [MBECTM] device) and biotic (lettuce) surfaces at different temperatures. The effectiveness of bacteriophage BPECO 19 in reducing preformed biofilms on these surfaces was further evaluated by treating the surfaces with a phage suspension (108 PFU/mL) for 2 h. The results indicated that the phage treatment significantly reduced ($P < 0.05$) the number of adhered cells in all the surfaces. Following phage treatment, the viability of adhered cells was reduced by >/=3 log CFU/cm2 , 2.4 log CFU/cm2 , and 3.1 log CFU/peg in biofilms grown on stainless steel, rubber, and the MBECTM device, respectively. Likewise, the phage treatment reduced cell viability by >/=2 log CFU/cm2 in biofilms grown on lettuce. Overall, these results suggested that bacteriophages such as BPECO 19 could be effective in reducing the viability of biofilm-adhered cells.

Samoylova, T. I., Braden, T. D., Spencer, J. A., and Bartol, F. F. Immunocontraception: Filamentous Bacteriophage as a Platform for Vaccine Development. Curr.Med.Chem. 9-11-2017; PM: 28901276

ABSTRACT: Population control of domestic, wild and invasive species of animals is a global issue of importance to public health, animal welfare and the economy. Although many methods for regulation of animal reproduction are available, the need for effective, safe, and inexpensive contraceptives remains. Immunocontraceptives (contraceptive vaccines) are designed to stimulate the immune system in order to block critical events in the reproductive process and suppress fertility. Platforms used for vaccine development play a critical role in vaccine efficacy, safety, and practicality. One nontraditional platform used for development of contraceptive vaccines is based on filamentous bacteriophages (shortened phages). Filamentous phages comprise a

group of rod-shaped bacterial viruses. The core of the virion is a DNA molecule, which is surrounded by phage coat proteins. Phages can be engineered to display fusion (non-phage) peptides as a part of their coat proteins. Such modifications can be accomplished via genetic manipulations of phage DNA or by chemical conjugation of synthetic peptides to phage surface proteins. Phage fusions with antigenic determinants induce humoral as well as cell-mediated immune responses in animals, making them attractive vaccine carriers. Additional advantages of the phage platform include environmental stability, low cost, and safety of phage-based preparations for immunized animals and those administering the vaccines.

Sarhan, W. A. and Azzazy, H. M. Apitherapeutics and phage-loaded nanofibers as wound dressings with enhanced wound healing and antibacterial activity. Nanomedicine.(Lond). 2017; 12(17):2055-2067; PM: 28805554

*ABSTRACT**: AIM***: Develop green wound dressings which exhibit enhanced wound-healing ability and potent antibacterial effects. ***METHODS***: Honey, polyvinyl alcohol, chitosan nanofibers were electrospun and loaded with bee venom, propolis and/or bacteriophage against the multidrug-resistant Pseudomonas aeruginosa and examined for their antibacterial, wound-healing ability and cytotoxicity. ***RESULTS***: Among different formulations of nanofibers, honey, polyvinyl alcohol, chitosan-bee venom/bacteriophage exhibited the most potent antibacterial activity against all tested bacterial strains (Gram-positive and -negative strains) and achieved nearly complete killing of multidrug-resistant P. aeruginosa. In vivo testing revealed enhanced wound-healing results and cytotoxicity testing proved improved biocompatibility. ***CONCLUSION***: The developed biocompatible nanofibers represent competitive wound-healing dressings with potent antibacterial and wound-healing activity.

Saucedo-Mora, M. A., Castaneda-Tamez, P., Cazares, A., Perez-Velazquez, J., Hense, B. A., Cazares, D., Figueroa, W., Carballo, M., Guarneros, G., Perez-Eretza, B., Cruz, N., Nishiyama, Y., Maeda, T., Belmont-Diaz, J. A., Wood, T. K., and Garcia-Contreras, R. Selection of Functional Quorum Sensing Systems by Lysogenic Bacteriophages in Pseudomonas aeruginosa. Front Microbiol. 2017; 8:1669; PM: 28912771

ABSTRACT: Quorum sensing (QS) in Pseudomonas aeruginosa coordinates the expression of virulence factors, some of which are used as public goods. Since their production is a cooperative behavior, it is susceptible to social cheating in which non-cooperative QS deficient mutants use the resources without investing in their production. Nevertheless, functional QS systems are abundant; hence, mechanisms regulating the amount of cheating should exist. Evidence that demonstrates a tight relationship between QS and the susceptibility of bacteria against the attack of lytic phages is increasing; nevertheless, the relationship between temperate phages and QS has been much less explored. Therefore, in this work, we studied the effects of having a functional QS system on the susceptibility to temperate bacteriophages and how this affects the bacterial and phage dynamics. We find that both experimentally and using mathematical models, that the lysogenic bacteriophages D3112 and JBD30 select QS-proficient P. aeruginosa phenotypes as compared to the QS-deficient mutants during competition experiments with mixed strain populations in vitro and in vivo in Galleria mellonella, in spite of the fact that both phages replicate better in the wild-type background. We show that this phenomenon restricts social cheating, and we propose that temperate phages may constitute an important selective pressure toward the conservation of bacterial QS.

Schmidt, I., Riedel, T., Schober, I., Bunk, B., Sproer, C., Bierbrodt, A., Lehnherr, H., and Wittmann, J. Genome Sequence of Escherichia coli E28, a Multidrug-Resistant Strain Isolated from a Chicken Carcass, and Its Spontaneously Inducible Prophage. Genome Announc. 6-1-2017; 5(22); PM: 28572305

ABSTRACT: In this study, we sequenced the complete genome of the multidrug-resistant Escherichia coli strain E28, which was used as an indicator strain for phage therapy in vivo We used a combination of single-molecule real-time and Illumina sequencing technology to reveal the presence of a spontaneously inducible prophage.

Schooley, R. T., Biswas, B., Gill, J. J., Hernandez-Morales, A., Lancaster, J., Lessor, L., Barr, J. J., Reed, S. L., Rohwer, F., Benler, S., Segall, A. M., Taplitz, R., Smith, D. M., Kerr, K., Kumaraswamy, M., Nizet, V., Lin, L., McCauley, M. D., Strathdee, S. A., Benson, C. A., Pope, R. K., Leroux, B. M., Picel, A. C., Mateczun, A. J., Cilwa, K. E., Regeimbal, J. M., Estrella, L. A., Wolfe, D. M., Henry, M. S., Quinones, J., Salka, S., Bishop-Lilly, K. A., Young, R., and Hamilton, T. Development and use of personalized bacteriophage-based therapeutic cocktails to treat a patient with a disseminated resistant Acinetobacter baumannii infection. Antimicrob.Agents Chemother. 8-14-2017; PM: 28807909

ABSTRACT: Widespread antibiotic use in clinical medicine and the livestock industry has contributed to the global spread of multidrug-resistant (MDR) bacterial pathogens, including Acinetobacter baumannii We report on a method used to produce a personalized bacteriophage-based therapeutic treatment for a 68-year old diabetic patient with necrotizing pancreatitis complicated by a MDR A. baumannii infection. Despite multiple antibiotic courses and efforts at percutaneous drainage of a pancreatic pseudocyst, the patient deteriorated over a four-month period. In the absence of effective antibiotics, two laboratories identified nine different bacteriophages with lytic activity for an A. baumannii isolate from the patient. Administration of these bacteriophages intravenously and percutaneously into the abscess cavities was associated with reversal of the patient's downward clinical trajectory, clearance of the A. baumannii infection, and a return to health. The outcome of this case suggests that the methods described here for the production of bacteriophage therapeutics could be applied to similar cases and that more concerted efforts to investigate the use of therapeutic bacteriophages for MDR bacterial infections are warranted.

Scott, Brady T., Merrill, B. D., Hilton, J. A., Payne, A. M., Stephenson, M. B., and Hope, S. Bacteriophages as an Alternative to Conventional Antibiotic use for the Prevention or Treatment of Paenibacillus larvae in Honeybee Hives. J.Invertebr.Pathol. 9-13-2017; PM: 28917651

ABSTRACT: American Foulbrood (AFB) is an infectious disease caused by the bacteria, Paenibacillus larvae. P. larvae phages were isolated and tested to determine each phages' host range amongst 59 field isolate strains of P. larvae. Three phages were selected to create a phage cocktail for the treatment of AFB infections according to the combined phages' ability to lyse all tested strains of bacteria. Studies were performed to demonstrate the safety and efficacy of the phage cocktail treatment as a replacement for traditional antibiotics for the prevention of AFB and the treatment of active infections. Safety verification studies confirmed that the phage cocktail did not adversely affect the rate of bee death even when administered as an overdose. In a comparative study of healthy hives, traditional prophylactic antibiotic treatment experienced a 38+/-0.7%

decrease in overall hive health, which was statistically lower than hive health observed in control hives. Hives treated with phage cocktail decreased 19+/-0.8%, which was not statistically different than control hives, which decreased by 10+/-1.0%. In a study of beehives at-risk for a natural infection, 100+/-0.5% of phage-treated hives were protected from AFB infection, while 80+/-0.5% of untreated controls became infected. AFB infected hives began with an average Hitchcock score of 2.25 out of 4 and 100+/-0.5% of the hives recovered completely within two weeks of treatment with phage cocktail. While the n numbers for the latter two studies are small, the results for both the phage protection rate and the phage cure rate were statistically significant (alpha=0.05). These studies demonstrate the powerful potential of using a phage cocktail against AFB and establish phage therapy as a feasible treatment.

Seco, E. M. and Ayora, S. Bacillus subtilis DNA polymerases, PolC and DnaE, are required for both leading and lagging strand synthesis in SPP1 origin-dependent DNA replication. Nucleic Acids Res. 8-21-2017; 45(14):8302-8313; PM: 28575448

ABSTRACT: Firmicutes have two distinct replicative DNA polymerases, the PolC leading strand polymerase, and PolC and DnaE synthesizing the lagging strand. We have reconstituted in vitro Bacillus subtilis bacteriophage SPP1 theta-type DNA replication, which initiates unidirectionally at oriL. With this system we show that DnaE is not only restricted to lagging strand synthesis as previously suggested. DnaG primase and DnaE polymerase are required for initiation of DNA replication on both strands. DnaE and DnaG synthesize in concert a hybrid RNA/DNA 'initiation primer' on both leading and lagging strands at the SPP1 oriL region, as it does the eukaryotic Pol alpha complex. DnaE, as a RNA-primed DNA polymerase, extends this initial primer in a reaction modulated by DnaG and one single-strand binding protein (SSB, SsbA or G36P), and hands off the initiation primer to PolC, a DNA-primed DNA polymerase. Then, PolC, stimulated by DnaG and the SSBs, performs the bulk of DNA chain elongation at both leading and lagging strands. Overall, these modulations by the SSBs and DnaG may contribute to the mechanism of polymerase switch at Firmicutes replisomes.

Secor, P. R., Sass, G., Nazik, H., and Stevens, D. A. Effect of acute predation with bacteriophage on intermicrobial aggression by Pseudomonas aeruginosa. PLoS.One. 2017; 12(6):e0179659; PM: 28622385

ABSTRACT: In persons with structural lung disease, particularly those with cystic fibrosis (CF), chronic airway infections cause progressive loss of lung function. CF airways can be colonized by a variety of microorganisms; the most frequently encountered bacterial and fungal pathogens are Pseudomonas aeruginosa and Aspergillus fumigatus, respectively. Co-infection with P. aeruginosa and A. fumigatus often results in a more rapid loss of lung function, indicating that interactions between these pathogens affect infection pathogenesis. There has been renewed interest in the use of viruses (bacteriophage, mycoviruses) as alternatives to antibiotics to treat these infections. In previous work, we found that filamentous Pf bacteriophage produced by P. aeruginosa directly inhibited the metabolic activity of A. fumigatus by binding to and sequestering iron. In the current study, we further examined how filamentous Pf bacteriophage affected interactions between P. aeruginosa and A. fumigatus. Here, we report that the antifungal properties of supernatants collected from P. aeruginosa cultures infected with Pf bacteriophage were substantially less inhibitory towards A. fumigatus biofilms. In particular, we found that acute infection of P. aeruginosa by Pf bacteriophage inhibited

the production of the virulence factor pyoverdine. Our results raise the possibility that the reduced production of antimicrobials by P. aeruginosa infected by Pf bacteriophage may promote conditions in CF airways that allow co-infection with A. fumigatus to occur, exacerbating disease severity. Our results also highlight the importance of considering how the use of bacteriophage as therapeutic agents could affect the behavior and composition of polymicrobial communities colonizing sites of chronic infection.

Sergueev, K. V., Filippov, A. A., and Nikolich, M. P. Highly Sensitive Bacteriophage-Based Detection of Brucella abortus in Mixed Culture and Spiked Blood. Viruses. 6-10-2017; 9(6); PM: 28604602

ABSTRACT: For decades, bacteriophages (phages) have been used for Brucella species identification in the diagnosis and epidemiology of brucellosis. Traditional Brucella phage typing is a multi-day procedure including the isolation of a pure culture, a step that can take up to three weeks. In this study, we focused on the use of brucellaphages for sensitive detection of the pathogen in clinical and other complex samples, and developed an indirect method of Brucella detection using real-time quantitative PCR monitoring of brucellaphage DNA amplification via replication on live Brucella cells. This assay allowed the detection of single bacteria (down to 1 colony-forming unit per milliliter) within 72 h without DNA extraction and purification steps. The technique was equally efficient with Brucella abortus pure culture and with mixed cultures of B. abortus and alpha-proteobacterial near neighbors that can be misidentified as Brucella spp., Ochrobactrum anthropi and Afipia felis. The addition of a simple short sample preparation step enabled the indirect phage-based detection of B. abortus in spiked blood, with the same high sensitivity. This indirect phage-based detection assay enables the rapid and sensitive detection of live B. abortus in mixed cultures and in blood samples, and can potentially be applied for detection in other clinical samples and other complex sample types.

Serwer, P. and Wright, E. T. ATP-Driven Contraction of Phage T3 Capsids with DNA Incompletely Packaged In Vivo. Viruses. 5-19-2017; 9(5); PM: 28534826

ABSTRACT: Adenosine triphosphate (ATP) cleavage powers packaging of a double-stranded DNA (dsDNA) molecule in a pre-assembled capsid of phages that include T3. Several observations constitute a challenge to the conventional view that the shell of the capsid is energetically inert during packaging. Here, we test this challenge by analyzing the in vitro effects of ATP on the shells of capsids generated by DNA packaging in vivo. These capsids retain incompletely packaged DNA (ipDNA) and are called ipDNA-capsids; the ipDNA-capsids are assumed to be products of premature genome maturation-cleavage. They were isolated via preparative Nycodenz buoyant density centrifugation. For some ipDNA-capsids, Nycodenz impermeability increases hydration and generates density so low that shell hyper-expansion must exist to accommodate associated water. Electron microscopy (EM) confirmed hyper-expansion and low permeability and revealed that 3.0 mM magnesium ATP (physiological concentration) causes contraction of hyper-expanded, lowpermeability ipDNA-capsids to less than mature size; 5.0 mM magnesium ATP (border of supraphysiological concentration) or more disrupts them. Additionally, excess sodium ADP reverses 3.0 mM magnesium ATP-induced contraction and re-generates hyper-expansion. The Nycodenz impermeability implies assembly perfection that suggests selection for function in DNA packaging. These findings support the above challenge and can be explained via the assumption that T3

DNA packaging includes a back-up cycle of ATP-driven capsid contraction and hyper-expansion.

Sharma, J., Uchida, M., Miettinen, H. M., and Douglas, T. Modular interior loading and exterior decoration of a virus-like particle. Nanoscale. 7-27-2017; 9(29):10420-10430; PM: 28702648

ABSTRACT: Virus-like particles (VLPs) derived from the bacteriophage P22 offer an interesting and malleable platform for encapsulation and multivalent presentation of cargo molecules. The packaging of cargo in P22 VLP is typically achieved through genetically enabled directed in vivo encapsulation. However, this approach does not allow control over the packing density and composition of the encapsulated cargos. Here, we have adopted an in vitro assembly approach to gain control over cargo packaging in P22. The packaging was controlled by closely regulating the stoichiometric ratio of cargo-fused-scaffold protein and wild-type scaffold protein during the in vitro assembly. In a "one-pot assembly reaction" coat protein subunits were incubated with varied ratios of wild-type scaffold protein and cargo-fused-scaffold protein, which resulted in the encapsulation of both components in a co-assembled capsid. These experiments demonstrate that an input stoichiometry can be used to achieve controlled packaging of multiple cargos within the VLP. The porous nature of P22 allows the escape and re-entry of wild-type scaffold protein from the assembled capsid but scaffold protein fused to a protein-cargo cannot traverse the capsid shell due to the size of the cargo. This has allowed us to control and alter the packing density by selectively releasing wild-type scaffold protein from the co-assembled capsids. We have demonstrated these concepts in the P22 system using an encapsulated streptavidin protein and have shown its highly selective interaction with biotin or biotin derivatives. Additionally, this system can be used to encapsulate small molecules coupled to biotin, or display large proteins, that cannot enter the capsid and thus remain available for the multivalent display on the exterior of the capsid when attached to a flexible biotinylated linker. Thus, we have developed a P22 system with controlled protein cargo composition and packing density, to which both small and large molecules can be attached at high copy number on the interior or exterior of the capsid.

Shen, Y., Boulos, S., Sumrall, E., Gerber, B., Julian-Rodero, A., Eugster, M. R., Fieseler, L., Nystrom, L., Ebert, M. O., and Loessner, M. J. Structural and functional diversity in Listeria cell wall teichoic acids. J.Biol.Chem. 9-14-2017; PM: 28912268

ABSTRACT: Wall teichoic acids (WTAs) are the most abundant glycopolymers found on the cell wall of many Gram-positive bacteria, whose diverse surface structures play key roles in multiple biological processes. Despite recent technological advances in glycan analysis, structural elucidation of WTAs remains challenging due to their complex nature. Here, we employed a combination of UPLC-MS/MS and NMR to determine the structural complexity of WTAs from Listeria species. We unveiled more than 10 different types of WTA polymers that vary in their linkage and repeating units. Disparity in GlcNAc to ribitol connectivity, as well as variable O-acetylation and glycosylation of GlcNAc contribute to the structural diversity of WTAs. Notably, SPR analysis indicated that constitution of WTA determines the recognition by bacteriophage endolysins. Collectively, these findings provide detailed insight into Listeria cell wall-associated carbohydrates, and will guide further studies on the structure-function relationship of WTAs.

Shende, R. K., Hirpurkar, S. D., Sannat, C., Rawat, N., and Pandey, V. Isolation and characterization of bacteriophages with lytic activity against common bacterial pathogens. Vet.World. 2017; 10(8):973-978; PM: 28919692

*ABSTRACT**: AIM***: Present investigation was conducted to isolate and characterize bacteriophages with lytic activity against common bacterial pathogens. ***MATERIALS AND METHODS***: A total of 60 samples of animal waste disposal from cattle (42) and buffalo (18) farms were collected from three different strata, i.e., top, mid, and bottom of collection tank. Samples were primarily subjected to rapid detection methods, and then isolation of phage was done by double agar layer method using Bacillus subtilis (BsH) and Escherichia coli (EH) as host system. Phages were characterized on the basis of plaque morphology, temperature, pH susceptibility, and host range. ***RESULTS***: Recovery of phages was higher from dairy cattle farm waste (78.57%) as compared to buffalo farm waste (72.22%) and bottom layer of tank showed maximum recovery. Bacillus subtilis (91%) supported the growth of more phages as compared to E. coli (9%). Three different phage morphotypes were observed each against Bacillus subtilis (BsHR1, BsHR2, and BsHR3) and E. coli (EHR1, EHR2, and EHR3). Mean phage titer of above six phage isolates ranged between 3x1010 and 5x1012 plaque forming units/ml. Viability of phages was by, and large unaffected at 70 degrees C within 2-3 min, and phage isolates were completely inactivated below pH 3 and above 11. Coliphage EHR1 had widest host range followed by BsHR1 and BsHR2 while EHR2, EHR3, and BsHR3 had low lytic activity. ***CONCLUSION***: It could be concluded from the present study that the Bacillus and Coli phage has wide host range and thus exhibits the potential to be used as drug substitute tool against common bacterial pathogens.

Shiley, J. R., Comfort, K. K., and Robinson, J. B. Immunogenicity and antimicrobial effectiveness of Pseudomonas aeruginosa specific bacteriophage in a human lung in vitro model. Appl.Microbiol.Biotechnol. 9-15-2017; PM: 28914348

ABSTRACT: The rise of antibiotic resistant bacteria is posing a serious threat to human health. For example, resistant strains of Pseudomonas aeruginosa have resulted in untreatable and potentially lethal infections in both cystic fibrosis and immunocompromised patients. Due to the growing need for alternative treatment options, bacteriophage, or phage, therapy is gaining considerable attention. While previous studies have demonstrated the effectiveness of phage in combating persistent bacterial infections, there is currently a lack of knowledge regarding the host immunological response following phage exposure. In the present study, the bioresponses of an enhanced in vitro model were characterized following exposure to either DMS3 or PEV2, P. aeruginosa targeting phages. Results demonstrated a PEV2-dependent increase in IL-6 and TNF-alpha production, but no changes associated with DMS3 exposure. Additionally, following the establishment of an in vitro infection model, DMS3 was found to successfully protect mammalian lung cells from P. aeruginosa. Taken together, the biocompatibility and antibacterial effectiveness distinguish DMS3 bacteriophage as a strong candidate for phage therapy. However, as DMS3 is pilin dependent and bacterial receptor expression varies significantly, this work highlights the necessity of generating phage cocktails.

Shimabuku, Q. L., Arakawa, F. S., Fernandes, Silva M., Ferri, Coldebella P., Ueda-Nakamura, T., Fagundes-Klen, M. R., and Bergamasco, R. Water treatment with exceptional virus

inactivation using activated carbon modified with silver (Ag) and copper oxide (CuO) nanoparticles. Environ.Technol. 2017; 38(16):2058-2069; PM: 27766917

ABSTRACT: Continuous flow experiments (450 mL min-1) were performed in household filter in order to investigate the removal and/or inactivation of T4 bacteriophage, using granular activated carbon (GAC) modified with silver and/or copper oxide nanoparticles at different concentrations. GAC and modified GAC were characterized by X-ray diffractometry, specific surface area, pore size and volume, pore average diameter, scanning electron microscopy, transmission electron microscopy, zeta potential and atomic absorption spectroscopy. The antiviral activity of the produced porous media was evaluated by passing suspensions of T4 bacteriophage (approximately 105 UFP/mL) through filters. The filtered water was analyzed for the presence of the bacteriophage and the release of silver and copper oxide. The porous media containing silver and copper oxide nanoparticles showed high inactivation capacity, even reaching reductions higher than 3 log. GAC6 (GAC/Ag0.5%Cu1.0%) was effective in the bacteriophage inactivation, reaching 5.53 log reduction. The levels of silver and copper released in filtered water were below the recommended limits (100 ppb for silver and 1000 ppb for copper) in drinking water. From this study, it is possible to conclude that activated carbon modified with silver and copper oxide nanoparticles can be used as a filter for virus removal in the treatment of drinking water.

Sidhu, J. P. S., Ahmed, W., Palmer, A., Smith, K., Hodgers, L., and Toze, S. Optimization of sampling strategy to determine pathogen removal efficacy of activated sludge treatment plant. Environ.Sci.Pollut.Res.Int. 6-28-2017; PM: 28656581

ABSTRACT: Large-scale wastewater schemes rely on multi-barrier approach for the production of safe and sustainable recycled water. In multi-barrier wastewater reclamation systems, conventional activated sludge process (ASP) often constitutes a major initial treatment step. The main aim of this research was to determine most appropriate sampling approach to establish pathogen removal efficacy of ASP. The results suggest that ASP is capable of reducing human adenovirus (HAdV) and polyomavirus (HPyV) by up to 3 log10. The virus removal data suggests that HAdV removal is comparable to somatic bacteriophage belonging to Microviridae family. Due to the high removal of Escherichia coli (>3 log10) and very poor correlation with the enteric virus, it is not recommended that E. coli be used as a surrogate for enteric virus removal. The results also demonstrated no statistically significant differences (t test, P > 0.05) in calculated log removal values (LRVs) for HAdV, HPyV, and Microviridae from samples collected on hydraulic retention time (HRT) or simultaneous paired samples collected for influent and effluent. This indicates that a more practical approach of simultaneous sampling for influent and effluent could be used to determine pathogen removal efficiency of ASP. The results also suggest that a minimum of 10, preferably 20 samples, are required to fully capture variability in the removal of virus. In order to cover for the potential seasonal prevalence of viruses such as norovirus and rotavirus, sampling should be spread across all seasons.

Sinumvayo, J. P., Yang, S., Chen, J., Du, G., and Kang, Z. [Engineering and characterization of new intrinsic transcriptional terminators in Bacillus subtilis 168]. Sheng Wu Gong.Cheng Xue.Bao. 7-25-2017; 33(7):1091-1100; PM: 28869729

ABSTRACT: Terminators as regulatory signals are typically placed behind the last coding

sequence to block the transcription of DNA to RNA and release the transcript. In the present study, the hairpin and the U-rich sequence of the bacteriophage lambdato terminator were first modified to investigate their effects on termination efficiency and mRNA stability in Bacillus subtilis 168. Compared with the native lambdato terminator, the terminator variants M3, M11 and M12 showed higher termination efficiency values. Moreover, the variantsM3, M4 and M11 showed significant positive effects on the mRNA stability of the upstream gfp gene. Additionally, insertion of RNase site also increased the mRNA stability. The results of this study suggested that the composition of the hairpin loop is not required for effective intrinsic termination in B. subtilis. Our results also showed that the terminator could also be used as a potential tool for increasing mRNA stability and the corresponding enzyme production in B. subtilis.

Smith, W. D., Bardin, E., Cameron, L., Edmondson, C. L., Farrant, K. V., Martin, I., Murphy, R. A., Soren, O., Turnbull, A. R., Wierre-Gore, N., Alton, E. W., Bundy, J. G., Bush, A., Connett, G. J., Faust, S. N., Filloux, A., Freemont, P. S., Jones, A. L., Takats, Z., Webb, J. S., Williams, H. D., and Davies, J. C. Current and future therapies for Pseudomonas aeruginosa infection in patients with cystic fibrosis. FEMS Microbiol.Lett. 8-1-2017; 364(14); PM: 28854668

ABSTRACT: Pseudomonas aeruginosa opportunistically infects the airways of patients with cystic fibrosis and causes significant morbidity and mortality. Initial infection can often be eradicated though requires prompt detection and adequate treatment. Intermittent and then chronic infection occurs in the majority of patients. Better detection of P. aeruginosa infection using biomarkers may enable more successful eradication before chronic infection is established. In chronic infection P. aeruginosa adapts to avoid immune clearance and resist antibiotics via efflux pumps, beta-lactamase expression, reduced porins and switching to a biofilm lifestyle. The optimal treatment strategies for P. aeruginosa infection are still being established, and new antibiotic formulations such as liposomal amikacin, fosfomycin in combination with tobramycin and inhaled levofloxacin are being explored. Novel agents such as the alginate oligosaccharide OligoG, cysteamine, bacteriophage, nitric oxide, garlic oil and gallium may be useful as anti-pseudomonal strategies, and immunotherapy to prevent infection may have a role in the future. New treatments that target the primary defect in cystic fibrosis, recently licensed for use, have been associated with a fall in P. aeruginosa infection prevalence. Understanding the mechanisms for this could add further strategies for treating P. aeruginosa in future.

Srinivasan, P. and Ramasamy, P. Morphological characterization and biocontrol effects of Vibrio vulnificus phages against Vibriosis in the shrimp aquaculture environment. Microb.Pathog. 9-13-2017; PM: 28917670

ABSTRACT: The re-emerging field of phage therapy is the potential biocontrol agents for the transfer of virulence factor and to kill their bacterial hosts. In this study, the lytic Vibrio vulnificus phages were studied to provide a better understanding of phage-host interactions and development of phage therapy. Four new V. vulnificus phages were detected from shrimp aquaculture system, named VV1, VV2, VV3 and VV4. All lytic V. vulnificus phages are the Tecviruses of the family Tectiviridae with typical double layered elongated icosahedral head and tailless morphology. Lytic V. vulnificus phages which infect other Vibrio isolates were further characterized by long term storage, enzymes treatment, organic solvents treatment, detergents treatment, pH stability, temperature stability, agar bioassay method and one-step growth experiment. The effects of

chloroform, acetone, ethyl alcohol, methyl alcohol, ribonuclease (RNase), trypsin, protease, Triton-X100 treatments were not affected the growth of VV1, VV2, VV3 and VV4 phages. These phages (VV1-VV4) were inactivated completely with temperature (over 60 degrees C), pH (<3 or >12), lysozyme and sodium dodecyl sulfate (SDS) treatment. One-step growth experiments indicated that the latent period was at 3 h and burst size was at 37 degrees C. Agar bioassay method indicated that the percentage of inhibition was 75% (VV1) and 70% (VV2, VV3 & VV4), respectively. SDS-PAGE analysis of all V. vulnificus phages had similar protein patterns with molecular weight masses of 260, 249, 204, 148, 63, 59, 22 and 15 kDa. Hence, it could be concluded that V. vulnificus phage had a broad lytic spectrum and potential biocontrol of luminous Vibriosis in the shrimp aquaculture system.

Stachler, E., Kelty, C., Sivaganesan, M., Li, X., Bibby, K., and Shanks, O. C. Quantitative CrAssphage PCR Assays for Human Fecal Pollution Measurement. Environ.Sci.Technol. 8-15-2017; 51(16):9146-9154; PM: 28700235

ABSTRACT: Environmental waters are monitored for fecal pollution to protect public health and water resources. Traditionally, general fecal-indicator bacteria are used; however, they cannot distinguish human fecal waste from other animal pollution sources. Recently, a novel bacteriophage, crAssphage, was discovered by metagenomic data mining and reported to be abundant in and closely associated with human fecal waste. To confirm bioinformatic predictions, 384 primer sets were designed along the length of the crAssphage genome. Based on initial screening, two novel crAssphage qPCR assays (CPQ_056 and CPQ_064) were designed and evaluated in reference fecal samples and water matrices. The assays exhibited high specificities (98.6%) when tested against an animal fecal reference library, and crAssphage genetic markers were highly abundant in raw sewage and sewage-impacted water samples. In addition, CPQ_056 and CPQ_064 performance was compared to HF183/BacR287 and HumM2 assays in paired experiments. Findings confirm that viral crAssphage qPCR assays perform at a similar level to well-established bacterial human-associated fecal-source-identification approaches. These new viral-based assays could become important water quality management and research tools.

Strauss, B. S. A Physicist's Quest in Biology: Max Delbruck and "Complementarity". Genetics. 2017; 206(2):641-650; PM: 28592501

ABSTRACT: Max Delbruck was trained as a physicist but made his major contribution in biology and ultimately shared a Nobel Prize in Physiology or Medicine. He was the acknowledged leader of the founders of molecular biology, yet he failed to achieve his key scientific goals. His ultimate scientific aim was to find evidence for physical laws unique to biology: so-called "complementarity." He never did. The specific problem he initially wanted to solve was the nature of biological replication but the discovery of the mechanism of replication was made by others, in large part because of his disdain for the details of biochemistry. His later career was spent investigating the effect of light on the fungus Phycomyces, a topic that turned out to be of limited general interest. He was known both for his informality but also for his legendary displays of devastating criticism. His life and that of some of his closest colleagues was acted out against a background of a world in conflict. This essay describes the man and his career and searches for an explanation of his profound influence.

Sun, G. and Riggs, A. D. A Simple and Cost-Effective Approach for In Vitro Production of Sliced siRNAs as Potent Triggers for RNAi. Mol.Ther.Nucleic Acids. 9-15-2017; 8:345-355; PM: 28918034

ABSTRACT: We have studied the molecular properties of in-vitro-transcribed sliced small interfering RNAs (tsli-siRNAs) as an alternative RNAi agent for chemically synthesized siRNA. We describe here a simple and cost-effective procedure for high-purity production of tsli-siRNA using bacteriophage T7 RNA polymerases. tsli-siRNAs exhibit potent gene knockdown effects, with efficacy comparable with that of chemically synthesized sli-siRNAs and classical siRNAs. Furthermore, we found that it is very easy to prepare potent tsli-siRNAs with modified bases, such as 2'-fluorine- or biotin-16-modified tsli-siRNAs. tsli-siRNAs can cause a mild innate immune response, which can be easily eliminated by alkaline phosphatase treatment. On the other hand, this feature, which can be useful as a trigger of the innate immune response, can be enhanced by polynucleotide kinase treatment. Because of the simplicity of preparation and purification, the procedure presented here could be useful for the production of RNAi or immunostimulatory reagents.

Sun, Y., Li, Y., Wu, B., Wang, J., Lu, X., Qu, S., Weng, J., and Feng, B. Biological responses to M13 bacteriophage modified titanium surfaces in vitro. Acta Biomater. 2017; 58:527-538; PM: 28624655

ABSTRACT: Phage-based materials have showed great potential in tissue engineering application. However, it is unknown what inflammation response will happen to this kind of materials. This work is to explore the biological responses to M13 bacteriophage (phage) modified titanium surfaces in vitro from the aspects of their interaction with macrophages, osteoblasts and mineralization behavior. Pretreated Ti surface, Ti surfaces with noncrosslinked phage film (APP) and crosslinked phage film (APPG) were compared. Phage films could limit the macrophage adhesion and activity due to inducing adherent-cell apoptosis. The initial inflammatory activity (24h) caused by phage films was relatively high with more production of TNF-alpha, but in the later stage (7-10days) inflammatory response was reduced with lower TNF-alpha, IL-6 and higher IL-10. In addition, phage films improved osteoblast adhesion, differentiation, and hydroapatite (HA)-forming via a combination of topographical and biochemcial cues. The noncrosslinked phage film displayed the best immunomodulatory property, osteogenic activity and HA mineralization ability. This work provides better understanding of inflammatory and osteogenetic activity of phage-based materials and contributes to their future application in tissue engineering. STATEMENT OF SIGNIFICANCE: In vivo, the bone and immune cells share a common microenvironment, and are being affected by similar cytokines, signaling molecules, transcription factors and membrane receptors. Ideal implants should cause positive biological response, including adequate and appropriate inflammatory reaction, well-balanced bone formation and absorption. Phage-based materials have showed great potential in tissue engineering application. However, at present it is unknown what inflammation response will happen to this kind of materials. A good understanding of the immune response possibly induced by phage-based materials is needed. This work studied the osteoimmunomodulation property of phage films on titanium surface, involving inflammatory response, osteogenic activity and biomineralization ability. It provides more understanding of the phage-based materials and contributes to their future application in tissue engineering.

Suster, K., Podgornik, A., and Cor, A. Quick bacteriophage-mediated bioluminescence assay for detecting Staphylococcus spp. in sonicate fluid of orthopaedic artificial joints. New Microbiol. 2017; 40(3):190-196; PM: 28675248

ABSTRACT: Staphylococcus spp. accounts for up to two thirds of all microorganisms causing prosthetic joint infections, with Staphylococcus aureus and Staphylococcus epidermidis being the major cause. The present study describes a diagnostic model to detect staphylococci using a specific bacteriophage and bioluminescence detection, exploring the possibility of its use on sonicate fluid of orthopaedic artificial joints. Intracellular adenosine-5'-triphosphate release by bacteriophage mediated lysis of staphylococci was assessed to determine optimal parameters for detection. With the optimized method, a limit of detection of around 103 CFU/mL was obtained after incubation with bacteriophage for 2 h. Importantly, sonicate fluid did not prevent the ability of bacteriophage to infect bacteria and all simulated infected sonicate fluid as well as 6 clinical samples with microbiologically proven staphylococcal infection were detected as positive. The total assay took approximately 4 h. Collectively, the results indicate that the developed method promises a rapid, inexpensive and specific diagnostic detection of staphylococci in sonicate fluid of infected prosthetic joints. In addition, the unlimited pool of different existing bacteriophages, with different specificity for all kind of bacteria gives the opportunity for further investigations, improvements of the current model and implementation in other medical fields for the purpose of the establishment of a rapid diagnosis.

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.

Temmam, S., Davoust, B., Chaber, A. L., Lignereux, Y., Michelle, C., Monteil-Bouchard, S., Raoult, D., and Desnues, C. Screening for Viral Pathogens in African Simian Bushmeat Seized at A French Airport. Transbound.Emerg.Dis. 2017; 64(4):1159-1167; PM: 26876732

ABSTRACT: Illegal bushmeat traffic is an important threat to biodiversity conservation of several endangered species and may contribute to the emergence and spread of infectious diseases in humans. The hunting, manipulation and consumption of wildlife-based products, especially those of primate origin, may be a threat to human health; however, few studies have investigated the role of bushmeat trade and consumption as

a potential source of human infections to date. In this study, we report the screening of viral pathogens in African simian game seized by French customs at Toulouse Blagnac Airport. Epifluorescence microscopy revealed the presence of virus-like particles in the samples, and further metagenomic sequencing of the DNA and RNA viromes confirmed the presence of sequences related to the Siphoviridae, Myoviridae and Podoviridae bacteriophage families; some of them infecting bacterial hosts that could be potentially pathogenic for humans. To increase the sensitivity of detection, twelve pan-generic PCRs targeting several viral zoonoses were performed, but no positive signal was detected. A large-scale inventory of bacteria, viruses and parasites is urgently needed to globally assess the risk for human health of the trade, manipulation and consumption of wildlife-related bushmeat.

Tetz, G. V., Ruggles, K. V., Zhou, H., Heguy, A., Tsirigos, A., and Tetz, V. Bacteriophages as potential new mammalian pathogens. Sci.Rep. 8-1-2017; 7(1):7043; PM: 28765534

ABSTRACT: Increased intestinal permeability and translocation of gut bacteria trigger various polyaetiological diseases associated with chronic inflammation and underlie a variety of poorly treatable pathologies. Previous studies have established a primary role of the microbiota composition and intestinal permeability in such pathologies. Using a rat model, we examined the effects of exposure to a bacteriophage cocktail on intestinal permeability and relative abundance of taxonomic units in the gut bacterial community. There was an increase in markers of impaired gut permeability, such as the lactulose/mannitol ratio, plasma endotoxin concentrations, and serum levels of inflammation-related cytokines, following the bacteriophage challenge. We observed significant differences in the alpha diversity of faecal bacterial species and found that richness and diversity index values increased following the bacteriophage challenge. There was a reduction in the abundance of Blautia, Catenibacterium, Lactobacillus, and Faecalibacterium species and an increase in Butyrivibrio, Oscillospira and Ruminococcus after bacteriophage administration. These findings provide novel insights into the role of bacteriophages as potentially pathogenic for mammals and their possible implication in the development of diseases associated with increased intestinal permeability.

Tewari, K., Dahuja, A., Sachdev, A., Kumar, V., Ali, K., Kumar, A., and Kumari, S. Molecular cloning, heterologous expression and functional characterization of gamma tocopherol methyl transferase (gamma-TMT) from Glycine max. Protein Expr.Purif. 2017; 140:81-89; PM: 28811265

ABSTRACT: gamma-Tocopherol methyltransferase (gamma-TMT) (EC 2.1.1.95) is the last enzyme in the tocopherol biosynthetic pathway and it catalyzes the conversion of gamma-tocopherol into alpha-tocopherol, the nutritionally significant and most bioactive form of vitamin E. Although the gamma-TMT gene has been successfully overexpressed in many crops to enhance their alpha-tocopherol content but still only few attempts have been made to uncover its structural, functional and regulation aspects at protein level. In this study, we have cloned the complete 909bp coding sequence of Glycine max gamma-TMT (Gm gamma-TMT) gene that encodes the corresponding protein comprising of 302 amino acid residues. The deduced Gm gamma-TMT protein showed 74-87% sequence identity with other characterized plant gamma-TMTs. Gm gamma-TMT belongs to Class I Methyl Transferases that have a Rossmann-like fold which consists of a seven-stranded beta sheet joined by alpha

helices. Heterologous expression of Gm gamma-TMT in pET29a expression vector under the control of bacteriophage T7 promoter produced a 37.9 kDa recombinant Gm gamma-TMT protein with histidine hexamer tag at its C-terminus. The expression of recombinant Gm gamma-TMT protein was confirmed by western blotting using anti-His antibody. The recombinant protein was purified by Ni2+-NTA column chromatography. The purified protein showed SAM dependent methyltransferase activity. The alpha-tocopherol produced in the in-vitro reaction catalyzed by the purified enzyme was detected using reverse phase HPLC. This study has laid the foundation to unveil the biochemical understanding of Gm gamma-TMT enzyme which can be further explored by studying its kinetic behaviour, substrate specificity and its interaction with other biomolecules.

Tinoco, J. M., Liss, N., Zhang, H., Nissan, R., Gordon, W., Tinoco, E., Sassone, L., and Stevens, R. Antibacterial effect of genetically-engineered bacteriophage varphiEf11/varphiFL1C(Delta36)PnisA on dentin infected with antibiotic-resistant Enterococcus faecalis. Arch.Oral Biol. 2017; 82:166-170; PM: 28646693

ABSTRACT: ***OBJECTIVE***: Enterococcus faecalis is a gram-positive facultative anaerobic bacterium, which is present in 30-89% of teeth with postendodontic treatment failures. E. faecalis is capable of penetrating dentinal tubules and surviving as a monoculture after conventional endodontic therapy, indicating that it is resistant to commonly used endodontic disinfection protocols. Different E. faecalis strains have shown resistance to several antibiotics, and have been associated with both dental pathology and systemic infections. The aim of this study was to evaluate the efficacy of a genetically engineered bacteriophage to disinfect dentin infected with antibiotic resistant strains of E. faecalis. ***METHODS***: Extracted human dentin root segments were cemented into sealable two-chamber devices, fabricated from syringe needle caps to form in vitro infected-dentin models. The models were inoculated with an overnight suspension of either E. faecalis V583 (vancomycin resistant strain) or E. faecalis JH2-2 (fusidic acid and rifampin resistant, vancomycin sensitive strain). After 7days of incubation at 37 degrees C, a suspension of a genetically engineered phage, varphiEf11/varphiFL1C(Delta36)PnisA, was added to the root canal of each infected dentin segment, and the incubation was continued for an additional 72-h. Dentin was harvested from the walls of each root canal and assayed for the residual titer of E. faecalis cells. ***RESULTS***: The recovered E. faecalis titer was reduced by 18% for the JH2-2 infected models, and by 99% for the V583 infected models. ***CONCLUSION***: Treatment: of E. faecalis-infected dentin with bacteriophage varphiEf11/varphiFL1C(Delta36)PnisA consistently resulted in a decrease in the residual bacterial population of both vancomycin-sensitive and resistant strains.

Totte, J., de, Wit J., Pardo, L., Schuren, F., van, Doorn M., and Pasmans, S. Targeted anti-staphylococcal therapy with endolysins in atopic dermatitis and the effect on steroid use, disease severity and the microbiome: study protocol for a randomized controlled trial (MAAS trial). Trials. 8-31-2017; 18(1):404; PM: 28859690

ABSTRACT: ***BACKGROUND***: Atopic dermatitis (AD) is associated with reduced skin microbial diversity and overgrowth of Staphylococcus (S.) aureus. However, the importance of S. aureus colonisation in the complex pathogenesis remains unclear and studies on the effect of anti-staphylococcal therapy in non-infected AD show contradictory results. Long-term interventions against S. aureus might be needed to restore the microbial balance, but carry the risk of bacterial resistance induction. Staphefekt, an engineered bacteriophage endolysin, specifically kills S. aureus leaving

other skin commensals unharmed. Bacterial resistance towards endolysins has not been reported, nor is it expected, which allows us to study its effect as long-term anti-staphylococcal treatment in non-infected AD. ***METHODS***: This is a multi-centre, placebo-controlled, double-blinded and randomized superiority trial with a parallel group design. A total of 100 participants, aged 18 years or older, diagnosed with moderate to severe AD and using a topical corticosteroid in the weeks before enrolment are included in the study. The study is executed in the Erasmus MC University Medical Centre Rotterdam in collaboration with the Havenziekenhuis Rotterdam. After a 2-week run-in period to standardize the corticosteroid use with triamcinolone acetonide 0.1% cream, participants will be randomized to either treatment with Staphefekt in a cetomacrogol-based cream or a placebo for 12 weeks, followed by an 8-week follow-up period. The primary objective is to assess the difference in the need for corticosteroid co-therapy between the Staphefekt and the placebo group, measuring the number of days per week of corticosteroid cream (triamcinolone) use. Secondary outcomes include the difference in use of corticosteroid cream measured in grams, differences in clinical efficacy, quality of life (QoL), microbial composition (includi23ng S. aureus) between the Staphefekt and the placebo group, and the safety and tolerability. ***DISCUSSION***: The results of this trial will provide data about the effect of long-term anti-staphylococcal therapy with Staphefekt on corticosteroid use, clinical symptoms and QoL in patients with moderate to severe AD. Additional data about growth characteristics of the skin microbiome, including S. aureus, will give insight into the role of the microbiome as a factor in the pathophysiology of AD. ***TRIAL REGISTRATION***: ClinicalTrials.gov, NCT02840955 . Registered on 11 July 2016.

Tram, N. D. T. and Ee, P. L. R. Macromolecular Conjugate and Biological Carrier Approaches for the Targeted Delivery of Antibiotics. Antibiotics.(Basel). 7-4-2017; 6(3); PM: 28677631

ABSTRACT: For the past few decades, the rapid rise of antibiotic multidrug-resistance has presented a palpable threat to human health worldwide. Meanwhile, the number of novel antibiotics released to the market has been steadily declining. Therefore, it is imperative that we utilize innovative approaches for the development of antimicrobial therapies. This article will explore alternative strategies, namely drug conjugates and biological carriers for the targeted delivery of antibiotics, which are often eclipsed by their nanomedicine-based counterparts. A variety of macromolecules have been investigated as conjugate carriers, but only those most widely studied in the field of infectious diseases (e.g., proteins, peptides, antibodies) will be discussed in detail. For the latter group, blood cells, especially erythrocytes, have been successfully tested as homing carriers of antimicrobial agents. Bacteriophages have also been studied as a candidate for similar functions. Once these alternative strategies receive the amount of research interest and resources that would more accurately reflect their latent applicability, they will inevitably prove valuable in the perennial fight against antibiotic resistance.

Trend, S., Fonceca, A. M., Ditcham, W. G., Kicic, A., and Cf, A. The potential of phage therapy in cystic fibrosis: Essential human-bacterial-phage interactions and delivery considerations for use in Pseudomonas aeruginosa-infected airways. J.Cyst.Fibros. 7-15-2017; PM: 28720345

ABSTRACT: As antimicrobial-resistant microbes become increasingly common and a significant global issue, novel approaches to treating these infections particularly in those at high risk are required. This is evident in people with cystic fibrosis (CF), who suffer from

chronic airway infection caused by antibiotic resistant bacteria, typically Pseudomonas aeruginosa. One option is bacteriophage (phage) therapy, which utilises the natural predation of phage viruses upon their host bacteria. This review summarises the essential and unique aspects of the phage-microbe-human lung interactions in CF that must be addressed to successfully develop and deliver phage to CF airways. The current evidence regarding phage biology, phage-bacterial interactions, potential airway immune responses to phages, previous use of phages in humans and method of phage delivery to the lung are also summarised.

Triana, V. and Derda, R. Tandem Wittig/Diels-Alder diversification of genetically encoded peptide libraries. Org.Biomol.Chem. 9-7-2017; PM: 28880027

ABSTRACT: In this paper, we developed a tandem of two carbon-carbon bond-forming reactions to chemically diversify the libraries of peptides displayed on a bacteriophage. The Wittig reaction of a biotin-ester from a stabilized phosphorane ylide with model peptides containing N-terminal glyoxal exhibits reaction rates of 0.07 to 5 M-1 s-1 in water at pH 6.5-8. The log(k) scaled linearly with pH from pH 6 to 8; above pH 9 the reaction is accompanied by the hydrolysis of the ester functionality. Capture of the phage displaying the biotinylated product by streptavidin beads confirmed the rate of this reaction in a library of 108 peptides (k = 0.23 M-1 s-1 at pH = 6.5) and also confirmed the regioselectivity of this modification. Olefins introduced into the Wittig reaction can act as Michael acceptors: addition of glutathione, cysteamine, and DYKDDDDKC ("FLAG-Cys") peptide occurs with k = 0.12-4.1 M-1 s-1 at pH 7.8. Analogous reactions with the DYKDDDDKC peptide take place on phage-displayed peptides modified via the Wittig reaction. This reaction is manifested as a progressive emergence of a FLAG-epitope on the phage and detected by the capture of this phage using an anti-FLAG antibody. Olefins introduced into the Wittig reaction also act as dienophiles in the Diels-Alder reaction with cyclopentadiene. The conversion of the dienophile to norbornene-like adducts on the phage was observed by monitoring the disappearance of the thiol-reactive olefin on the phage. This report broadens the reaction scope of genetically-encoded peptide libraries displayed on the phage, expanding the structural diversity of these platforms and increasing their potential to be used in screening against important protein targets. The possibility of monitoring tandem reactions by the use of different labels illustrates the feasibility of obtaining highly functionalized peptides with chemical motifs impossible to achieve using conventional translational machinery.

Uchiyama, J., Taniguchi, M., Kurokawa, K., Takemura-Uchiyama, I., Ujihara, T., Shimakura, H., Sakaguchi, Y., Murakami, H., Sakaguchi, M., and Matsuzaki, S. Adsorption of Staphylococcus viruses S13' and S24-1 on Staphylococcus aureus strains with different glycosidic linkage patterns of wall teichoic acids. J.Gen.Virol. 2017; 98(8):2171-2180; PM: 28730979

ABSTRACT: The group of phages belonging to the family Podoviridae, genus P68virus, including Staphylococcus viruses S13' and S24-1, are important because of their benefits in phage therapy against Staphylococcus aureus infections. The O-glycosidic linkage patterns of wall teichoic acids (WTAs) in S. aureus cell walls seem to be important for adsorption of this phage group. In this study, the adsorption of Staphylococcus viruses S13' and S24-1 to S. aureus was examined using strains with modified WTA glycosidic linkage patterns. We found that the beta-O-N-acetylglucosamine of WTAs was essential for S13' adsorption, while N-acetylglucosamine, regardless of the alpha- and beta-O-

glycosidic linkages of the WTAs, was essential for S24-1 adsorption. Next, examining the binding activities of their receptor-binding proteins (RBPs) to cell walls with different WTA glycosidic patterns, the beta-O-N-acetylglucosamine of the WTAs was essential for S13' RBP binding, while N-acetylglucosamine, regardless of the alpha- and beta-O-glycosidic linkages of the WTAs, was essential for S24-1 RBP binding. Therefore, the results of the RBP binding assays were consistent with those of the phage adsorption assays. Bioinformatic analysis suggested that the RBPs of Staphylococcus viruses S13' and S24-1 were structurally similar to the RBPs of phage phi11 of thefamily Siphoviridae. Phylogenetic analysis of the RBPs indicated that two phylogenetic subclusters in the family Podoviridae were related to the glycosidic linkage patterns required for phage adsorption, possibly mediated by RBPs. We hope that this study will encourage the future development of therapeutic phages.

Uldahl, K. B., Walk, S. T., Olshefsky, S. C., Young, M. J., and Peng, X. SMV1, an extremely stable thermophilic virus platform for nanoparticle trafficking in the mammalian GI tract. J.Appl.Microbiol. 9-11-2017; PM: 28891224

*ABSTRACT**: AIMS***: analysis of the stability and safety of Sulfolobus monocaudavirus 1 (SMV1) during passage through the mammalian GI tract. ***METHODS AND RESULTS***: A major challenge of using nano-vectors to target gut microbiome is their survival during passage through the extremely acidic and proteolytic environment of the mammalian GI tract. Here we investigated the thermo-acidophilic archaeal virus SMV1 as a candidate therapeutic nano-vector for the distal mammalian GI tract microbiome. We investigated the anatomical distribution, vector stability, and immunogenicity of this virus following oral ingestion in mice and compared these traits to the more classically used Inovirus vector M13KE. We found that SMV1 particles were highly stable under both simulated GI tract conditions (in vitro) and in mice (in vivo). Moreover, SMV1 could not be detected in tissues outside the GI tract and it elicited a nearly undetectable inflammatory response. Finally, we used human intestinal organoids (HIOs) to show that labeled SMV1 did not invade or otherwise perturb the human GI tract epithelium. ***CONCLUSION***: SMV1 appeared stable and safe during passage though the mammalian GI tract. ***SIGNIFICANCE AND IMPACT***: this is the first study evaluating an archaeal virus as a potential therapeutic nanoparticle delivery system and it opens new possibilities for future development of novel nanoplatforms. This article is protected by copyright. All rights reserved.

Valerio, N., Oliveira, C., Jesus, V., Branco, T., Pereira, C., Moreirinha, C., and Almeida, A. Effects of single and combined use of bacteriophages and antibiotics to inactivate Escherichia coli. Virus Res. 8-15-2017; 240:8-17; PM: 28746884

ABSTRACT: A major concern of phage therapy is the emergency of phage-resistant mutants. This limitation can be overcome by the combined use of phages and antibiotics. It has been shown that the combination of antibiotics and phages is an alternative that cannot only be effective at reducing bacterial numbers, but also to contribute to the management of resistance levels. However, this view has only been discussed with regard to antibiotic resistance and not to control phage-mutant emergence. In our study we compared not only the resistance of the bacteria to the four antibiotics tested with and without phages addition, but also the resistance to the phages in the presence and absence of antibiotics. The aim of this study was to evaluate the potential synergistic effect of phages and antibiotics in the inactivation of

Escherichia coli in order to control infections, namely urinary tract infection (UTI), and to reduce the development of bacterial resistance to phages. Phage therapy combined with antibiotics (ampicillin, piperacillin, kamanycin, tetracycline, chloramphenicol and ciprofloxacin) was evaluated in the inactivation of E. coli, both in saline solution and urine samples. Phage and antibiotic combinations could result in high synergistic effects in the inactivation of bacteria. The combination of phage and ciprofloxacin at sublethal concentration decreased the bacterial counts in urine samples by 7.8+/-0.1 log CFU/ml after 8h, but when phages or the antibiotic were tested alone, the decrease was of 3.9+/-0.3 log CFU/mL and 1.2+/-0.1 log CFU/mL, respectively, after the same time. The efficacy of the combination of the two therapies depends on the antibiotic resistance status of the targeted bacteria to the employed antibiotic and of the antibiotic type (bactericide or bacteriostatic), causing the same or less bacterial resistance than phages and antibiotics applied alone (1.2+/-1.0x10-5 to 2.4+/-1.5x10-7 CFU/mL for the combined treatment, 2.7+/-0.2x10-4 CFU/mL for the antibiotics and 5.0+/-1.5x10-6 CFU/mL for the phages). The addition of antibiotics, at subinhibitory concentration, during phage treatment can control the phage-mutant. The high bacterial inactivation efficiency of these combined techniques and the long periods of phage survival in urine, pave the way for depth studies to control UTI and to overcome the development of resistances by bacteria.

van Nassau, T. J., Lenz, C. A., Scherzinger, A. S., and Vogel, R. F. Combination of endolysins and high pressure to inactivate Listeria monocytogenes. Food Microbiol. 2017; 68:81-88; PM: 28800829

ABSTRACT: Outbreaks of listeriosis are often related to the consumption of low-processed ready-to-eat food products (e.g. soft cheeses or smoked fish) contaminated with Listeria monocytogenes. Traditional preservation techniques, such as heat treatment, cannot eliminate Listeria from these products without strongly affecting the quality of the foods. We therefore investigated the use of endolysin (PlyP40, Ply511, or PlyP825) in combination with high hydrostatic pressure processing to kill L. monocytogenes in buffer. The results demonstrated a more than additive effect when both treatments were combined. For example, whereas 0.16 mug/mL PlyP825 or 300 MPa (1 min, 30 degrees C) applied individually reduced the cell count by 0.2 and 0.3 log cfu, respectively, a combined treatment resulted in a reduction of 5.5 log cfu. Similar results were obtained for the other endolysins combined with high pressure processing. We also showed that the synergistic inactivation of cells by endolysin and HHP is possible at a pressure level of only 200 MPa (2 min, 30 degrees C). Thus, the application of endolysins did not only substantially increase the bactericidal effect of high pressure, but it also enabled the inactivation of bacterial cells at much lower pressure levels. This shows the potential of using such combined processes for the inactivation of L. monocytogenes and food preservation.

Vongkamjan, K., Benjakul, S., Kim Vu, H. T., and Vuddhakul, V. Longitudinal monitoring of Listeria monocytogenes and Listeria phages in seafood processing environments in Thailand. Food Microbiol. 2017; 66:11-19; PM: 28576358

ABSTRACT: Listeria monocytogenes is a foodborne pathogen commonly found in environments of seafood processing, thus presenting a challenge for eradication from seafood processing facilities. Monitoring the prevalence and subtype diversity of L. monocytogenes together with phages that are specific to Listeria spp. ("Listeria phages") will provide knowledge on the bacteria-phage ecology in food processing plants. In this

work, a total of 595 samples were collected from raw material, finished seafood products and environmental samples from different sites of a seafood processing plant during 17 sampling visits in 1.5 years of study. L. monocytogenes and Listeria spp. (non-monocytogenes) were found in 22 (3.7%) and 43 (7.2%) samples, respectively, whereas 29 Listeria phages were isolated from 9 (1.5%) phage-positive samples. DNA fingerprint analysis of L. monocytogenes isolates revealed 11 Random Amplified Polymorphic DNA (RAPD) profiles, with two subtypes were frequently observed over time. Our data reveal a presence of Listeria phages within the same seafood processing environments where a diverse set of L. monocytogenes subtypes was also found. Although serotype 4b was observed at lower frequency, data indicate that isolates from this seafood processing plant belonged to both epidemiologically important serotypes 1/2a and 4b, which may suggest a potential public health risk. Phages (all showed a unique genome size of 65 +/- 2 kb) were classified into 9 host range groups, representing both broad- and narrow-host range. While most L. monocytogenes isolates from this facility were susceptible to phages, five isolates showed resistance to 12-20 phages. Variations in phage host range among Listeria phages isolated from food processing plant may affect a presence of a diverse set of L. monocytogenes isolates derived from the same processing environment in Thailand.

Wang, L., Qu, K., Li, X., Cao, Z., Wang, X., Li, Z., Song, Y., and Xu, Y. Use of Bacteriophages to Control Escherichia coli O157:H7 in Domestic Ruminants, Meat Products, and Fruits and Vegetables. Foodborne.Pathog.Dis. 2017; 14(9):483-493; PM: 28636835

ABSTRACT: Escherichia coli O157:H7 is an important foodborne pathogen that causes severe bloody diarrhea, hemorrhagic colitis, and hemolytic uremic syndrome. Ruminant manure is a primary source of E. coli O157:H7 contaminating the environment and food sources. Therefore, effective interventions targeted at reducing the prevalence of fecal excretion of E. coli O157:H7 by cattle and sheep and the elimination of E. coli O157:H7 contamination of meat products as well as fruits and vegetables are required. Bacteriophages offer the prospect of sustainable alternative approaches against bacterial pathogens with the flexibility of being applied therapeutically or for biological control purposes. This article reviews the use of phages administered orally or rectally to ruminants and by spraying or immersion of fruits and vegetables as an antimicrobial strategy for controlling E. coli O157:H7. The few reports available demonstrate the potential of phage therapy to reduce E. coli O157:H7 carriage in cattle and sheep, and preparation of commercial phage products was recently launched into commercial markets. However, a better ecological understanding of the phage E. coli O157:H7 will improve antimicrobial effectiveness of phages for elimination of E. coli O157:H7 in vivo.

Wernicki, A., Nowaczek, A., and Urban-Chmiel, R. Bacteriophage therapy to combat bacterial infections in poultry. Virol.J. 9-16-2017; 14(1):179; PM: 28915819

ABSTRACT: Infections in poultry are an economic and health problem in Europe and worldwide. The most common infections are associated with salmonellosis, colibacillosis, campylobacteriosis, and others. The prevalence of Campylobacter-positive poultry flocks in European countries varies from 18% to 90%. In the United States, the prevalence of infected flocks is nearly 90%. A similar percentage of infection has been noted for salmonellosis (about 75-90%) and E. coli (90-95%). The occurence of Clostridium perfringens is a major problem for the poultry industry, with some estimates suggesting colonization of as many as 95% of chickens, resulting in clinical or subclinical infections. In

the US, annual economic losses due to Salmonella infections run from $1.188 billion to over $11.588 billion, based on an estimated 1.92 million cases. Similar costs are observed in the case of other types of infections. In 2005 economic losses in the the poultry industry due to mortalities reached 1,000,000 USD.Infections caused by these pathogens, often through poultry products, are also a serious public health issue.The progressive increase in the number of multi-drug resistant bacteria and the complete ban on the use of antibiotics in livestock feed in the EU, as well as the partial ban in the US, have led to the growth of research on the use of bacteriophages to combat bacterial infections in humans and animals.The high success rate and safety of phage therapy in comparison with antibiotics are partly due to their specificity for selected bacteria and the ability to infect only one species, serotype or strain. This mechanism does not cause the destruction of commensal bacterial flora. Phages are currently being used with success in humans and animals in targeted therapies for slow-healing infections. They have also found application in the US in eliminating pathogens from the surface of foods of animal and plant origin. At a time of growing antibiotic resistance in bacteria and the resulting restrictions on the use of antibiotics, bacteriophages can provide an alternative means of eliminating pathogens.

Westbye, A. B., Beatty, J. T., and Lang, A. S. Guaranteeing a captive audience: coordinated regulation of gene transfer agent (GTA) production and recipient capability by cellular regulators. Curr.Opin.Microbiol. 6-6-2017; 38:122-129; PM: 28599143

ABSTRACT: Gene transfer agents (GTAs) are bacteriophage-like particles produced by many prokaryotes. Several members of the Alphaproteobacteria produce a class of genetically-related GTAs that is best studied in Rhodobacter capsulatus. DNA transfer by the R. capsulatus GTA (RcGTA) combines aspects of both transduction and natural transformation, as recipient cells require a natural transformation-like system to incorporate donated DNA. The genes involved in RcGTA production and recipient capability are located at multiple loci in the bacterial genome; however, a conserved phosphorelay containing the response regulator CtrA and a quorum sensing system regulate both RcGTA production and recipient capability. This review highlights recent discoveries in RcGTA biology, and focuses on the co-regulation of genes involved in RcGTA production and recipient capability.

Westbye, A. B., O'Neill, Z., Schellenberg-Beaver, T., and Beatty, J. T. The Rhodobacter capsulatus gene transfer agent is induced by nutrient depletion and the RNAP omega subunit. Microbiology. 2017; 163(9):1355-1363; PM: 28869409

ABSTRACT: Small bacteriophage-like particles called gene transfer agents (GTAs) that mediate DNA transfer between cells are produced by a variety of prokaryotes. The model GTA, produced by the alphaproteobacterium Rhodobacter capsulatus (RcGTA), is controlled by several cellular regulators, and production is induced upon entry into the stationary phase. We report that RcGTA production and gene transfer are stimulated by nutrient depletion. Cells depleted of organic carbon or blocked for amino acid biosynthesis increased RcGTA production and release from cells. Furthermore, cells lacking the sole RelA-SpoT homologue produced decreased levels of RcGTA, and the RNA polymerase omega (omega) subunit was required for appreciable production of RcGTA.

Wu, Y., You, L., Li, S., Ma, M., Wu, M., Ma, L., Bock, R., Chang, L., and Zhang, J. In vivo Assembly in Escherichia coli of Transformation Vectors for Plastid Genome Engineering. Front Plant Sci. 2017; 8:1454; PM: 28871270

ABSTRACT: Plastid transformation for the expression of recombinant proteins and entire metabolic pathways has become a promising tool for plant biotechnology. However, large-scale application of this technology has been hindered by some technical bottlenecks, including lack of routine transformation protocols for agronomically important crop plants like rice or maize. Currently, there are no standard or commercial plastid transformation vectors available for the scientific community. Construction of a plastid transformation vector usually requires tedious and time-consuming cloning steps. In this study, we describe the adoption of an in vivo Escherichia coli cloning (iVEC) technology to quickly assemble a plastid transformation vector. The method enables simple and seamless build-up of a complete plastid transformation vector from five DNA fragments in a single step. The vector assembled for demonstration purposes contains an enhanced green fluorescent protein (GFP) expression cassette, in which the gfp transgene is driven by the tobacco plastid ribosomal RNA operon promoter fused to the 5' untranslated region (UTR) from gene10 of bacteriophage T7 and the transcript-stabilizing 3'UTR from the E. coli ribosomal RNA operon rrnB. Successful transformation of the tobacco plastid genome was verified by Southern blot analysis and seed assays. High-level expression of the GFP reporter in the transplastomic plants was visualized by confocal microscopy and Coomassie staining, and GFP accumulation was ~9% of the total soluble protein. The iVEC method represents a simple and efficient approach for construction of plastid transformation vector, and offers great potential for the assembly of increasingly complex vectors for synthetic biology applications in plastids.

Wyatt, L. S., Xiao, W., Americo, J. L., Earl, P. L., and Moss, B. Novel Nonreplicating Vaccinia Virus Vector Enhances Expression of Heterologous Genes and Suppresses Synthesis of Endogenous Viral Proteins. MBio. 6-6-2017; 8(3); PM: 28588133

ABSTRACT: Viruses are used as expression vectors for protein synthesis, immunology research, vaccines, and therapeutics. Advantages of poxvirus vectors include the accommodation of large amounts of heterologous DNA, the presence of a cytoplasmic site of transcription, and high expression levels. On the other hand, competition of approximately 200 viral genes with the target gene for expression and immune recognition may be disadvantageous. We describe a vaccinia virus (VACV) vector that uses an early promoter to express the bacteriophage T7 RNA polymerase; has the A23R intermediate transcription factor gene deleted, thereby restricting virus replication to complementing cells; and has a heterologous gene regulated by a T7 promoter. In noncomplementing cells, viral early gene expression and DNA replication occurred normally but synthesis of intermediate and late proteins was prevented. Nevertheless, the progeny viral DNA provided templates for abundant expression of heterologous genes regulated by a T7 promoter. Selective expression of the Escherichia coli lac repressor gene from an intermediate promoter reduced transcription of the heterologous gene specifically in complementing cells, where large amounts might adversely impact VACV replication. Expression of heterologous proteins mediated by the A23R deletion vector equaled that of a replicating VACV, was higher than that of a nonreplicating modified vaccinia virus Ankara (MVA) vector used for candidate vaccines in vitro and in vivo, and was similarly immunogenic in mice. Unlike the MVA vector, the A23R deletion vector still expresses numerous early genes that can restrict immunogenicity as demonstrated here by the failure of the prototype vector to induce interferon alpha. By deleting

immunomodulatory genes, we anticipate further improvements in the system. ***IMPORTANCE***: Vaccines provide an efficient and effective way of preventing infectious diseases. Nevertheless, new and better vaccines are needed. Vaccinia virus, which was used successfully as a live vaccine to eradicate smallpox, has been further attenuated and adapted as a recombinant vector for immunization against other pathogens. However, since the initial description of this vector system, only incremental improvements largely related to safety have been implemented. Here we described novel modifications of the platform that increased expression of the heterologous target gene and decreased expression of endogenous vaccinia virus genes while providing safety by preventing replication of the candidate vaccine except in complementing cells used for vector propagation.

Xing, S., Zhang, X., Sun, Q., Wang, J., Mi, Z., Pei, G., Huang, Y., An, X., Fu, K., Zhou, L., Zhao, B., and Tong, Y. Complete genome sequence of a novel, virulent Ahjdlikevirus bacteriophage that infects Enterococcus faecium. Arch.Virol. 8-16-2017; PM: 28812171

ABSTRACT: A novel virulent bacteriophage named vB_EfaP_IME199 that specifically infects Enterococcus faecium was isolated and characterized. Its optimal multiplicity of infection was 0.01, and it had a 30 minute outbreak period. High-throughput sequencing revealed that the phage has a dsDNA genome of 18,838 bp with 22 open reading frames. The genome has very low homology to all other bacteriophage sequences in the GenBank database. Run-off sequencing experiments confirmed that vB_EfaP_IME199 has short inverted terminal repeats. Phylogenetic analysis indicated that vB_EfaP_IME199 can be taxonomically classified as a new member of the genus Ahjdlikevirus of family Podoviridae.

Xu, C., Sun, X., Jin, M., and Zhang, X. A Novel Benzoquinone Compound Isolated from Deep-Sea Hydrothermal Vent Triggers Apoptosis of Tumor Cells. Mar.Drugs. 6-26-2017; 15(7); PM: 28672882

ABSTRACT: Microorganisms are important sources for screening bioactive natural products. However, natural products from deep-sea microbes have not been extensively explored. In this study, the metabolites of bacteriophage GVE2 -infected (Geobacillus sp. E263 virus) thermophilic bacterium Geobacillus sp. E263, which was isolated from a deep-sea hydrothermal vent, were characterized. A novel quinoid compound, which had anti-tumor activity, was isolated from the phage-challenged thermophile. The chemical structure analysis showed that this novel quinoid compound was 2-amino-6-hydroxy-[1,4]-benzoquinone. The results indicated that 2-amino-6-hydroxy-[1,4]-benzoquinone and its two derivatives could trigger apoptosis of gastric cancer cells and breast cancer cells by inducing the accumulation of intracellular reactive oxygen species. Therefore, our study highlighted that the metabolites from the phage-challenged deep-sea microbes might be a kind of promising sources for anti-tumor drug discovery, because of the similarity of metabolic disorder between bacteriophage-infected microbes and tumor cells.

Xu, H., Bao, X., Lu, Y., Liu, Y., Deng, B., Wang, Y., Xu, Y., and Hou, J. Immunogenicity of T7 bacteriophage nanoparticles displaying G-H loop of foot-and-mouth disease virus (FMDV). Vet.Microbiol. 2017; 205:46-52; PM: 28622860

ABSTRACT: Foot-and-mouth disease (FMD) is a highly contagious disease of cloven-

hoofed animals that causes severe economic losses worldwide. The G-H loop of the FMDV VP1 structural protein is the major neutralizing antigenic site. However, a fully protective G-H loop peptide vaccine requires the addition of promiscuous Th sites from a source outside VP1. Thus, we demonstrated the potential of T7 bacteriophage based nanoparticles displaying a genetically fused G-H loop peptide (T7-GH) as a FMDV vaccine candidate. Recombinant T7-GH phage was constructed by inserting the G-H loop coding region into the T7 Select 415-1b vector. Purified T7-GH phage nanoparticles were analyzed by SDS-PAGE, Western blot and Dot-ELISA. Pigs seronegative for FMDV exposure were immunized with T7-GH nanoparticles along with the adjuvant Montanide ISA206, and two commercially available FMDV vaccines (InactVac and PepVac). Humoral and cellular immune responses, as well as protection against virulent homologous virus challenge were assessed following single dose immunization. Pigs immunized T7-GH developed comparable anti-VP1 antibody titers to PepVac, although lower LPBE titers than was induced by InactVac. Antigen specific lymphocyte proliferation was detected in T7-GH group similar to that of PepVac group, however, weaker than InactVac group. Pigs immunized with T7-GH developed a neutralizing antibody response stronger than PepVac, but weaker than InactVac. Furthermore, 80% (4/5) of T7-GH immunized pigs were protected from challenge with virulent homologous virus. These findings demonstrate that the T7-GH phage nanoparticles were effective in eliciting antigen specific immune responses in pigs, highlighting the value of such an approach in the research and development of FMDV vaccines.

Xu, S., Attinti, R., Adams, E., Wei, J., Kniel, K., Zhuang, J., and Jin, Y. Mutually facilitated co-transport of two different viruses through reactive porous media. Water Res. 10-15-2017; 123:40-48; PM: 28646749

ABSTRACT: In this study, we quantified transport and retention behaviors of a human pathogenic virus (Adenovirus 41, abbreviated as Ad-41) and a model bacteriophage (varphiX174) through metal oxide-removed and goethite-coated sand under saturated flow conditions. Two sets of bench scale column experiments were conducted: transport of each type of viruses alone and co-transport of both viruses. All experiments were conducted at pH 7.5 using 2 mM artificial ground water (AGW) buffer as background solution. Experimental results revealed that goethite-coated sand (i.e., reactive sand) retained much more viruses relative to metal oxide-removed sand (i.e., non-reactive sand), with the difference more pronounced for varphiX174 (effluent concentration decreased by 92.1%) than for Ad-41 (effluent concentration decreased by 59.7%). Interestingly, lower retention of both viruses on goethite-coated sand was observed when they co-existed in the influent. The mutual promotion to the transport of the two viruses may be attributed to attachment site competition and steric hindrance effect (illustrated in the graphical abstract). Mass recovery results revealed that varphiX174 was largely reversibly attached, whereas Ad-41 was mostly irreversibly bound or inactivated. Force measurements using atomic force microscopy (AFM) demonstrated that varphiX174 had doubled affinity to goethite-coated sand compared with Ad-41, consistent with the transport behavior of each type of viruses when they existed alone. As expected, the extended DLVO theory cannot accurately estimate interfacial energy profiles for viruses and reactive sand that have heterogeneous surface properties (i.e., roughness and charge heterogeneity). The results of this study clearly demonstrate that caution must be taken when applying laboratory results, which are generally obtained from experiments employing a single virus species, to predict the mobility and environmental risks in natural systems where multiple agents are present.

Xu, Z., Sun, Y., Weber, J. K., Cao, Y., Wang, W., Jasinski, D., Guo, P., Zhou, R., and Li, J. Directional mechanical stability of Bacteriophage phi29 motor's 3WJ-pRNA: Extraordinary robustness along portal axis. Sci.Adv. 2017; 3(5):e1601684; PM: 28560321

ABSTRACT: The molecular motor exploited by bacteriophage phi29 to pack DNA into its capsid is regarded as one of the most powerful mechanical devices present in viral, bacterial, and eukaryotic systems alike. Acting as a linker element, a prohead RNA (pRNA) effectively joins the connector and ATPase (adenosine triphosphatase) components of the phi29 motor. During DNA packing, this pRNA needs to withstand enormous strain along the capsid's portal axis-how this remarkable stability is achieved remains to be elucidated. We investigate the mechanical properties of the phi29 motor's three-way junction (3WJ)-pRNA using a combined steered molecular dynamics and atomic force spectroscopy approach. The 3WJ exhibits strong resistance to stretching along its coaxial helices, demonstrating its super structural robustness. This resistance disappears, however, when external forces are applied to the transverse directions. From a molecular standpoint, we demonstrate that this direction-dependent stability can be attributed to two Mg clamps that cooperate and generate mechanical resistance in the pRNA's coaxial direction. Our results suggest that the asymmetric nature of the 3WJ's mechanical stability is entwined with its biological function: Enhanced rigidity along the portal axis is likely essential to withstand the strain caused by DNA condensation, and flexibility in other directions should aid in the assembly of the pRNA and its association with other motor components.

Yamaguchi, Y., Usuki, S., Kanai, Y., Yamatoya, K., Suzuki, N., Katsumata, K. I., Terashima, C., Suzuki, T., Fujishima, A., Sakai, H., Kudo, A., and Nakata, K. Selective Inactivation of Bacteriophage in the Presence of Bacteria by Use of Ground Rh-Doped SrTiO3 Photocatalyst and Visible Light. ACS Appl.Mater.Interfaces. 9-5-2017; PM: 28872820

ABSTRACT: Bacteriophage (denoted as phage) infection in the bacterial fermentation industry is a major problem, leading to the loss of fermented products such as alcohol and lactic acid. Currently, the prevention of phage infection is limited to biological approaches, which are difficult to apply in an industrial setting. Herein, we report an alternative chemical approach using ground Rh-doped SrTiO3 (denoted as g-STO:Rh) as a visible-light-driven photocatalyst. The g-STO:Rh showed selective inactivation of phage without bactericidal activity when irradiated with visible light (lambda > 440 nm). After inactivation, the color of g-STO:Rh changed from gray to purple, suggesting that the Rh valence state partially changed from 3+ to 4+ induced by photocatalysis, as confirmed by diffuse reflectance spectroscopy. To study the effect of the Rh4+ ion on phage inactivation under visible-light irradiation, the survival rate of phage for g-STO:Rh was compared to that for ground Rh,Sb-codoped SrTiO3 (denoted as g-STO:Rh,Sb), where the change of Rh valence state from 3+ to 4+ is almost suppressed under visible-light irradiation due to charge compensation by the Sb5+ ion. Only g-STO:Rh effectively inactivated phage, which indicated that Rh4+ ion induced by photocatalysis particularly contributed to phage inactivation under visible-light irradiation. These results suggested that g-STO:Rh has potential as an antiphage material in bacterial fermentation.

Yan, G., Liu, J., Ma, Q., Zhu, R., Guo, Z., Gao, C., Wang, S., Yu, L., Gu, J., Hu, D., Han, W., Du, R., Yang, J., and Lei, L. The N-terminal and central domain of colicin A enables phage lysin

to lyse Escherichia coli extracellularly. Antonie Van Leeuwenhoek. 7-20-2017; PM: 28730370

ABSTRACT: Multidrug-resistant Escherichia coli has seriously threatened antibiotic resources and international public health. Bacteriophage lysin preparations have been widely considered as valid agents for solving multidrug resistances. Many lysins have been derived to treat diseases caused by Gram-positive bacteria, but only a few lysin preparations have been found that successively treat diseases caused by Gram-negative bacteria. The outer membrane of Gram-negative bacteria effectively blocks the interactions between peptidoglycan in the periplasmic space and bacteriophage lysins, which therefore hampers the antimicrobial effects of bacteriophage lysins. In this study, a new fusion protein (Colicin-Lysep3) was constructed by fusing the translocation and receptor binding domains of colicin A with an E. coli phage lysin, which endows Colicin-Lysep3 bactericidal activity against E. coli from outside of Gram-negative bacteria. These results show that Colicin-Lysep3 could lyse the E. coli broadly in vitro and significantly reduce the number of E. coli in an intestinal infection mouse model. Overall, our findings first demonstrated that a colicin A fragment could enable a bacteriophage lysin to lyse E. coli from the outside, promoting the application of phage lysin preparations in control of Gram-negative bacteria.

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.

York, A. Viral infection: A bacteriophage-like entry pathway in eukaryotes. Nat.Rev.Microbiol. 9-13-2017; 15(10):577; PM: 28900309

No Abstract Available.

Yosef, I., Goren, M. G., Globus, R., Molshanski-Mor, S., and Qimron, U. Extending the Host Range of Bacteriophage Particles for DNA Transduction. Mol.Cell. 6-1-2017; 66(5):721-728; PM: 28552617

ABSTRACT: A major limitation in using bacteriophage-based applications is their narrow host range. Approaches for extending the host range have focused primarily on lytic phages in hosts supporting their propagation rather than approaches for extending the ability of DNA transduction into phage-restrictive hosts. To extend the host range of T7 phage for DNA transduction, we have designed hybrid particles displaying various phage tail/tail fiber proteins. These modular particles were programmed to package and transduce DNA into hosts that restrict T7 phage propagation. We have also developed an innovative generalizable platform that considerably enhances DNA transfer into new hosts by artificially selecting tails that efficiently transduce DNA. In addition, we have demonstrated that the hybrid particles transduce desired DNA into desired hosts. This study thus critically extends and improves the ability of the particles to transduce DNA into novel phage-restrictive hosts, providing a platform for myriad applications that require this ability.

Yu, X., Jih, J., Jiang, J., and Zhou, Z. H. Atomic structure of the human cytomegalovirus capsid with its securing tegument layer of pp150. Science. 6-30-2017; 356(6345); PM: 28663444

ABSTRACT: Herpesviruses possess a genome-pressurized capsid. The 235-kilobase genome of human cytomegalovirus (HCMV) is by far the largest of any herpesvirus, yet it has been unclear how its capsid, which is similar in size to those of other herpesviruses, is stabilized. Here we report a HCMV atomic structure consisting of the herpesvirus-conserved capsid proteins MCP, Tri1, Tri2, and SCP and the HCMV-specific tegument protein pp150-totaling ~4000 molecules and 62 different conformers. MCPs manifest as a complex of insertions around a bacteriophage HK97 gp5-like domain, which gives rise to three classes of capsid floor-defining interactions; triplexes, composed of two "embracing" Tri2 conformers and a "third-wheeling" Tri1, fasten the capsid floor. HCMV-specific strategies include using hexon channels to accommodate the genome and pp150 helix bundles to secure the capsid via cysteine tetrad-to-SCP interactions. Our structure should inform rational design of countermeasures against HCMV, other herpesviruses, and even HIV/AIDS.

Zago, M., Orru, L., Rossetti, L., Lamontanara, A., Fornasari, M. E., Bonvini, B., Meucci, A., Carminati, D., Cattivelli, L., and Giraffa, G. Survey on the phage resistance mechanisms displayed by a dairy Lactobacillus helveticus strain. Food Microbiol. 2017; 66:110-116; PM: 28576359

ABSTRACT: In this study the presence and functionality of phage defence mechanisms in Lactobacillus helveticus ATCC 10386, a strain of dairy origin which is sensitive to PhiLh56, were investigated. After exposure of ATCC 10386 to PhiLh56, the whole-genome sequences of ATCC 10386 and of a phage-resistant derivative (LhM3) were compared. LhM3 showed deletions in the S-layer protein and a higher expression of the genes involved in the restriction/modification (R/M) system. Genetic data were substantiated by measurements of bacteriophage adsorption rates, efficiency of plaquing, cell wall protein size and by gene expression analysis. In LhM3 two phage resistance mechanisms, the inhibition of phage adsorption and the upregulation of Type I R/M genes, take place and explain its resistance to PhiLh56. Although present in both ATCC 10386 and LhM3 genomes, the CRISPR machinery did not seem to play a role in the phage resistance of LhM3. Overall, the natural selection of phage resistant strains resulted successful in detecting variants carrying multiple phage defence mechanisms in L. helveticus. The concurrent presence of multiple phage-resistance systems should provide starter strains with increased fitness and robustness in dairy ecosystems.

Zhang, J., Gao, Q., Zhang, Q., Wang, T., Yue, H., Wu, L., Shi, J., Qin, Z., Zhou, J., Zuo, J., and Yang, Y. Bacteriophage-prokaryote dynamics and interaction within anaerobic digestion processes across time and space. Microbiome. 5-31-2017; 5(1):57; PM: 28569210

*ABSTRACT**: BACKGROUND***: Bacteriophage-prokaryote dynamics and interaction are believed to be important in governing microbiome composition and ecosystem functions, yet our limited knowledge of the spatial and temporal variation in phage and prokaryotic community compositions precludes accurate assessment of their roles and impacts. Anaerobic digesters are ideal model systems to examine phage-host interaction, owing to easy access, stable operation, nutrient-rich environment, and consequently enormous numbers of phages and prokaryotic cells. ***RESULTS***: Equipped with high-throughput, cutting-edge environmental genomics techniques, we examined

phage and prokaryotic community composition of four anaerobic digesters in full-scale wastewater treatment plants across China. Despite the relatively stable process performance in biogas production, phage and prokaryotic groups fluctuated monthly over a year of study period, showing significant correlations between those two groups at the alpha- and beta-diversity levels. Strikingly, phages explained 40.6% of total variations of the prokaryotic community composition, much higher than the explanatory power by abiotic factors (14.5%). Consequently, phages were significantly ($P < 0.010$) linked to parameters related to process performance including biogas production and volatile solid concentrations. Association network analyses showed phage-prokaryote pairs were shallowly conserved since they were detected only within small viral clades. ***CONCLUSIONS***: Those results collectively demonstrate phages as a major biotic factor in controlling prokaryotic composition and process performance. Therefore, phages may play a larger role in shaping prokaryotic community dynamics and process performance of anaerobic digesters than currently appreciated.

Zhang, L. New Insights into DNA Polymerase Function Revealed by Phosphonoacetic Acid-Sensitive T4 DNA Polymerases. Chem.Res.Toxicol. 9-15-2017; PM: 28872853

ABSTRACT: The bacteriophage T4 DNA polymerase (pol) and the closely related RB69 DNA pol have been developed into model enzymes to study family B DNA pols. While all family B DNA pols have similar structures and share conserved protein motifs, the molecular mechanism underlying natural drug resistance of nonherpes family B DNA pols and drug sensitivity of herpes DNA pols remains unknown. In the present study, we constructed T4 phages containing G466S, Y460F, G466S/Y460F, P469S, and V475W mutations in DNA pol. These amino acid substitutions replace the residues in drug-resistant T4 DNA pol with residues found in drug-sensitive herpes family DNA pols. We investigated whether the T4 phages expressing the engineered mutant DNA pols were sensitive to the antiviral drug phosphonoacetic acid (PAA) and characterized the in vivo replication fidelity of the phage DNA pols. We found that G466S substitution marginally increased PAA sensitivity, whereas Y460F substitution conferred resistance. The phage expressing a double mutant G466S/Y460F DNA pol was more PAA-sensitive. V475W T4 DNA pol was highly sensitive to PAA, as was the case with V478W RB69 DNA pol. However, DNA replication was severely compromised, which resulted in the selection of phages expressing more robust DNA pols that have strong ability to replicate DNA and contain additional amino acid substitutions that suppress PAA sensitivity. Reduced replication fidelity was observed in all mutant phages expressing PAA-sensitive DNA pols. These observations indicate that PAA sensitivity and fidelity are balanced in DNA pols that can replicate DNA in different environments.

Zhang, Y. and Tanner, N. A. Isothermal Amplification of Long, Discrete DNA Fragments Facilitated by Single-Stranded Binding Protein. Sci.Rep. 8-17-2017; 7(1):8497; PM: 28819114

ABSTRACT: Isothermal amplification methods for detection of DNA and RNA targets have expanded significantly in recent years, promising a new wave of simple and rapid molecular diagnostics. Current isothermal methods result in the generation of short fragments (<150 base pairs) or highly branched long DNA products. Here we report the amplification of discrete target fragments of several kilobases at 37 degrees C from both double- and single-stranded circular template DNA using specific primer pairs. In contrast to existing methods, this amplification requires only the single-stranded DNA-binding protein gp32 from bacteriophage T4 and a strand-displacing DNA polymerase. In

addition to the discrete amplicon products, this method also produces higher molecular weight products consisting of multiple repeated copies of the amplicon and template DNA. We demonstrate that two features of gp32 enable this amplification: a facilitation of primer strand invasion into double-stranded DNA, and a suppression of non-homologous primer annealing and nonspecific amplification. The ability presented here to produce long, discrete DNA products in an isothermal reaction extends the scope of isothermal amplification to enable more useful applications of these promising methods.

Zhang, Y., Yan, C., Yang, H., Yu, J., and Wei, H. Rapid and selective detection of E. coli O157:H7 combining phagomagnetic separation with enzymatic colorimetry. Food Chem. 11-1-2017; 234:332-338; PM: 28551244

ABSTRACT: Mammal IgG antibodies are normally used in conventional immunoassays for E. coli O157:H7, which could lead to false positive results from the presence of protein A producing S. aureus. In this study, a natural specific bacteriophage was isolated and then conjugated with magnetic beads as a capture element in a sandwich format for the rapid and selective detection of E. coli O157:H7. To the best of our knowledge, it was the first time to utilize a natural bacteriophage to develop a phagomagnetic separation combined with colorimetric assay for E. coli O157:H7. The method has an overall time less than 2h with a detection limit of 4.9x104CFU/mL. No interference from S. aureus was observed. Furthermore, the proposed method was successfully applied to detect E. coli O157:H7 in spiked skim milk. The proposed detection system provided a potential method for E. coli O157:H7 and other pathogenic bacteria in food samples.

Zhang, Y., Matsuzaka, T., Yano, H., Furuta, Y., Nakano, T., Ishikawa, K., Fukuyo, M., Takahashi, N., Suzuki, Y., Sugano, S., Ide, H., and Kobayashi, I. Restriction glycosylases: involvement of endonuclease activities in the restriction process. Nucleic Acids Res. 2-17-2017; 45(3):1392-1403; PM: 28180312

ABSTRACT: All restriction enzymes examined are phosphodiesterases generating 3-OH and 5-P ends, but one restriction enzyme (restriction glycosylase) excises unmethylated bases from its recognition sequence. Whether its restriction activity involves endonucleolytic cleavage remains unclear. One report on this enzyme, R.PabI from a hyperthermophile, ascribed the breakage to high temperature while another showed its weak AP lyase activity generates atypical ends. Here, we addressed this issue in mesophiles. We purified R.PabI homologs from Campylobacter coli (R.CcoLI) and Helicobacter pylori (R.HpyAXII) and demonstrated their DNA cleavage, DNA glycosylase and AP lyase activities in vitro at 37 degrees C. The AP lyase activity is more coupled with glycosylase activity in R.CcoLI than in R.PabI. R.CcoLI/R.PabI expression caused restriction of incoming bacteriophage/plasmid DNA and endogenous chromosomal DNA within Escherichia coli at 37 degrees C. The R.PabI-mediated restriction was promoted by AP endonuclease action in vivo or in vitro. These results reveal the role of endonucleolytic DNA cleavage in restriction and yet point to diversity among the endonucleases. The cleaved ends are difficult to repair in vivo, which may indicate their biological significance. These results support generalization of the concept of restriction-modification system to the concept of self-recognizing epigenetic system, which combines any epigenetic labeling and any DNA damaging.

Zhao, G., Vatanen, T., Droit, L., Park, A., Kostic, A. D., Poon, T. W., Vlamakis, H., Siljander, H., Harkonen, T., Hamalainen, A. M., Peet, A., Tillmann, V., Ilonen, J., Wang, D., Knip, M., Xavier, R. J., and Virgin, H. W. Intestinal virome changes precede autoimmunity in type I diabetes-susceptible children. Proc.Natl.Acad.Sci.U.S.A. 7-25-2017; 114(30):E6166-E6175; PM: 28696303

ABSTRACT: Viruses have long been considered potential triggers of autoimmune diseases. Here we defined the intestinal virome from birth to the development of autoimmunity in children at risk for type 1 diabetes (T1D). A total of 220 virus-enriched preparations from serially collected fecal samples from 11 children (cases) who developed serum autoantibodies associated with T1D (of whom five developed clinical T1D) were compared with samples from controls. Intestinal viromes of case subjects were less diverse than those of controls. Among eukaryotic viruses, we identified significant enrichment of Circoviridae-related sequences in samples from controls in comparison with cases. Enterovirus, kobuvirus, parechovirus, parvovirus, and rotavirus sequences were frequently detected but were not associated with autoimmunity. For bacteriophages, we found higher Shannon diversity and richness in controls compared with cases and observed that changes in the intestinal virome over time differed between cases and controls. Using Random Forests analysis, we identified disease-associated viral bacteriophage contigs after subtraction of age-associated contigs. These disease-associated contigs were statistically linked to specific components of the bacterial microbiome. Thus, changes in the intestinal virome preceded autoimmunity in this cohort. Specific components of the virome were both directly and inversely associated with the development of human autoimmune disease.

Zhao, J., Liu, Y., Xiao, C., He, S., Yao, H., and Bao, G. Efficacy of Phage Therapy in Controlling Rabbit Colibacillosis and Changes in Cecal Microbiota. Front Microbiol. 2017; 8:957; PM: 28611755

ABSTRACT: Phage therapy is a valid weapon that we could use to fight against pathogens. Bacteriophages kill bacteria and self-proliferate in the digestive tract. Furthermore, it was assumed that phage therapy could preserve the existing gut microbiota. In this study, 45 rabbits were equally divided into three groups after they were orally inoculated with pathogenic Escherichia coli to induce gut infection. Each group was treated with bacteriophage ZRP1 (Group P), ciprofloxacin lactate (Group A), or phosphate-buffered solution (PBS) (Group N). Another 15 healthy rabbits composed the control group (Group C). The body weight gain decreased significantly, but the white blood cell (WBC) count, especially the percentage of large WBCs, and the serum endotoxin levels increased significantly after infection. The result of microscopic examination of the ileum showed that E. coli ZR1 adhered to villi and caused hemorrhage inside the villi. Groups P and A rabbits recovered after treatments, and both bacteriophage and antibiotic treatment significantly decreased the eaeA gene concentration in cecal contents. The microbiota in cecal contents changed in infected rabbits that were treated with PBS. The relative abundance of Clostridiales and YS2 decreased but the relative abundance of Enterobacteriales increased significantly. According to the principal components analysis, the microbiota of Groups P and C rabbits were similar to one another in type and relative abundance but different from those of Groups N and A rabbits. The results demonstrated that oral administration of bacteriophage can cure gut infection with minimal impact on the cecal microbiota.

Zheng, W., Wang, F., Taylor, N. M. I., Guerrero-Ferreira, R. C., Leiman, P. G., and Egelman, E. H. Refined Cryo-EM Structure of the T4 Tail Tube: Exploring the Lowest Dose Limit. Structure. 9-5-2017; 25(9):1436-1441; PM: 28757144

ABSTRACT: The bacteriophage T4 contractile tail (containing a tube and sheath) was the first biological assembly reconstructed in three dimensions by electron microscopy at a resolution of approximately 35 A in 1968. A single-particle reconstruction of the T4 baseplate was able to generate a 4.1 A resolution map for the first two rings of the tube using the overall baseplate for alignment. We have now reconstructed the T4 tail tube at a resolution of 3.4 A, more than a 1,000-fold increase in information content for the tube from 1968. We have used legacy software (Spider) to show that we can do better than the typical 2/3 Nyquist frequency. A reasonable map can be generated with only 1.5 electrons/A2 using the higher dose images for alignment, but increasing the dose results in a better map, consistent with other reports that electron dose does not represent the main limitation on resolution in cryo-electron microscopy.

Zhou, Z., Zuber, S., Cantergiani, F., Butot, S., Li, D., Stroheker, T., Devlieghere, F., Lima, A., Piantini, U., and Uyttendaele, M. Inactivation of viruses and bacteria on strawberries using a levulinic acid plus sodium dodecyl sulfate based sanitizer, taking sensorial and chemical food safety aspects into account. Int.J.Food Microbiol. 9-18-2017; 257:176-182; PM: 28668727

ABSTRACT: The efficacy of levulinic acid (LVA) in combination with sodium dodecyl sulfate (SDS) in removal of foodborne viruses, enteric bacterial pathogens and their surrogates on fresh strawberries was investigated. Inoculated strawberries were treated with potable water, sodium hypochlorite solution (50ppm), 0.5% LVA plus 0.5% SDS solution, and 5% LVA plus 2% SDS solution respectively for 2min, followed by spray-rinsing with potable water. Water washing removed at least 1.0-log of the tested viral and bacterial strains from the strawberries' surfaces. The 50ppm chlorine wash induced 3.4, 1.5 and 2.1-log reductions for hepatitis A virus (HAV), murine norovirus-1 (MNV-1) and MS2 bacteriophage, respectively. In comparison, the tested bacterial strains showed uniform reductions around 1.6-log CFU/ml. The 0.5% LVA plus 0.5% SDS wash induced 2.7, 1.4 and 2.4-log reductions for HAV, MNV-1 and MS2, which were comparable with the reductions induced by chlorine ($P>0.05$). For bacteria, over 2.0-log reductions were obtained for Enterococcus faecium, Listeria monocytogenes and Salmonella, while Escherichia coli O157:H7 and Escherichia coli P1 showed reductions of 1.9 and 1.8-log CFU/ml. Higher concentration of LVA plus SDS showed no significantly higher reductions ($P>0.05$). Sensory tests of washed strawberries and chemical residue analysis of LVA on strawberries after washing were also performed. In conclusion, this study demonstrates good performance of 0.5% LVA plus 0.5% SDS to reduce the levels of enteric pathogens if present on strawberries without altering taste and introducing chemical safety issues.

Zhvania, P., Hoyle, N. S., Nadareishvili, L., Nizharadze, D., and Kutateladze, M. Phage Therapy in a 16-Year-Old Boy with Netherton Syndrome. Front Med.(Lausanne). 2017; 4:94; PM: 28717637

ABSTRACT: Netherton syndrome (NS) is a rare autosomal recessive disorder, characterized by a classical triad of clinical features, including congenital ichthyosiform erythroderma, trichorrhexis invaginata, and atopic diathesis coupled with frequent bacterial infections (1). The genetic basis for the disease has been recently identified with

mutations in gene SPINK5, which is involved in the regulation of formation of skin barriers. We report on a 16-year-old male with all the typical manifestations of NS, including atopic diathesis and ongoing serious staphylococcal infections and allergy to multiple antibiotics whose family sought help at the Eliava Phage Therapy Center when all other treatment options were failing. Treatment with several antistaphylococcal bacteriophage preparations led to significant improvement within 7 days and very substantial changes in his symptoms and quality of life after treatment for 6 months, including return visits to the Eliava Phage Therapy Center after 3 and 6 months of ongoing use of phage at home.

Zinke, M., Fricke, P., Samson, C., Hwang, S., Wall, J. S., Lange, S., Zinn-Justin, S., and Lange, A. Bacteriophage Tail-Tube Assembly Studied by Proton-Detected 4D Solid-State NMR. Angew.Chem.Int.Ed Engl. 8-1-2017; 56(32):9497-9501; PM: 28644511

ABSTRACT: Obtaining unambiguous resonance assignments remains a major bottleneck in solid-state NMR studies of protein structure and dynamics. Particularly for supramolecular assemblies with large subunits (>150 residues), the analysis of crowded spectral data presents a challenge, even if three-dimensional (3D) spectra are used. Here, we present a proton-detected 4D solid-state NMR assignment procedure that is tailored for large assemblies. The key to recording 4D spectra with three indirect carbon or nitrogen dimensions with their inherently large chemical shift dispersion lies in the use of sparse non-uniform sampling (as low as 2 %). As a proof of principle, we acquired 4D (H)COCANH, (H)CACONH, and (H)CBCANH spectra of the 20 kDa bacteriophage tail-tube protein gp17.1 in a total time of two and a half weeks. These spectra were sufficient to obtain complete resonance assignments in a straightforward manner without use of previous solution NMR data.

Zoued, A., Durand, E., Santin, Y. G., Journet, L., Roussel, A., Cambillau, C., and Cascales, E. TssA: The cap protein of the Type VI secretion system tail. Bioessays. 8-17-2017; PM: 28817192

ABSTRACT: The Type VI secretion system (T6SS) is a multiprotein and mosaic apparatus that delivers protein effectors into prokaryotic or eukaryotic cells. Recent data on the enteroaggregative Escherichia coli (EAEC) T6SS have provided evidence that the TssA protein is a key component during T6SS biogenesis. The T6SS comprises a trans-envelope complex that docks the baseplate, a cytoplasmic complex that represents the assembly platform for the tail. The T6SS tail is structurally, evolutionarily and functionally similar to the contractile tails of bacteriophages. We have shown that TssA docks to the membrane complex, recruits the baseplate complex and initiates and coordinates the polymerization of the inner tube with that of the sheath. Here, we review these recent findings, discuss the variations within TssA-like proteins, speculate on the role of EAEC TssA in T6SS biogenesis and propose future research perspectives.

Zuo, T., Wong, S. H., Lam, K., Lui, R., Cheung, K., Tang, W., Ching, J. Y. L., Chan, P. K. S., Chan, M. C. W., Wu, J. C. Y., Chan, F. K. L., Yu, J., Sung, J. J. Y., and Ng, S. C. Bacteriophage transfer during faecal microbiota transplantation in Clostridium difficile infection is associated with treatment outcome. Gut. 5-24-2017; PM: 28539351

*ABSTRACT**: OBJECTIVE***: Faecal microbiota transplantation (FMT) is effective for the

treatment of recurrent Clostridium difficile infection (CDI). Studies have shown bacterial colonisation after FMT, but data on viral alterations in CDI are scarce. We investigated enteric virome alterations in CDI and the association between viral transfer and clinical outcome in patients with CDI. ***DESIGN***: Ultra-deep metagenomic sequencing of virus-like particle preparations and bacterial 16S rRNA sequencing were performed on stool samples from 24 subjects with CDI and 20 healthy controls. We longitudinally assessed the virome and bacterial microbiome changes in nine CDI subjects treated with FMT and five treated with vancomycin. Enteric virome alterations were assessed in association with treatment response. ***RESULTS***: Subjects with CDI demonstrated a significantly higher abundance of bacteriophage Caudovirales and a lower Caudovirales diversity, richness and evenness compared with healthy household controls. Significant correlations were observed between bacterial families Proteobacteria, Actinobacteria and Caudovirales taxa in CDI. FMT treatment resulted in a significant decrease in the abundance of Caudovirales in CDI. Cure after FMT was observed when donor-derived Caudovirales contigs occupied a larger fraction of the enteric virome in the recipients (p=0.024). In treatment responders, FMT was associated with alterations in the virome and the bacterial microbiome, while vancomycin treatment led to alterations in the bacterial community alone. ***CONCLUSIONS***: In a preliminary study, CDI is characterised by enteric virome dysbiosis. Treatment response in FMT was associated with a high colonisation level of donor-derived Caudovirales taxa in the recipient. Caudovirales bacteriophages may play a role in the efficacy of FMT in CDI. ***TRIAL REGISTRATION NUMBER***: NCT02570477.



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I. Probiotics & Bacteriotherapy

What are Probiotics? Am.Fam.Physician. 8-1-2017; 96(3):Online; PM: 28762700

No Abstract Available.

Aaron, J. G., Sobieszczyk, M. E., Weiner, S. D., Whittier, S., and Lowy, F. D. Lactobacillus rhamnosus Endocarditis After Upper Endoscopy. Open.Forum Infect.Dis. 2017; 4(2):ofx085; PM: 28695143

ABSTRACT: Lactobacillus rhamnosus is commonly found in gastrointestinal flora and used in probiotics but is a rare human pathogen. We report a case of L. rhamnosus endocarditis following upper endoscopy in a frequent consumer of yogurt containing the organism, who required aortic and mitral valve replacement for cure.

Abdelazez, A., Muhammad, Z., Zhang, Q. X., Zhu, Z. T., Abdelmotaal, H., Sami, R., and Meng, X. C. Production of a Functional Frozen Yogurt Fortified with Bifidobacterium spp. Biomed.Res.Int. 2017; 2017:6438528; PM: 28691028

ABSTRACT: Frozen dairy products have characteristics of both yogurt and ice cream and could be the persuasive carriers of probiotics. Functions of the frozen yogurt containing viable bifidobacterial cells are recognized and favored by the people of all ages. We developed a kind of yogurt supplemented by Bifidobacterium species. Firstly, five strains of Bifidobacterium spp. (Bifidobacterium bifidum ATCC 11547, Bifidobacterium longum ATCC 11549, Bifidobacterium infantis ATCC 11551, Bifidobacterium adolescentis ATCC 11550, and Bifidobacterium breve ATCC 11548) were evaluated based on the feasibility criteria of probiotics, comprising acid production, bile tolerance, and adhesion to epithelial cells. Formerly, we combined the optimum strains with yogurt culture (Lactobacillus delbrueckii subsp. bulgaricus EMCC 11102 and Streptococcus salivarius subsp. thermophilus EMCC 11044) for producing frozen yogurt. Finally, physiochemical properties and sensory evaluation of the frozen yogurt were investigated during storage of 60 days at -18 degrees C. Results directed that Bifidobacterium adolescentis ATCC 11550 and Bifidobacterium infantis ATCC 11551 could be utilized with yogurt culture for producing frozen yogurt. Moreover, the frozen yogurt fermented by two bifidobacterial strains and yogurt culture gained the high evaluation in the physiochemical properties and sensory evaluation. In summary, our results revealed that there was no significant difference between frozen yogurt fermented by Bifidobacterium spp. and yogurt culture and that fermented by yogurt culture only.

Abhisingha, M., Dumnil, J., and Pitaksutheepong, C. Selection of Potential Probiotic Lactobacillus with Inhibitory Activity Against Salmonella and Fecal Coliform Bacteria. Probiotics.Antimicrob.Proteins. 7-15-2017; PM: 28712023

ABSTRACT: Three hundred and sixty presumptive lactic acid bacteria (LAB) isolated from pregnant sows, newborn, suckling, and weaned piglets were preliminarily screened for anti-Salmonella activity. Fifty-eight isolates consisting of Lactobacillus reuteri (n = 32), Lactobacillus salivarius (n = 10), Lactobacillus mucosae (n = 8), Lactobacillus johnsonii (n

= 5), and Lactobacillus crispatus (n = 3) were selected and further characterized for probiotic properties including production of antimicrobial substances, acid and bile tolerance, and cell adherence to Caco-2 cells. Eight isolates including Lact. johnsonii LJ202 and Lact. reuteri LR108 were identified as potential probiotics. LJ202 was selected for further use in co-culture studies of two-bacterial and multiple-bacterial species to examine its inhibitory activity against Salmonella enterica serovar Enteritidis DMST7106 (SE7106). Co-culture of LJ202 and SE7106 showed that LJ202 could completely inhibit the growth of SE7106 in 10 h of co-culture. In co-culture of multiple-bacterial species, culturable fecal bacteria from pig feces were used as representative of multiple-bacterial species. The study was performed to examine whether interactions among multiple-bacterial species would influence antagonistic activity of LJ202 against SE7106 and fecal coliform bacteria. Co-culture of SE7106 with different combinations of fecal bacteria and probiotic (LJ202 and LR108) or non-probiotic (Lact. mucosae LM303) strains revealed that the growth of SE7106 was completely inhibited either in the presence or in the absence of probiotic strains. Intriguingly, LJ202 exhibited notable inhibitory activity against fecal coliform bacteria while LR108 did not. Taken together, the results of co-culture studies suggested that LJ202 is a good probiotic candidate for further study its inhibitory effects against pathogen infections in pigs.

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. 2017; 65:33-42; 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.

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.

Abrahamsson, T. R. Using probiotics to prevent necrotising enterocolitis. Acta Paediatr. 9-15-2017; PM: 28914455

No Abstract Available.

Abrao, F. O., Duarte, E. R., Pessoa, M. S., Santos, V. L. D., Freitas Junior, L. F., Barros, K. O., Hughes, A. F. D. S., Silva, T. D., and Rodriguez, N. M. Notable fibrolytic enzyme production by Aspergillus spp. isolates from the gastrointestinal tract of beef cattle fed in lignified pastures. PLoS.One. 2017; 12(8):e0183628; PM: 28850605

ABSTRACT: Fungi have the ability to degrade vegetal cell wall carbohydrates, and their presence in the digestive tract of ruminants can minimize the effects of lignified forage on ruminal fermentation. Here, we evaluated enzyme production by Aspergillus spp. isolates from the digestive tracts of cattle grazed in tropical pastures during the dry season. Filamentous fungi were isolated from rumen and feces by culture in cellulose-based medium. Ninety fungal strains were isolated and identified by rDNA sequence analysis, microculture, or both. Aspergillus terreus was the most frequently isolated species, followed by Aspergillus fumigatus. The isolates were characterized with respect to their cellulolytic, xylanolytic, and lignolytic activity through qualitative evaluation in culture medium containing a specific corresponding carbon source. Carboxymethyl cellulase (CMCase) activity was quantified by the reducing sugar method. In the avicel and xilan degradation test, the enzyme activity (EA) at 48 h was significantly higher other periods ($P < 0.05$). Intra- and inter-specific differences in EA were verified, and high levels of phenoloxidases, which are crucial for lignin degradation, were observed in 28.9% of the isolates. Aspergillus terreus showed significantly higher EA for avicelase (3.96 +/-1.77) and xylanase (3.13 +/-.091) than the other Aspergillus species at 48 h of incubation. Isolates AT13 and AF69 showed the highest CMCase specific activity (54.84 and 33.03 U

mg-1 protein, respectively). Selected Aspergillus spp. isolates produced remarkable levels of enzymes involved in vegetal cell wall degradation, suggesting their potential as antimicrobial additives or probiotics in ruminant diets.

Abriouel, H., Perez, Montoro B., Casimiro-Soriguer, C. S., Perez Pulido, A. J., Knapp, C. W., Caballero, Gomez N., Castillo-Gutierrez, S., Estudillo-Martinez, M. D., Galvez, A., and Benomar, N. Insight into Potential Probiotic Markers Predicted in Lactobacillus pentosus MP-10 Genome Sequence. Front Microbiol. 2017; 8:891; PM: 28588563

ABSTRACT: Lactobacillus pentosus MP-10 is a potential probiotic lactic acid bacterium originally isolated from naturally fermented Alorena green table olives. The entire genome sequence was annotated to in silico analyze the molecular mechanisms involved in the adaptation of L. pentosus MP-10 to the human gastrointestinal tract (GIT), such as carbohydrate metabolism (related with prebiotic utilization) and the proteins involved in bacteria-host interactions. We predicted an arsenal of genes coding for carbohydrate-modifying enzymes to modify oligo- and polysaccharides, such as glycoside hydrolases, glycoside transferases, and isomerases, and other enzymes involved in complex carbohydrate metabolism especially starch, raffinose, and levan. These enzymes represent key indicators of the bacteria's adaptation to the GIT environment, since they involve the metabolism and assimilation of complex carbohydrates not digested by human enzymes. We also detected key probiotic ligands (surface proteins, excreted or secreted proteins) involved in the adhesion to host cells such as adhesion to mucus, epithelial cells or extracellular matrix, and plasma components; also, moonlighting proteins or multifunctional proteins were found that could be involved in adhesion to epithelial cells and/or extracellular matrix proteins and also affect host immunomodulation. In silico analysis of the genome sequence of L. pentosus MP-10 is an important initial step to screen for genes encoding for proteins that may provide probiotic features, and thus provides one new routes for screening and studying this potentially probiotic bacterium.

Aceti, A., Maggio, L., Beghetti, I., Gori, D., Barone, G., Callegari, M. L., Fantini, M. P., Indrio, F., Meneghin, F., Morelli, L., Zuccotti, G., and Corvaglia, L. Probiotics Prevent Late-Onset Sepsis in Human Milk-Fed, Very Low Birth Weight Preterm Infants: Systematic Review and Meta-Analysis. Nutrients. 8-22-2017; 9(8); PM: 28829405

ABSTRACT: Growing evidence supports the role of probiotics in reducing the risk of necrotizing enterocolitis, time to achieve full enteral feeding, and late-onset sepsis (LOS) in preterm infants. As reported for several neonatal clinical outcomes, recent data have suggested that nutrition might affect probiotics' efficacy. Nevertheless, the currently available literature does not explore the relationship between LOS prevention and type of feeding in preterm infants receiving probiotics. Thus, the aim of this systematic review and meta-analysis was to evaluate the effect of probiotics for LOS prevention in preterm infants according to type of feeding (exclusive human milk (HM) vs. exclusive formula or mixed feeding). Randomized-controlled trials involving preterm infants receiving probiotics and reporting on LOS were included in the systematic review. Only trials reporting on outcome according to feeding type were included in the meta-analysis. Fixed-effects models were used and random-effects models were used when significant heterogeneity was found. The results were expressed as risk ratio (RR) with 95% confidence interval (CI). Twenty-five studies were included in the meta-analysis. Overall, probiotic supplementation resulted in a significantly lower incidence of LOS (RR 0.79 (95%

CI 0.71-0.88), p < 0.0001). According to feeding type, the beneficial effect of probiotics was confirmed only in exclusively HM-fed preterm infants (RR 0.75 (95% CI 0.65-0.86), p < 0.0001). Among HM-fed infants, only probiotic mixtures, and not single-strain products, were effective in reducing LOS incidence (RR 0.68 (95% CI 0.57-0.80) p < 0.00001). The results of the present meta-analysis show that probiotics reduce LOS incidence in exclusively HM-fed preterm infants. Further efforts are required to clarify the relationship between probiotics supplementation, HM, and feeding practices in preterm infants.

Acurcio, L. B., Sandes, S. H. C., Bastos, R. W., Sant'anna, F. M., Pedroso, S. H. S. P., Reis, D. C., Nunes, A. C., Cassali, G. D., Souza, M. R., and Nicoli, J. R. Milk fermented by Lactobacillus species from Brazilian artisanal cheese protect germ-free-mice against Salmonella Typhimurium infection. Benef.Microbes. 8-24-2017; 8(4):579-588; PM: 28789560

ABSTRACT: Ingestion of milks fermented by Lactobacillus strains showing probiotic properties is an important tool to maintain gastrointestinal health. In this study, Lactobacillus rhamnosus D1 and Lactobacillus plantarum B7, isolated from Brazilian artisanal cheese, were used as starters for the functional fermented milks to assess their probiotic properties in a gnotobiotic animal model. Male germ-free Swiss mice received a single oral dose of milk fermented by each sample, and were challenged with Salmonella Typhimurium five days afterwards. Milk fermented by both Lactobacillus strains maintained counts above 108 cfu/ml during cold storage. Lactobacillus strains colonised the gut of the germ-free-mice, maintaining their antagonistic effect. This colonisation led to a protective effect against Salmonella challenge, as demonstrated by reduced pathogen translocation and histological lesions, when compared to control group, especially for Lactobacillus rhamnosus D1. Additionally, mRNA expression of inflammatory (interferon gamma, interleukin (IL)-6, tumour necrosis factor alpha) and anti-inflammatory (transforming growth factor beta1) cytokines was augmented in animals previously colonised and then challenged, when compared to other experimental groups. Lactobacillus plantarum B7 colonisation also promoted higher expression of IL-17, showing a proper maturation of colonised germ-free-mice immune system. IL-5 was stimulated by both strains' colonisation and not by S. Typhimurium challenge.

Adhikari, B. and Kwon, Y. M. Characterization of the Culturable Subpopulations of Lactobacillus in the Chicken Intestinal Tract as a Resource for Probiotic Development. Front Microbiol. 2017; 8:1389; PM: 28798730

ABSTRACT: To gain better understanding of the distributions of the culturable Lactobacillus species in the chicken intestinal tract, we collected ceca, and distal ileum from 10 3-weeks-old broiler chickens. Lactobacillus strains from cecal lumen contents (M-CL), and those associated with mucosa of ceca (M-CM) and ileum (M-IM) were recovered on de Man, Rogosa and Sharpe (MRS) agar plates, and used for microbiota analysis. The total cecal content (T-CL) was also used directly for microbiota analysis. We purposefully focused on MRS-recovered populations to gain understanding of the culturable subpopulations of Lactobacillus, since the culturability is an important phenotype in order to exploit the chicken gut microbiota as a resource for development of probiotics. The V1-V3 regions of 16S rRNA gene was amplified from genomic DNA samples, and the pooled amplicons were analyzed by MiSeq sequencing with paired-end read 300 cycle option. Among MRS groups, Firmicutes were significantly higher in M-IM and M-CL as compared to M-CM, whereas Proteobacteria were significantly higher in

M-CM as compared to M-IM and M-CL at $p < 0.05$. Among Lactobacillus, L. salivarius (36%) and L. johnsonii (21%) were higher in M-IM as compared to M-CL (L. salivarius, 28%; L. johnsonii, 15%), and M-CM (L. salivarius, 20%; L. johnsonii, 11%). L. crispatus was found significantly higher in M-CL as compared to M-IM ($p < 0.01$) whereas L. gasseri was found significantly higher in M-IM as compared to M-CM ($p < 0.05$). L. aviarius, and L. fornicalis were only observed in T-CL. In summary, Lactobacillus populations recovered on MRS vary with different regions and locations in chicken GIT, which might indicate their distinct functional roles in different gastrointestinal tract (GIT) niches, and some species of Lactobacillus are not culturable on MRS agar media. This study is the first attempt to define culturable Lactobacillus subpopulations in the chicken intestinal tract comprehensively using 16S rRNA gene profiling, and the findings of this study will be used as a platform to develop a new strategy for isolation of effective Lactobacillus probiotic candidates based on comparative analyses of chicken gut microbiota.

Ai, R., Wei, J., Ma, D., Jiang, L., Dan, H., Zhou, Y., Ji, N., Zeng, X., and Chen, Q. A meta-analysis of randomized trials assessing the effects of probiotic preparations on oral candidiasis in the elderly. Arch.Oral Biol. 4-30-2017; 83:187-192; PM: 28783552

ABSTRACT: ***OBJECTIVE***: Oral candidiasis is the most common fungal infection and can be attributed in part to dysbiosis, an imbalance in the resident oral microflora. Therefore, probiotics, which counter pathogenic microorganisms through competitive, antagonistic, and immunological effects, have been used by some clinicians. To date, the effect of probiotics in preventing oral candidiasis in the elderly is controversial. A systematic review that summarizes and critically appraises the available clinical trials is therefore necessary. ***DESIGN***: Electronic searches were performed using the Pubmed, Embase, and Cochrane databases. Only randomized controlled trials were included. The Mantel-Haenszel test was used to appraise the odds ratio for single studies and an overall combined odds ratio for all studies combined. ***RESULTS***: Three studies matched the inclusion criteria and were homogeneous. The data from one study that estimated candida growth from plaque and saliva were subdivided, thus a total of four studies with 595 people were included. The overall combined odds ratio was 0.54 (95% CI: 0.38-0.77). Three studies provided that active treatment reduced the risk of oral candidiasis more than placebo: Hatakka et al. (OR 0.51, 95% CI 0.26 to 0.97; 192 participants, plaque); Kraft-Bodi et al. (OR 0.46, 95% CI 0.24 to 0.86; 174 participants, palatal); Kraft-Bodi et al. (OR 0.50, 95% CI 0.26 to 0.98; 174 participants, plaque), while one study provided reverse result: Ishikawa et al. (OR 1.24, 95% CI 0.48 to 3.58; 55 participants, saliva). ***CONCLUSION***: Probiotics have a preventative effect on oral candidiasis in the elderly.

Aitbaev, K. A., Murkamilov, I. T., and Fomin, V. V. [Liver diseases: The pathogenetic role of the gut microbiome and the potential of treatment for its modulation]. Ter.Arkh. 2017; 89(8):120-128; PM: 28914862

ABSTRACT: The paper gives an update on the role of the gut microbiome (GM) in the development of nonalcoholic fatty liver disease, nonalcoholic steatohepatitis, alcoholic liver disease, liver cirrhosis (LC), and its complications, such as hepatic encephalopathy (HE) and hepatocellular carcinoma (HCC), and discusses the possibilities of its correction with prebiotics, probiotics, synbiotics, antibiotics, and fecal microbiota transplantation (FMT). The pathophysiology of the liver diseases in question demonstrates some common features that are characterized by pathogenic changes in the composition of the gastrointestinal tract microflora, by intestinal barrier impairments, by development of

endotoxemia, by increased liver expression of proinflammatory factors, and by development of liver inflammation. In progressive liver disease, the above changes are more pronounced, which contributes to the development of LC, HE, and HCC. GM modulation using prebiotics, probiotics, synbiotics, antibiotics, and FMT diminishes dysbacteriosis, strengthens the intestinal mucosal barrier, reduces endotoxemia and liver damage, and positively affects the clinical manifestations of HE. Further investigations are needed, especially in humans, firstly, to assess a relationship of GM to the development of liver diseases in more detail and, secondly, to obtain evidence indicating the therapeutic efficacy of GM-modulating agents in large-scale, well-designed, randomized, controlled, multicenter studies.

Aitoro, R., Paparo, L., Amoroso, A., Di, Costanzo M., Cosenza, L., Granata, V., Di, Scala C., Nocerino, R., Trinchese, G., Montella, M., Ercolini, D., and Berni, Canani R. Gut Microbiota as a Target for Preventive and Therapeutic Intervention against Food Allergy. Nutrients. 6-28-2017; 9(7); PM: 28657607

ABSTRACT: The gut microbiota plays a pivotal role in immune system development and function. Modification in the gut microbiota composition (dysbiosis) early in life is a critical factor affecting the development of food allergy. Many environmental factors including caesarean delivery, lack of breast milk, drugs, antiseptic agents, and a low-fiber/high-fat diet can induce gut microbiota dysbiosis, and have been associated with the occurrence of food allergy. New technologies and experimental tools have provided information regarding the importance of select bacteria on immune tolerance mechanisms. Short-chain fatty acids are crucial metabolic products of gut microbiota responsible for many protective effects against food allergy. These compounds are involved in epigenetic regulation of the immune system. These evidences provide a foundation for developing innovative strategies to prevent and treat food allergy. Here, we present an overview on the potential role of gut microbiota as the target of intervention against food allergy.

Akhtar, N. and Pathak, K. Probiotics as a Tool to Biosynthesize Metallic Nanoparticles: Research Reports and Patents Survey. Recent Pat Drug Deliv.Formul. 2017; 11(1):5-18; PM: 28294074

*ABSTRACT**: BACKGROUND***: Probiotics are the live microbes that exert beneficial effects on the health of the host cell, creating novel nanoformulations via probiotic bacteria, thus gaining 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 the focus of research nowadays due to several applications. Research inputs have led to the 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.

Aluwong, T., Sumanu, V. O., Ayo, J. O., Ocheja, B. O., Zakari, F. O., and Minka, N. S. Daily rhythms of cloacal temperature in broiler chickens of different age groups administered with zinc gluconate and probiotic during the hot-dry season. Physiol Rep. 2017; 5(12); PM: 28637707

ABSTRACT: The aim of the experiment was to evaluate effects of zinc gluconate (ZnGlu) and probiotic administration on the daily rhythm of cloacal temperature (tcloacal) in broiler chickens of different age groups during the hot-dry season. One-day-old broiler chicks (n = 60) were divided into groups I-IV of 15 chicks per group, and treated for 35 days: Group I (control) was given deionized water; Group II, ZnGlu (50 mg/kg); Group III, probiotic (4.125 x 106 cfu/100 mL), and Group IV, ZnGlu (50 mg/kg) + probiotic (4.125 x 106 cfu/100 mL). Air dry-bulb temperature (tdb), relative humidity (RH), and temperature-humidity index (THI) inside the pen, and tcloacal of each broiler chick were obtained bihourly over a 24-h period; on days 21, 28, and 35 of the study. Values of tdb (32.10 +/- 0.49 degrees C), RH (49.94 +/- 1.91%), and THI (38.85 +/- 0.42) obtained were outside the thermoneutral zone for broiler chickens, and suggested that the birds were subjected to heat stress. Application of the periodic model showed disruption of daily rhythm of tcloacal in broilers on day 21, which was synchronized by probiotic administration. The administration of probiotics or ZnGlu + probiotics to a greater extent decreased the mesor and amplitude, delayed the acrophases of tcloacal in broilers, especially at day 35, as compared to the controls. Overall, the tcloacal values in broiler chickens administered with probiotic alone (41.25 +/- 0.05 degrees C) and ZnGlu + probiotic (41.52 +/- 0.05 degrees C) were lower ($P < 0.001$) than that of the controls (41.94 +/- 0.06 degrees C). In conclusion, probiotic alone synchronized tcloacal of the birds at day 21, and, in addition, decreased tcloacal response most, followed by its coadministration with ZnGlu, the antioxidants may be beneficial in modulating daily rhythmicity of tcloacal and alleviating adverse effects of heat stress on broiler chickens during the hot-dry season.

Amenyogbe, N., Kollmann, T. R., and Ben-Othman, R. Early-Life Host-Microbiome Interphase: The Key Frontier for Immune Development. Front Pediatr. 2017; 5:111; PM: 28596951

ABSTRACT: Human existence can be viewed as an "animal in a microbial world." A healthy interaction of the human host with the microbes in and around us heavily relies on a well-functioning immune system. As development of both the microbiota and the host immune system undergo rapid changes in early life, it is not surprising that even minor alterations during this co-development can have profound consequences. Scrutiny of existing data regarding pre-, peri-, as well as early postnatal modulators of newborn microbiota indeed suggest strong associations with several immune-mediated diseases with onset far beyond the newborn period. We here summarize these data and extract overarching themes. This same effort in turn sets the stage to guide effective countermeasures, such as probiotic administration. The objective of our review is to highlight the interaction of host immune ontogeny with the developing microbiome in early life as a critical window of susceptibility for lifelong disease, as well as to identify the enormous potential to protect and promote lifelong health by specifically targeting this window of opportunity.

Andersen, A. D., Cilieborg, M. S., Lauridsen, C., Morkbak, A. L., and Sangild, P. T. Supplementation with Lactobacillus paracasei or Pediococcus pentosaceus does not prevent diarrhoea in neonatal pigs infected with Escherichia coli F18. Br.J.Nutr. 2017; 118(2):109-120; PM: 28720151

ABSTRACT: Infectious diarrhoea is a worldwide problem in newborns. Optimal bacterial colonisation may enhance gut maturation and protect against pathogenic bacteria after birth. We hypothesised that lactic acid bacteria (LAB) administration prevents pathogen-induced diarrhoea in formula-fed newborns. Newborn caesarean-delivered, colostrum-deprived term piglets on parenteral nutrition for the first 15 h, were used as models for sensitive newborn infants. A commercially available probiotic strain, Lactobacillus paracasei F19 (LAP, 2.6x108 colony-forming units (CFU)/kg per d) and a novel LAB isolate, Pediococcus pentosaceus (PEP, 1.3x1010 CFU/kg per d), were administered for 5 d with or without inoculation of the porcine pathogen, Escherichia coli F18 (F18, 1010 CFU/d). This resulted in six treatment groups: Controls (n 9), LAP (n 10), PEP (n 10), F18 (n 10), F18-LAP (n 10) and F18-PEP (n 10). The pathogen challenge increased diarrhoea and density of F18 in the intestinal mucosa ($P<0.05$). LAB supplementation further increased the diarrhoea score, relative to F18 alone ($P<0.01$). Intestinal structure and permeability were similar among groups, whereas brush border enzymes were affected in variable intestinal regions with decreased activities in most cases after F18 and LAB inoculation. Bacterial density in colon mucosa increased after F18 inoculation ($P<0.05$) but was unaffected by LAB supplementation. In colon contents, acetic and butyric acids were increased by PEP ($P<0.05$). The LAB used in this study failed to reduce E. coli-induced diarrhoea in sensitive newborn pigs. In vulnerable newborns there may be a delicate balance among bacterial composition and load, diet and the host. Caution may be required when administering LAB to compromised newborns suffering from enteric infections.

Angurana, S. K. Probiotics in the Pediatric ICU: Beyond Blurred Lines. Chest. 2017; 152(3):685-686; PM: 28889889

No Abstract Available.

Ansari, F., Pourjafar, H., Jodat, V., Sahebi, J., and Ataei, A. Effect of Eudragit S100 nanoparticles and alginate chitosan encapsulation on the viability of Lactobacillus acidophilus and Lactobacillus rhamnosus. AMB.Express. 2017; 7(1):144; PM: 28687035

ABSTRACT: In this study, we examined a novel method of microencapsulation with calcium alginate-chitosan and Eudragit S100 nanoparticles for the improving viability of probiotic bacteria, Lactobacillus acidophilus and Lactobacillus rhamnosus. Extrusion technique was carried out in microencapsulation process. The viability of two probiotics in single coated beads (with only chitosan), double coated beads (with chitosan and Eudragit nanoparticles), and as free cells (unencapsulated) were conducted in simulated gastric juice (pH 1.55, without pepsin) followed by incubation in simulated intestinal juice (pH 7.5, with 1% bile salt). In case of single coated beads, presumably, lack of sufficient strength of chitosan under simulated gastric condition was the main reason of 4-log and 5-log reduction of the counts of the L. acidophilus and L. rhamnosus respectively. The results showed that with the second coat forming (Eudragit

nanoparticles) over the first coat (chitosan), the strength of the beads and then viability rate of the bacteria were increased in comparison with the single coated beads.

Araujo, J. R., Tomas, J., Brenner, C., and Sansonetti, P. J. Impact of high-fat diet on the intestinal microbiota and small intestinal physiology before and after the onset of obesity. Biochimie. 5-29-2017; PM: 28571979

ABSTRACT: The modulation of the intestinal microbiota by high-fat diet (HFD) has a major impact on both immunological and metabolic functions of the host. Taking this into consideration, the aim of this contribution is to review the impact of HFD on microbiota profile and small intestinal physiology before and after the onset of obesity and its metabolic complications. Evidence from animal studies suggest that before the onset of obesity and its metabolic complications, HFD induces intestinal dysbiosis - encompassing changes in composition balance and massive redistribution with bacteria occupying intervillous spaces and crypts - associated with early physiopathological changes, predominantly in the ileum, such as low-grade inflammation, decreased antimicrobial peptides expression, impaired mucus production, secretion and layer's thickness, and decreased expression of tight junction proteins. With time, major inflammatory signals (e.g. toll-like receptor-4 dependent) become activated, thereby stimulating proinflammatory cytokines secretion in the small intestine. This inflammatory state might subsequently exacerbate disruption of the mucus layer barrier and increase epithelial permeability of the small intestine, thereby creating an environment that facilitates the passage of bacterial components (e.g. lipopolysaccharide, peptidoglycan and flagellin) and metabolites from the intestinal lumen (e.g. secondary bile acids) to the circulation and peripheral tissues (i.e. leaky gut), eventually promoting the development of systemic inflammation, obesity, adiposity, insulin resistance and glucose intolerance preceding hyperglycemia. Although the mechanisms are still not completely understood, prebiotics, probiotics, polyphenols, peroxisome proliferator-activated receptor-gamma agonists (such as rosiglitazone) and exercise have been shown to reverse HFD-induced intestinal phenotype and to attenuate the severity of obesity and its associated metabolic complications.

Artene, D. V., Bordea, C. I., and Blidaru, A. Results of 1-year Diet and Exercise Interventions for ER+/PR+/-/. Chirurgia.(Bucur.). 2017; 112(4):457-468; PM: 28862123

*ABSTRACT**: PURPOSE***: Many breast cancer patients gain weight during chemotherapy and antiestrogenic treatment increasing recurrence, oncologic specific and all-cause mortality risks. Patients and Methods: 165 ER+/PR+/-/.

Ashwar, B. A., Gani, A., Gani, A., Shah, A., and Masoodi, F. A. Production of RS4 from rice starch and its utilization as an encapsulating agent for targeted delivery of probiotics. Food Chem. 1-15-2018; 239:287-294; PM: 28873571

ABSTRACT: The research reported in this article is based on the hypothesis that crosslinking of starch can make it a potential wall material for targeted delivery of probiotics by altering its digestion. Three probiotic strains namely Lactobacillus casei, Lactobacillus brevis and Lactobacillus plantarum were microencapsulated with resistant starch. Encapsulation yield (%) of resistant starch microspheres was in the range of 43.01-48.46. The average diameter of resistant starch microparticles was in the range of 45.53-49.29mum. Fourier transform infrared (FT-IR) spectroscopy of microcapsules showed

peaks in the region of 900-1300cm-1 and 2918-2925cm-1 which corresponds to the presence of bacteria. Differential Scanning Calorimeter (DSC) showed better thermal stability of resistant starch microcapsules. Microencapsulated probiotics survived well in simulated gastrointestinal conditions and adverse heat conditions. The viability of the microcapsulated lactobacilli also remained high (>7 log cfu g-1) for 2months at 4 degrees C. The results revealed that resistant starch is the potential new delivery carrier for oral administration of probiotics.

Ayyash, M., Al-Nuaimi, A. K., Al-Mahadin, S., and Liu, S. Q. In vitro investigation of anticancer and ACE-inhibiting activity, alpha-amylase and alpha-glucosidase inhibition, and antioxidant activity of camel milk fermented with camel milk probiotic: A comparative study with fermented bovine milk. Food Chem. 1-15-2018; 239:588-597; PM: 28873609

ABSTRACT: This study aimed to investigate in vitro the health-promoting benefits (anticancer activity, alpha-amylase and alpha-glucosidase inhibition, angiotensin-converting-enzyme (ACE)-inhibition, antioxidant and proteolytic activity) of camel milk fermented with indigenous probiotic strains of Lactobacillus spp., compared with fermented bovine milk. The three camel milk probiotic strains Lb. reuteri-KX881777, Lb. plantarum-KX881772, Lb. plantarum-KX881779 and a control strain Lb. plantarum DSM2468 were employed to ferment camel and bovine milks separately. The proteolytic and antioxidant activity of water soluble extracts (WSEs) from all fermented camel milks were higher than those of fermented bovine milk. alpha-Amylase inhibition of WSEs were >34% in both milk types fermented with all strains during storage periods, except the WSE of camel milk fermented by Lp.K772. The highest ACE-inhibition of the WSE from camel milk fermented by Lr.K777 was >80%. The proliferations of Caco-2, MCF-7 and HELA cells were more inhibited when treated with the WSE of fermented camel milk.

Azhar, N. S., Md Zin, N. H., and Hamid, T. H. T. A. Lactococcus Lactis Strain A5 Producing Nisin-like Bacteriocin Active against Gram Positive and Negative Bacteria. Trop.Life Sci.Res. 2017; 28(2):107-118; PM: 28890764

ABSTRACT: In this study, a Lactic acid bacteria (LAB) strain was isolated on MRS medium from gastro-intestinal tissues of Broadhead catfish (Clarias macrocephalus). Out of 50 isolates, 25 isolates were found to be positive on lactose utilisation test and were identified to be gram positive cocci. Using disc diffusion methods, one out of 22 isolates, i.e., a strain A5 demonstrated inhibitions against three indicator organisms; Bacillus cereus, Staphylococcus aureus and Salmonella thyphimurium. Partial 16S rDNA sequencing identified isolate A5 as a member of Lactococcus lactis, with 100% DNA homology. Cell free supernatant fluid from Lactococcus lactis A5 showed inhibitory activities against both gram positive pathogens (Bacillus cereus and Staphylococcus aureus) and gram negative pathogens (Salmonella thyphimurium). Chloroform precipitated bacteriocin retained antagonistic activities in the presence of catalase and lysozyme; and was completely inactivated by Proteinase K treatment. The bacteriocin has a molecular weight of 3.4 kDa, based on SDS-PAGE analysis and the extract was heat stable at 37 degrees C and 65 degrees C, for 15 minutes. The antibacterial activity was suppressed with the addition of EDTA but was significantly increased with the addition of SDS, Triton X-100, Tween 20 and Tween 80. This bacteriocin belongs to class 1 bacteriocin, which was shown to have a nisin-like properties. This strain can be used as potential probiotics in animal or aquaculture feeding; and the bacteriocin it produces will be useful in food preservative.

Bailey, J. R., Vince, V., Williams, N. A., and Cogan, T. A. Streptococcus thermophilus NCIMB 41856 ameliorates signs of colitis in an animal model of inflammatory bowel disease. Benef.Microbes. 8-24-2017; 8(4):605-614; PM: 28618865

ABSTRACT: Treatment of inflammatory bowel disease (IBD) is mainly based on suppression of symptoms, often with numerous side effects. Trials of probiotics in IBD have frequently produced disappointing results. The majority of probiotics are unusual, since they do not require iron for growth, unlike many bacteria resident in the intestine. The IBD intestine is iron-rich due to bleeding and use of oral iron supplements; conventional probiotics would be rapidly outcompeted. We have evaluated an iron-responsive Streptococcus thermophilus strain for its potential to reduce signs of colitis. Efficacy of S. thermophilus was evaluated in the dextran sodium sulphate mouse model of colitis. Treated animals were given 1x108 cfu S. thermophilus per day and clinical observations were taken daily. At termination, gross and histopathological signs of disease, cellular infiltration, location of bacteria, and cytokine expression in the intestine were determined. S. thermophilus delayed onset of colitis and reduced clinical signs of disease, including bodyweight loss and gastrointestinal bleeding. It reduced bacterial translocation into the colonic tissue. Increased numbers of CD8+ intraepithelial lymphocytes were seen in control animals treated with S. thermophilus. S. thermophilus had no effect on gross pathology, histopathology or cytokine production in either colitic or control animals. We propose that S. thermophilus promotes maintenance of mucosal barrier function which reduces bacterial translocation, thereby reducing immune stimulation and associated inflammation. This allows mucosal healing, reducing gastrointestinal bleeding and weight loss. This could be studied as a locally-acting adjunct or alternative to current IBD treatments.

Bailey, M. T. and Cryan, J. F. The microbiome as a key regulator of brain, behavior and immunity: Commentary on the 2017 named series. Brain Behav.Immun. 8-23-2017; PM: 28843452

ABSTRACT: The focus on the microbiome for the 2017 Named Series in Brain, Behavior, and Immunity reflects the rapidly growing interest in commensal microbes and the effects that they can have on physiological processes often studied in PsychoNeuroImmunology Research. The studies included in this Named Series show that commensal microbes can impact immune system activity, as well as brain and behavioral processes across the lifespan, and are involved in behavioral and immunological responses to social stresses. The studies also show that dietary effects on brain, behavior, and immunity often involve alterations of the gut microbiota. Thus, diet can be used therapeutically for diseases and conditions involving the brain, behavior, and immunity, as can treatment with both pre- and probiotics. While this has been widely tested in animal models, fewer studies have focused on pre- and probiotic treatment in humans. The studies in this Named Series highlight the challenges of probiotic research in human populations, but also highlight the future promise of probiotics for human health. While emotional disorders, such as anxiety and depression have been often been linked to alterations in the gut microbiota, studies in this Named Series identify new domains involving interactions between the microbiota, brain, behavior, and immunity, including schizophrenia, traumatic brain injury, and stroke. As a whole, this collection of work demonstrates the importance of the microbiome in regulating key aspects of immunity, brain, and behavior, and provides important rationale for extending the work so that findings can be translated into clinical practice.

Bajpai, V. K., Chandra, V., Kim, N. H., Rai, R., Kumar, P., Kim, K., Aeron, A., Kang, S. C., Maheshwari, D. K., Na, M., Rather, I. A., and Park, Y. H. Ghost probiotics with a combined regimen: a novel therapeutic approach against the Zika virus, an emerging world threat. Crit Rev.Biotechnol. 9-7-2017; 1-17; PM: 28877637

ABSTRACT: The Zika virus (ZIKV) used to be an obscure flavivirus closely related to dengue virus (DENV). Transmission of this epidemic pathogen occurs mainly via mosquitoes, but it is also capable of placental and sexual transmission. Although the characteristics of these viruses are well defined, infections are unpredictable in terms of disease severity, unusual clinical manifestations, unexpected methods of transmission, long-term persistence, and the development of new strains. Recently, ZIKV has gained huge medical attention following the large-scale epidemics around the world, and reported cases of congenital abnormalities associated with Zika virus infections which have created a public health emergency of international concern. Despite continuous research on ZIKV, no specific treatment or vaccine has been developed, excepting a preventive strategy for congenital ZIKV infection. Probiotics, known as GRAS, are bacteria that confer various health beneficial effects, and have been shown to be effective at curing a number of viral diseases by modulating the immune system. Furthermore, probiotic preparations consisting of dead cells and cellular metabolites, so-called "Ghost probiotics", can also act as biological response modifiers. Here, we review available information on the epidemiology, transmission, and clinical features of ZIKV, and on treatment and prevention strategies. In addition, we emphasize the use of probiotics and plant-based natural remedies and describe their action mechanisms, and the green technologies for microbial conversion, which could contribute to the development of novel therapies that may reduce the pathogenicity of ZIKV. Accordingly, we draw attention to new findings, unanswered questions, unresolved issues, and controversies regarding ZIKV.

Banna, G. L., Torino, F., Marletta, F., Santagati, M., Salemi, R., Cannarozzo, E., Falzone, L., Ferrau, F., and Libra, M. Lactobacillus rhamnosus GG: An Overview to Explore the Rationale of Its Use in Cancer. Front Pharmacol. 2017; 8:603; PM: 28919861

ABSTRACT: Cancer is the second leading cause of death in the western world. In the era of precision medicine, a significant number of cancer patients can be cured with several anti-cancer therapeutic regimens. However, therapy failure may be caused by treatment side effects, such as diarrhea, especially occurring in patients with gastrointestinal or pelvic malignancies. In particular, diarrhea is one of the most frequent gastrointestinal toxicity during cancer treatment and it can result from nearly bot chemo- and radio-therapeutic strategies currently used. Diarrhea has a serious impact on patients' quality of life and treatment dosing and schedule modification due to its severity can negatively influence treatment outcomes. In this context, probiotics may play an interesting role in several human diseases with an inflammatory bowel involvement and, among these, Lactobacillus rhamnosus GG (LGG) is one of the most characterized and utilized. In particular, LGG is able to reverse intestinal dysbiosis and moderate diarrhea. Moreover, preclinical studies have documented its effects in reducing chronic inflammation associated with cancer development. This review summarizes the preclinical results of LGG on cancer cells proliferation and tumor invasion as well as the potential role of LGG use in cancer patients for the prevention and management of diarrhea associated with cancer treatment. Overall, these encouraging data support further investigation on the use of LGG in stratified patients undergoing

specific therapeutic protocols, including chemotherapy and pelvic radiotherapy, in order to reduce the development of severe diarrhea and thus improve the adherence to the therapy and patients' quality of life.

Barba-Vidal, E., Castillejos, L., Roll, V. F. B., Cifuentes-Orjuela, G., Moreno Munoz, J. A., and Martin-Orue, S. M. The Probiotic Combination of Bifidobacterium longum subsp. infantis CECT 7210 and Bifidobacterium animalis subsp. lactis BPL6 Reduces Pathogen Loads and Improves Gut Health of Weaned Piglets Orally Challenged with Salmonella Typhimurium. Front Microbiol. 2017; 8:1570; PM: 28861074

ABSTRACT: Probiotics have been demonstrated to be useful to enhance gut health and prevent gastrointestinal infections in humans. Additionally, some multi-strain probiotic combinations have been suggested to have greater efficacy than single strains. The objective of this study is to demonstrate the potential of a combination of the probiotic strains: Bifidobacterium longum subsp. infantis CECT 7210 (brand name B. infantis IM1(R)) and B. animalis subsp. lactis BPL6 to enhance gut health and to ameliorate the outcome of a Salmonella challenge using a weaning piglet model. Seventy-two 28-day-old weanling piglets, 7.7 (+/-0.28) kg of body-weight, were distributed in a 2 x 2 factorial design; treated or not with the probiotic combination and challenged or not with the pathogen. Animals were orally challenged after an adaptation period (Day 8) with a single dose (5 x 108 cfu) of Salmonella Typhimurium. One animal per pen was euthanized on Day 12 (Day 4 post-inoculation [PI]) and Day 16 (Day 8 PI). All parameters responded to the challenge and 4 deaths were registered, indicating a severe but self-limiting challenge. Improvements registered in the challenged animals due to the probiotic were: increased voluntary feed-intake (P probiotic x challenge = 0.078), reduced fecal excretion of Salmonella (P = 0.028 at Day 1 PI and P < 0.10 at Days 3 and 5 PI), decreased rectal temperature (P probiotic x day = 0.048) and improvements in the villous:crypt ratio (P probiotic x challenge < 0.001). Moreover, general probiotic benefits were observed in both challenged and non-challenged groups: decreased diarrhea scores of the PI period (P = 0.014), improved fermentation profiles on Day 8 PI (increased ileal acetic acid [P = 0.008] and a tendency to lower colonic ammonia concentrations [P = 0.078]), stimulation of intestinal immune response by increasing villous intraepithelial lymphocytes (P = 0.015 on Day 8 PI) and an improved villous:crypt ratio (P = 0.011). In conclusion, the multi-strain probiotic had a positive effect on reducing pathogen loads and alleviating animals in a Salmonella challenge. In addition, enhanced gut health and immunity was recorded in all animals receiving the probiotic, indicating an improvement in the post-weaning outcome.

Barraclough, H. Question 2 Probiotics in acute infectious diarrhoea: should we run with it? Arch.Dis.Child. 2017; 102(8):782-785; PM: 28724708

No Abstract Available.

Bazanella, M., Maier, T. V., Clavel, T., Lagkouvardos, I., Lucio, M., Maldonado-Gomez, M. X., Autran, C., Walter, J., Bode, L., Schmitt-Kopplin, P., and Haller, D. Randomized controlled trial on the impact of early-life intervention with bifidobacteria on the healthy infant fecal microbiota and metabolome. Am.J.Clin.Nutr. 9-6-2017; PM: 28877893

ABSTRACT: ***Background***: Early-life colonization of the intestinal tract is a dynamic process influenced by numerous factors. The impact of probiotic-supplemented infant formula on

the composition and function of the infant gut microbiota is not well defined. ***Objective***: We sought to determine the effects of a bifidobacteria-containing formula on the healthy human intestinal microbiome during the first year of life. ***Design***: A double-blind, randomized, placebo-controlled study of newborn infants assigned to a standard whey-based formula containing a total of 108 colony-forming units (CFU)/g of Bifidobacterium bifidum, Bifidobacterium breve, Bifidobacterium longum, B. longum subspecies infantis (intervention), or to a control formula without bifidobacteria (placebo). Breastfed controls were included. Diversity and composition of fecal microbiota were determined by 16S ribosomal RNA gene amplicon sequencing, and metabolite profiles were analyzed by ultrahigh-performance liquid chromatography-mass spectrometry over a period of 2 y. ***Results***: Infants (n = 106) were randomly assigned to either the interventional (n = 48) or placebo (n = 49) group; 9 infants were exclusively breastfed throughout the entire intervention period of 12 mo. Infants exposed to bifidobacteria-supplemented formula showed decreased occurrence of Bacteroides and Blautia spp. associated with changes in lipids and unknown metabolites at month 1. Microbiota and metabolite profiles of intervention and placebo groups converged during the study period, and long-term colonization (24 mo) of the supplemented Bifidobacterium strains was not detected. Significant differences in microbiota and metabolites were detected between infants fed breast milk and those fed formula ($P < 0.005$) and between infants birthed vaginally and those birthed by cesarean delivery ($P < 0.005$). No significant differences were observed between infant feeding groups regarding growth, antibiotic uptake, or other health variables ($P > 0.05$).***Conclusion***: The supplementation of bifidobacteria to infant diet can modulate the occurrence of specific bacteria and metabolites during early life with no detectable long-term effects. This trial was registered at germanctr.de as DRKS00003660.

Becattini, S., Littmann, E. R., Carter, R. A., Kim, S. G., Morjaria, S. M., Ling, L., Gyaltshen, Y., Fontana, E., Taur, Y., Leiner, I. M., and Pamer, E. G. Commensal microbes provide first line defense against Listeria monocytogenes infection. J.Exp.Med. 7-3-2017; 214(7):1973-1989; PM: 28588016

ABSTRACT: Listeria monocytogenes is a foodborne pathogen that causes septicemia, meningitis and chorioamnionitis and is associated with high mortality. Immunocompetent humans and animals, however, can tolerate high doses of L. monocytogenes without developing systemic disease. The intestinal microbiota provides colonization resistance against many orally acquired pathogens, and antibiotic-mediated depletion of the microbiota reduces host resistance to infection. Here we show that a diverse microbiota markedly reduces Listeria monocytogenes colonization of the gut lumen and prevents systemic dissemination. Antibiotic administration to mice before low dose oral inoculation increases L. monocytogenes growth in the intestine. In immunodeficient or chemotherapy-treated mice, the intestinal microbiota provides nonredundant defense against lethal, disseminated infection. We have assembled a consortium of commensal bacteria belonging to the Clostridiales order, which exerts in vitro antilisterial activity and confers in vivo resistance upon transfer into germ free mice. Thus, we demonstrate a defensive role of the gut microbiota against Listeria monocytogenes infection and identify intestinal commensal species that, by enhancing resistance against this pathogen, represent potential probiotics.

Bernardeau, M., Lehtinen, M. J., Forssten, S. D., and Nurminen, P. Importance of the gastrointestinal life cycle of Bacillus for probiotic functionality. J.Food Sci.Technol. 2017; 54(8):2570-2584; PM: 28740315

ABSTRACT: Bacillus spp. are widely used in animal production for their probiotic properties. In many animal species, feed supplementation with specific Bacillus strains can provide numerous benefits including improvement in digestibility, the gut microbiota and immune modulation, and growth performance. Bacilli are fed to animals as spores that can sustain the harsh feed processing and long storage. However, the spores are metabolically quiescent and it is widely accepted that probiotics should be in a metabolically active state to perform certain probiotic functions like secretion of antimicrobial compounds and enzymes, synthesis of short chain fatty acids, and competition for essential nutrients. These functions should become active in the host gastrointestinal tract (GIT) soon after digestion of spores in order to contribute to microbiota and host metabolism. Considering that bacterial spores are metabolically dormant and many health benefits are provided by vegetative cells, it is of particular interest to discuss the life cycle of Bacillus in animal GIT. This review aims to capture the main characteristics of spores and vegetative cells and to discuss the latest knowledge in the life cycle of beneficial Bacillus in various intestinal environments. Furthermore, we review how the life cycle may influence probiotic functions of Bacillus and their benefits for human and animal health.

Berni, Canani R., Di, Costanzo M., Bedogni, G., Amoroso, A., Cosenza, L., Di, Scala C., Granata, V., and Nocerino, R. Extensively hydrolyzed casein formula containing Lactobacillus rhamnosus GG reduces the occurrence of other allergic manifestations in children with cow's milk allergy: 3-year randomized controlled trial. J.Allergy Clin.Immunol. 2017; 139(6):1906-1913; PM: 28043872

*ABSTRACT**: BACKGROUND***: Children with cow's milk allergy (CMA) have an increased risk of other allergic manifestations (AMs). ***OBJECTIVE***: We performed a parallel-arm randomized controlled trial to test whether administration of an extensively hydrolyzed casein formula (EHCF) containing the probiotic Lactobacillus rhamnosus GG (LGG) can reduce the occurrence of other AMs in children with CMA. ***METHODS***: Children with IgE-mediated CMA were randomly allocated to the EHCF or EHCF+LGG groups and followed for 36 months. The main outcome was occurrence of at least 1 AM (eczema, urticaria, asthma, and rhinoconjunctivitis). The secondary outcome was tolerance acquisition, which was defined as the negativization of a double-blind food challenge results at 12, 24, and 36 months. AMs were diagnosed according to standardized criteria. Tolerance acquisition was evaluated every 12 months. ***RESULTS***: A total of 220 children (147 boys [67%]) with a median age of 5.0 months (interquartile range, 3.0-8.0 months) were randomized; 110 children were placed in the EHCF group, and 110 children were placed in the EHCF+LGG group. In the complete case analysis the absolute risk difference for the occurrence of at least 1 AM over 36 months was -0.23 (95% CI, -0.36 to -0.10; P < .001), and the absolute risk difference for the acquisition of cow's milk tolerance was 0.20 (95% CI, 0.05-0.35; P < .01) at 12 months, 0.24 (95% CI, 0.08-0.41; P < .01) at 24 months, and 0.27 (95% CI, 0.11-0.43; P < .001) at 36 months. In the sensitivity analysis the effect size of the main outcome was virtually unchanged when the occurrence of AMs was assigned to all 27 missing children. ***CONCLUSIONS***: EHCF+LGG reduces the incidence of other AMs and hastens the development of oral tolerance in children with IgE-mediated CMA.

Bhat, M., Pasini, E., Copeland, J., Angeli, M., Husain, S., Kumar, D., Renner, E., Teterina, A., Allard, J., Guttman, D. S., and Humar, A. Impact of Immunosuppression on the Metagenomic Composition of the Intestinal Microbiome: a Systems Biology Approach to Post-Transplant Diabetes. Sci.Rep. 8-31-2017; 7(1):10277; PM: 28860611

ABSTRACT: Solid organ transplantation (SOT) outcomes have continued to improve, although long-term use of immunosuppressants can lead to complications such as diabetes, compromising post-transplant outcomes. In this study, we have characterized the intestinal microbiome (IM) composition at the metagenomic level in the context of hyperglycemia induced by immunosuppressants. Sprague-Dawley rats were subjected to doses of tacrolimus and sirolimus that reliably induce hyperglycemia and an insulin-resistant state. Subsequent exposure to probiotics resulted in reversal of hyperglycemia. 16S rRNA and metagenomic sequencing of stool were done to identify the bacterial genes and pathways enriched in immunosuppression. Bacterial diversity was significantly decreased in sirolimus-treated rats, with 9 taxa significantly less present in both immunosuppression groups: Roseburia, Oscillospira, Mollicutes, Rothia, Micrococcaceae, Actinomycetales and Staphylococcus. Following probiotics, these changes were reversed to baseline. At the metagenomic level, the balance of metabolism was shifted towards the catabolic side with an increase of genes involved in sucrose degradation, similar to diabetes. Conversely, the control rats had greater abundance of anabolic processes and genes involved in starch degradation. Immunosuppression leads to a more catabolic microbial profile, which may influence development of diabetes after SOT. Modulation of the microbiome with probiotics may help in minimizing adverse long-term effects of immunosuppression.

Biagioli, M., Laghi, L., Carino, A., Cipriani, S., Distrutti, E., Marchiano, S., Parolin, C., Scarpelli, P., Vitali, B., and Fiorucci, S. Metabolic Variability of a Multispecies Probiotic Preparation Impacts on the Anti-inflammatory Activity. Front Pharmacol. 2017; 8:505; PM: 28804459

ABSTRACT: Background: In addition to strain taxonomy, the ability of probiotics to confer beneficial effects on the host rely on a number of additional factors including epigenetic modulation of bacterial genes leading to metabolic variability and might impact on probiotic functionality. Aims: To investigate metabolism and functionality of two different batches of a probiotic blend commercialized under the same name in Europe in models of intestinal inflammation. Methods: Boxes of VSL#3, a probiotic mixture used in the treatment of pouchitis, were obtained from pharmacies in UK subjected to metabolomic analysis and their functionality tested in mice rendered colitis by treatment with DSS or TNBS. Results: VSL#3-A (lot DM538), but not VSL#3-B (lot 507132), attenuated "clinical" signs of colitis in the DSS and TNBS models. In both models, VSL#3-A, but not VSL#3-B, reduced macroscopic scores, intestinal permeability, and expression of TNFalpha, IL-1beta, and IL-6 mRNAs, while increased the expression of TGFbeta and IL-10, occludin, and zonula occludens-1 (ZO-1) mRNAs and shifted colonic macrophages from a M1 to M2 phenotype ($P < 0.05$ vs. TNBS). In contrast, VSL#3-B failed to reduce inflammation, and worsened intestinal permeability in the DSS model ($P < 0.001$ vs. VSL#3-A). A metabolomic analysis of the two formulations allowed the identification of two specific patterns, with at least three-folds enrichment in the concentrations of four metabolites, including 1-3 dihydroxyacetone (DHA), an intermediate in the fructose metabolism, in VSL#3-B supernatants. Feeding mice with DHA, increased intestinal permeability. Conclusions: Two batches of a commercially available probiotic show divergent metabolic activities. DHA, a product of probiotic metabolism, increases intestinal permeability, highlighting the complex interactions between food, microbiota, probiotics, and intestinal inflammation.

Blackwood, B. P., Yuan, C. Y., Wood, D. R., Nicolas, J. D., Grothaus, J. S., and Hunter, C. J. Probiotic Lactobacillus Species Strengthen Intestinal Barrier Function and Tight Junction Integrity in Experimental Necrotizing Enterocolitis. J.Probiotics.Health. 2017; 5(1); PM: 28638850

ABSTRACT: Necrotizing enterocolitis (NEC) is a serious intestinal disease that occurs in newborn infants. It is associated with major morbidity and affects 5% of all infants admitted to neonatal intensive care units. Probiotics have variable efficacy in preventing necrotizing enterocolitis. Tight junctions (TJ) are protein complexes that maintain epithelial barrier integrity. We hypothesized that the probiotics Lactobacillus rhamnosus and Lactobacillus plantarum strengthen intestinal barrier function, promote TJ integrity, and protect against experimental NEC. Both an in vitro and an in vivo experimental model of NEC were studied. Cultured human intestinal Caco-2 cells were pretreated with L. rhamnosus and L. plantarum probiotics. TJ were then disrupted by EGTA calcium switch or LPS to mimic NEC in vitro. Trans-epithelial resistance (TER) and flux of fluorescein isothiocynate dextran was measured. TJ structure was evaluated by ZO-1 immunofluorescence. In vivo effects of ingested probiotics on intestinal injury and ZO-1 expression were assessed in a rat model of NEC infected with Cronobacter sakazakii (CS). Caco-2 cells treated with individual probiotics demonstrated higher TER and lower permeability compared to untreated cells ($p<0.0001$). ZO-1 immunofluorescence confirmed TJ stability in treated cells. Rat pups fed probiotics alone had more intestinal injury compared with controls ($p=0.0106$). Probiotics were protective against injury when given in combination with CS, with no difference in intestinal injury compared to controls ($p=0.21$). Increased permeability was observed in the probiotic and CS groups ($p=0.03$, $p=0.05$), but not in the probiotic plus CS group ($p=0.79$). Lactobacillus sp. strengthened intestinal barrier function and preserved TJ integrity in an in vitro experimental model of NEC. In vivo, probiotic bacteria were not beneficial when given alone, but were protective in the presence of CS in a rat model of NEC.

Bohm, S. and Kruis, W. [Diverticulitis : Domain of conservative or drug therapy?]. Internist (Berl). 2017; 58(7):745-752; PM: 28608124

ABSTRACT: Increasing interest in diverticular disease by the scientific community in the last 10-15 years has resulted in an increased number of publications. Among other things, nonevidence-based therapeutic paradigms were tested in randomized, controlled therapy studies. The importance of surgery in the therapy of diverticulitis has diminished in recent years; in particular, it has no role in the treatment of diverticulitis types 1a, 1b, and 2a according to the Classification of Diverticular Disease (CDD) treated successfully by conservative means. Surgery has only a subordinate role in recurrent type 3b diverticulitis according to the CDD. Diverticulitis is therefore increasingly treated using conservative or drug therapy. However, only the classic, established antibiotics are currently available as effective drugs for the treatment of diverticular disease. However, these are also decreasing in significance. Over 90% of patients with type 1a/1b diverticulitis can be safely treated according to current data without the use of antibiotics. It is possible that type 2a diverticulitis will also be successfully treated without antibiotics in the future. Substances such as rifaximin, mesalazine, or probiotics, which were tested above all in patients with chronic recurrent forms (CDD type 3a/3b), have not yet been established.

Bonatsou, S., Tassou, C. C., Panagou, E. Z., and Nychas, G. E. Table Olive Fermentation Using Starter Cultures with Multifunctional Potential. Microorganisms. 5-28-2017; 5(2); PM: 28555038

ABSTRACT: Table olives are one of the most popular plant-derived fermented products. Their enhanced nutritional value due to the presence of phenolic compounds and monounsaturated fatty acids makes olives an important food commodity of the Mediterranean diet. However, despite its economic significance, table olive fermentation is mainly craft-based and empirically driven by the autochthonous microbiota of the olives depending on various intrinsic and extrinsic factors, leading to a spontaneous process and a final product of variable quality. The use of microorganisms previously isolated from olive fermentations and studied for their probiotic potential and technological characteristics as starter cultures may contribute to the reduction of spoilage risk resulting in a controlled fermentation process. This review focuses on the importance of the development and implementation of multifunctional starter cultures related to olives with desirable probiotic and technological characteristics for possible application on table olive fermentation with the main purpose being the production of a health promoting and sensory improved functional food.

Borges, N. A., Carmo, F. L., Stockler-Pinto, M. B., de Brito, J. S., Dolenga, C. J., Ferreira, D. C., Nakao, L. S., Rosado, A., Fouque, D., and Mafra, D. Probiotic Supplementation in Chronic Kidney Disease: A Double-blind, Randomized, Placebo-controlled Trial. J.Ren Nutr. 9-6-2017; PM: 28888762

*ABSTRACT**: OBJECTIVE***: The objective of the study was to evaluate the effects of probiotic supplementation on the gut microbiota profile and inflammatory markers in chronic kidney disease patients undergoing maintenance hemodialysis (HD). ***DESIGN AND METHODS***: This was a randomized, double-blind, placebo-controlled study. Forty-six HD patients were assigned to receive 1 of 2 treatments: probiotic (n = 23; Streptococcus thermophilus, Lactobacillus acidophilus e Bifidobacterialongum, 90 billion colony-forming units per day) or placebo (n = 23) daily for 3 months. Blood and feces were collected at baseline and after intervention. The inflammatory markers (C-reactive protein and interleukin-6) were analyzed by immunoenzymatic assay (enzyme-linked immunosorbent assay). Uremic toxins plasma levels (indoxyl sulfate, p-cresyl sulfate, and indole-3-acetic acid) were obtained by Reversed-Phase High-Performance Liquid Chromatography. Routine laboratory parameters were measured by standard techniques. Fecal pH was measured by the colorimetric method, and the gut microbiota profile was assessed by Denaturing Gradient Gel Electrophoresis analysis. ***RESULTS***: Sixteen patients remained in the probiotic group (11 men, 53.6 +/- 11.0 year old, 25.3 +/- 4.6 kg/m2) and 17 in the placebo group (10 men, 50.3 +/- 8.5 year old, 25.2 +/- 5.7 kg/m2). After probiotic supplementation there was a significant increase in serum urea (from 149.6 +/- 34.2 mg/dL to 172.6 +/- 45.0 mg/dL, P = .02), potassium (from 4.4 +/- 0.4 mmol/L to 4.8 +/- 0.4 mmol/L, P = .02), and indoxyl sulfate (from 31.2 +/- 15.9 to 36.5 +/- 15.0 mg/dL, P = .02). The fecal pH was reduced from 7.2 +/- 0.8 to 6.5 +/- 0.5 (P = .01). These parameters did not change significantly in placebo group. Changes in the percentage delta (Delta) between groups were exhibited with no statistical differences observed. The inflammatory markers and gut profile were not altered by supplementation. ***CONCLUSIONS***: Aprobiotic supplementation failed to reduce uremic toxins and inflammatory markers. Therefore, probiotic therapy should be chosen with caution in HD

patients. Further studies addressing probiotic therapy in chronic kidney disease patients are needed.

Borycka-Kiciak, K., Strus, M., Pietrzak, P., Wawiernia, K., Mikolajczyk, D., Galecka, M., Heczko, P., and Tarnowski, W. Clinical and microbiological aspects of the use of Lactobacillus rhamnosus PL1 strains in proctological patients with symptoms of chronic proctitis. Pol.Przegl.Chir. 6-30-2017; 89(3):16-22; PM: 28703111

ABSTRACT: Recurrent proctitis and the symptoms associated therewith pose significant clinical problem in proctological patients. The objective of this study was to assess the impact of the probiotic Lactobacillus rhamnosus PL1 strain on the clinical presentation and composition of intestinal microbiota in patients with symptoms of proctitis in the course of hemorrhoidal disease and diverticulosis. Material consisted of 24 patients in whom no complete clinical improvement could be obtained after the treatment of the underlying disease. Subject to the assessment was the presence and the intensity of clinical symptoms as well as qualitative and quantitative changes in the composition of bacterial flora detected in the stool before, during and after a 9-week supplementation with the probiotic Lactobacillus rhamnosus PL1 strain. RESULTS: In the entire study group, the intensity of pain after 12 weeks was significantly lower (p=0,.011) compared to baseline; the intensity of flatulence and abdominal discomfort was reduced significantly as early as after 3 weeks, with the difference reaching a highly significant level after 12 weeks (pP<0,.0001). No significant difference was observed in the frequency of the reported episodes of diarrhea, constipation, as well as itching and burning in the anal region. As early as after 3 weeks of supplementation with the probiotic L. rhamnosus PL1 strain, significant qualitative and quantitative changes were observed in the composition of intestinal microbiota; the changes differed depending on the underlying disease. An increase in the total counts of the bacteria of Lactobacillus genus, particularly L. rhamnosus PL1 strain was observed regardless of the underlying disease. CONCLUSION: Tthe probiotic Lactobacillus rhamnosus PL1 strain appears to be useful in restoring appropriate ratios of bacterial populations in patients presenting with symptoms of proctitis in the course of the treatment of certain diseases of the lower gastrointestinal tract.

Bossa, L., Kline, K., McDougald, D., Lee, B. B., and Rice, S. A. Urinary catheter-associated microbiota change in accordance with treatment and infection status. PLoS.One. 2017; 12(6):e0177633; PM: 28628622

ABSTRACT: The use of long-term catheterisation to manage insensate bladders, often associated with spinal cord injury (SCI), increases the risk of microbial colonisation and infection of the urinary tract. Urinary tract infection (UTI) is typically diagnosed and treated based on the culturing of organisms from the urine, although this approach overlooks low titer, slow growing and non-traditional pathogens. Here, we present an investigation of the urinary tract microbiome in catheterised SCI individuals, using T-RFLP and metagenomic sequencing of the microbial community. We monitored three neurogenic patients over a period of 12 months, who were part of a larger study investigating the efficacy of probiotics in controlling UTIs, to determine how their urinary tract microbial community composition changed over time and in relation to probiotic treatment regimens. Bacterial biofilms adherent to urinary catheters were examined as a proxy for bladder microbes. The microbial community composition of the urinary tract

differed significantly between individuals. Probiotic therapy resulted in a significant change in the microbial community associated with the catheters. The community also changed as a consequence of UTI and this shift in community composition preceded the clinical diagnosis of infection. Changes in the microbiota due to probiotic treatment or infection were transient, resolving to microbial communities similar to their pre-treatment communities, suggesting that the native community was highly resilient. Based on these results, we propose that monitoring a patient's microbial community can be used to track the health of chronically catheterized patients and thus, can be used as part of a health-status monitoring program.

Bottari, B., Felis, G. E., Salvetti, E., Castioni, A., Campedelli, I., Torriani, S., Bernini, V., and Gatti, M. Effective identification of Lactobacillus casei group species: genome-based selection of the gene mutL as the target of a novel multiplex PCR assay. Microbiology. 2017; 163(7):950-960; PM: 28721852

ABSTRACT: Lactobacillus casei,Lactobacillus paracasei and Lactobacillusrhamnosus form a closely related taxonomic group (the L. casei group) within the facultatively heterofermentative lactobacilli. Strains of these species have been used for a long time as probiotics in a wide range of products, and they represent the dominant species of nonstarter lactic acid bacteria in ripened cheeses, where they contribute to flavour development. The close genetic relationship among those species, as well as the similarity of biochemical properties of the strains, hinders the development of an adequate selective method to identify these bacteria. Despite this being a hot topic, as demonstrated by the large amount of literature about it, the results of different proposed identification methods are often ambiguous and unsatisfactory. The aim of this study was to develop a more robust species-specific identification assay for differentiating the species of the L. casei group. A taxonomy-driven comparative genomic analysis was carried out to select the potential target genes whose similarity could better reflect genome-wide diversity. The gene mutL appeared to be the most promising one and, therefore, a novel species-specific multiplex PCR assay was developed to rapidly and effectively distinguish L. casei, L. paracasei and L. rhamnosus strains. The analysis of a collection of 76 wild dairy isolates, previously identified as members of the L. casei group combining the results of multiple approaches, revealed that the novel designed primers, especially in combination with already existing ones, were able to improve the discrimination power at the species level and reveal previously undiscovered intraspecific biodiversity.

Brandt, L. J. Fecal Microbiota Therapy with a Focus on C. difficile Infection. Psychosom.Med. 7-7-2017; PM: 28691996

ABSTRACT: There has been a paradigm shift in our view of bacteria away from their role as just pathogens. We now have a deepening appreciation of their critical influences in our health maintenance, including energy harvest, metabolism, intestinal development, cell proliferation, nervous system and immune function, as well as their role to protect against intestinal and other infections. A perturbed intestinal microbiome has been associated with an increasing number of gastrointestinal (GI) and non-GI diseases but particularly with C. difficile infection (CDI). While such association does not imply causation, it has been shown that fecal microbiota transplantation (FMT) can correct the dysbiosis that characterizes chronic and recurring CDI, and that FMT can effect a seemingly safe and rapidly effective cure for the majority of CDI patients so treated. FMT has been used to treat a wide range of other diseases, although conclusions about

efficacy in any disease other than CDI must await appropriate well-designed trials. More work needs to be done with FMT, especially to evaluate and ensure its long-term safety. Future studies are likely to narrow the spectrum of organisms that needs to be given to patients to cure CDI, and perhaps other diseases, and to elucidate the mechanisms whereby such therapeutic benefit occurs. FMT is but the first step in this journey.

Brenner, L. A., Stearns-Yoder, K. A., Hoffberg, A. S., Penzenik, M. E., Starosta, A. J., Hernandez, T. D., Hadidi, D. A., and Lowry, C. A. Growing literature but limited evidence: A systematic review regarding prebiotic and probiotic interventions for those with traumatic brain injury and/or posttraumatic stress disorder. Brain Behav.Immun. 2017; 65:57-67; PM: 28606462

ABSTRACT: Traumatic brain injury (TBI) is highly prevalent among a wide range of populations, including civilians, military personnel, and Veterans. TBI sequelae may be further exacerbated by symptoms associated with frequently occurring comorbid psychiatric conditions, including posttraumatic stress disorder (PTSD). This is particularly true among the population of military personnel from recent conflicts in Iraq and Afghanistan, with a history of mild TBI (mTBI) and PTSD. The need for efficacious treatments for TBI and comorbid PTSD is significant, and evidence-based interventions for these frequently co-occurring conditions are limited. Based on findings suggesting that inflammation may be an underlying mechanism of both conditions, anti-inflammatory/immunoregulatory agents, including probiotics, may represent a novel strategy to treat TBI and/or PTSD-related symptoms. The focus of this systematic review was to identify and evaluate existing research regarding prebiotic and probiotic interventions for the populations of individuals with a history of TBI and/or PTSD. Only 4 studies were identified (3 severe TBI, 1 PTSD, 0 co-occurring TBI and PTSD). Although findings suggested some promise, work in this area is nascent and results to date do not support some claims within the extensive coverage of probiotics in the popular press.

Brown, B. I. Nutritional Management of Metabolic Endotoxemia: A Clinical Review. Altern.Ther.Health Med. 2017; 23(4):42-54; PM: 28646814

ABSTRACT: Context * Diet-induced, metabolic endotoxemia is emerging as an important contributory factor to the development of a wide range of chronic diseases, including cardiometabolic, autoimmune, psychiatric, and neurodegenerative illnesses. Emerging human clinical studies have demonstrated that diet and dietary components are potent modifiers of circulating endotoxins and can be used to reduce plasma levels significantly and improve metabolic health. Objective * The aim of the current study was to explore briefly the concept of metabolic endotoxemia and its relationship to disease development, to examine the influence of diet and dietary components on circulating endotoxins, and, finally, discuss the clinical relevance of nutritional interventions for management of metabolic endotoxemia. Design * The researcher performed a literature review of dietary and nutritional interactions with metabolic endotoxemia with a focus on studies relevant to clinical practice. Setting * The study took place at the UK College of Nutrition and Health (London, England). Results * Improving dietary quality, optimizing the intake of phytonutrient-rich foods, improving micronutrient status, consuming fermented foods, manipulating the gut microflora with prebiotics and probiotics, and using specific nutritional supplements, such as glutamine, lactoferrin, resveratrol, and berberine, have been shown to be effective in targeting metabolic endotoxemia. Conclusions * Diet, dietary components, and nutritional supplements, including prebiotics

and probiotics, have demonstrated the ability to provide clinically important reductions in circulating endotoxins and improve related sequels, such as inflammation and other negative health markers. The development of personalized nutritional interventions for the management of metabolic endotoxemia is a promising area for future research due to the potential of such interventions to improve multiple aspects of human health and mitigate a wide range of chronic diseases.

Brunser, O. [Probiotics: innocuousness, prevention and risks]. Rev.Chil.Pediatr. 2017; 88(4):534-540; PM: 28898324

ABSTRACT: Probiotics have been defined as live microorganisms which, when ingested in adequate numbers, confer health benefits to the host. They are currently consumed without any age restrictions and adverse effects such as sepsis, a marker of the risk of invasion of the bloodstream, are extremely infrequent. However, some health professionals express doubts about probiotics being truly innocuous. This review discusses the incidence of sepsis secondary to probiotics use, mainly lactobacilli and bifidobacteria, evaluated through molecular biology or classic culture techniques, showing that sepsis in large numbers of individuals along decennia is extremely low, of the order of 0,02% en some centers or as low as 1 case/million population in France. These data are important considering the use different species and strains of these microorganisms. Few studies which have reported other adverse effects but many of these have problems with their design that cast doubt about the validity of their results. On the contrary, it has been shown that probiotic microorganisms exert positive stimulatory effects on innate and acquired immunity, with decrease of the manifestations of atopy and eczema. These positive effects are further evidenced by the beneficial effects of many species of probiotics in preventing necrotizing enterocolitis in patients as functionally labile as premature-born babies.

Brussow, H. Infection therapy: the problem of drug resistance - and possible solutions. Microb.Biotechnol. 7-24-2017; PM: 28737021

ABSTRACT: The rising antibiotic resistance in major bacterial pathogens together with the breakdown of the antibiotic discovery platform creates a critical situation for infection therapy. Recent developments reviving new antibiotic discovery from defining chemical rules for membrane-passing compounds to isolation chips for soil bacteria and exploring the human microbiome for antibiotic-producing bacteria are discussed. The potential of bacteriocins, tailocins, phage lysins, phages, probiotics and commensal blends as alternatives to antibiotics is evaluated.

bu-Braka, A. Z., Zaki, M. S., Abbas, H. H., Ismail, N. E. D. A., Khalil, R., Tanekhy, M., and Saad, T. Filed studies on some probiotics to minimize hazard effects of prevailing heavy metals contamination for improving immunity and growth performance of Oreochromis niloticus. Electron Physician. 2017; 9(4):4138-4144; PM: 28607647

*ABSTRACT**: AIM***: The objective of the present study was to determine the effect of some types of probiotics to minimize the hazard effect of cadmium on Oreochromis niloticus (O. niloticus) and to determine the influence of probiotics on the growth performance and immune status of O. niloticus. ***METHODS***: Fish were divided into four groups, the first one was fed on a diet without any additives (control group), and the second group was

fed on diet with the addition of 0.1 from (LC50) of cadmium 32 ppm in water. The third group was fed on a diet containing 1 gm/kg of Lactobacillus acidophilus. The fourth group was fed on a diet containing 1 gm/kg of L. acidophilus with 0.1 addition from (LC50) of cadmium 32 ppm. ***RESULTS***: The experiment lasted about 60 days which resulted in an improvement in growth performance, with a decrease in the number of micronucleus formation in the group which received the probiotic. The group which was affected with cadmium showed decrease in the growth performance with increase in the number of micronucleus formation while the group which received probiotics and treated with cadmium had significant improvement in growth performance and decreased in the number of micronucleus formation. ***CONCLUSIONS***: Probiotics decrease cadmium pollution.

bu-El-Haija, M., Kumar, S., Quiros, J. A., Balakrishnan, K., Barth, B., Bitton, S., Eisses, J. F., Foglio, E. J., Fox, V., Francis, D., Freeman, A. J., Gonska, T., Grover, A. S., Husain, S. Z., Kumar, R., Lapsia, S., Lin, T., Liu, Q. Y., Maqbool, A., Sellers, Z. M., Szabo, F., Uc, A., Werlin, S. L., and Morinville, V. D. The Management of Acute Pancreatitis in the Pediatric Population: A Clinical Report from the NASPGHAN Pancreas Committee. J.Pediatr.Gastroenterol.Nutr. 8-23-2017; PM: 28837512

*ABSTRACT****: BACKGROUND***: While the incidence of acute pancreatitis (AP) in children is increasing, management recommendations rely on adult published guidelines. Pediatric-specific recommendations are needed. ***METHODS***: The NASPGHAN Pancreas committee performed a MEDLINE review using several pre-selected key terms relating to management considerations in adult and pediatric AP. The literature was summarized, quality of evidence reviewed, and statements of recommendations developed. The authorship met to discuss the evidence, statements, and voted on recommendations. A consensus of at least 75% was required to approve a recommendation. ***RESULTS***: The diagnosis of pediatric AP should follow the published INSPPIRE definitions (by meeting at least two out of three criteria: (1) abdominal pain compatible with AP, (2) serum amylase and/or lipase values >/=3 times upper limits of normal, (3) imaging findings consistent with AP). Adequate fluid resuscitation with crystalloid appears key especially within the first 24 h. Analgesia may include opioid medications when opioid-sparing measures are inadequate. Pulmonary, cardiovascular, and renal status should be closely monitored particularly within the first 48 hours. Enteral nutrition should be started as early as tolerated, whether through oral, gastric, or jejunal route. Little evidence supports the use of prophylactic antibiotics, anti-oxidants, probiotics, and protease inhibitors. Esophago-gastro-duodenoscopy, endoscopic retrograde cholangiopancreatography and endoscopic ultrasonography have limited roles in diagnosis and management. Children should be carefully followed for development of early or late complications as well as recurrent attacks of AP. ***CONCLUSIONS***: This clinical report represents the first English-language recommendations for the management of pediatric AP. Future aims should include prospective multi-center pediatric studies to further validate these recommendations and optimize care for children with AP.

Burton, K. J., Rosikiewicz, M., Pimentel, G., Butikofer, U., von, Ah U., Voirol, M. J., Croxatto, A., Aeby, S., Drai, J., McTernan, P. G., Greub, G., Pralong, F. P., Vergeres, G., and Vionnet, N. Probiotic yogurt and acidified milk similarly reduce postprandial inflammation and both alter the gut microbiota of healthy, young men. Br.J.Nutr. 2017; 117(9):1312-1322; PM: 28558854

ABSTRACT: Probiotic yogurt and milk supplemented with probiotics have been investigated for their role in 'low-grade' inflammation but evidence for their efficacy is inconclusive. This study explores the impact of probiotic yogurt on metabolic and inflammatory biomarkers, with a parallel study of gut microbiota dynamics. The randomised cross-over study was conducted in fourteen healthy, young men to test probiotic yogurt compared with milk acidified with 2 % d-(+)-glucono-delta-lactone during a 2-week intervention (400 g/d). Fasting assessments, a high-fat meal test (HFM) and microbiota analyses were used to assess the intervention effects. Baseline assessments for the HFM were carried out after a run-in during which normal milk was provided. No significant differences in the inflammatory response to the HFM were observed after probiotic yogurt compared with acidified milk intake; however, both products were associated with significant reductions in the inflammatory response to the HFM compared with the baseline tests (assessed by IL6, TNFalpha and chemokine ligand 5) ($P<0.001$). These observations were accompanied by significant changes in microbiota taxa, including decreased abundance of Bilophila wadsworthia after acidified milk (log 2-fold-change (FC)=-1.5, P adj=0.05) and probiotic yogurt intake (FC=-1.3, P adj=0.03), increased abundance of Bifidobacterium species after acidified milk intake (FC=1.4, P adj=0.04) and detection of Lactobacillus delbrueckii spp. bulgaricus (FC=7.0, P adj<0.01) and Streptococcus salivarius spp. thermophilus (FC=6.0, P adj<0.01) after probiotic yogurt intake. Probiotic yogurt and acidified milk similarly reduce postprandial inflammation that is associated with a HFM while inducing distinct changes in the gut microbiota of healthy men. These observations could be relevant for dietary treatments that target 'low-grade' inflammation.

Byerley, L. O., Samuelson, D., Blanchard, E., Luo, M., Lorenzen, B. N., Banks, S., Ponder, M. A., Welsh, D. A., and Taylor, C. M. Changes in the gut microbial communities following addition of walnuts to the diet. J.Nutr.Biochem. 2017; 48:94-102; PM: 28797931

ABSTRACT: Walnuts are rich in omega-3 fatty acids, phytochemicals and antioxidants making them unique compared to other foods. Consuming walnuts has been associated with health benefits including a reduced risk of heart disease and cancer. Dysbiosis of the gut microbiome has been linked to several chronic diseases. One potential mechanism by which walnuts may exert their health benefit is through modifying the gut microbiome. This study identified the changes in the gut microbial communities that occur following the inclusion of walnuts in the diet. Male Fischer 344 rats (n=20) were randomly assigned to one of two diets for as long as 10 weeks: (1) walnut (W), and (2) replacement (R) in which the fat, fiber, and protein in walnuts were matched with corn oil, protein casein, and a cellulose fiber source. Intestinal samples were collected from the descending colon, the DNA isolated, and the V3-V4 hypervariable region of 16S rRNA gene deep sequenced on an Illumina MiSeq for characterization of the gut microbiota. Body weight and food intake did not differ significantly between the two diet groups. The diet groups had distinct microbial communities with animals consuming walnuts displaying significantly greater species diversity. Walnuts increased the abundance of Firmicutes and reduced the abundance of Bacteriodetes. Walnuts enriched the microbiota for probiotic-type bacteria including Lactobacillus, Ruminococcaceae, and Roseburia while significantly reducing Bacteroides and Anaerotruncus. The class Alphaproteobacteria was also reduced. Walnut consumption altered the gut microbial community suggesting a new mechanism by which walnuts may confer their beneficial health effects.

Cabana, M. D. and Merenstein, D. J. Probiotics in the Child Care Center: Context Matters. Pediatrics. 2017; 140(2); PM: 28674111

No Abstract Available.

Cahova, M., Bratova, M., and Wohl, P. Parenteral Nutrition-Associated Liver Disease: The Role of the Gut Microbiota. Nutrients. 9-7-2017; 9(9); PM: 28880224

ABSTRACT: Parenteral nutrition (PN) provides life-saving nutritional support in situations where caloric supply via the enteral route cannot cover the necessary needs of the organism. However, it does have serious adverse effects, including parenteral nutrition-associated liver disease (PNALD). The development of liver injury associated with PN is multifactorial, including non-specific intestine inflammation, compromised intestinal permeability, and barrier function associated with increased bacterial translocation, primary and secondary cholangitis, cholelithiasis, short bowel syndrome, disturbance of hepatobiliary circulation, lack of enteral nutrition, shortage of some nutrients (proteins, essential fatty acids, choline, glycine, taurine, carnitine, etc.), and toxicity of components within the nutrition mixture itself (glucose, phytosterols, manganese, aluminium, etc.). Recently, an increasing number of studies have provided evidence that some of these factors are directly or indirectly associated with microbial dysbiosis in the intestine. In this review, we focus on PN-induced changes in the taxonomic and functional composition of the microbiome. We also discuss immune cell and microbial crosstalk during parenteral nutrition, and the implications for the onset and progression of PNALD. Finally, we provide an overview of recent advances in the therapeutic utilisation of pro- and prebiotics for the mitigation of PN-associated liver complications.

Candido, F. G., Valente, F. X., Grzeskowiak, L. M., Moreira, A. P. B., Rocha, D. M. U. P., and Alfenas, R. C. G. Impact of dietary fat on gut microbiota and low-grade systemic inflammation: mechanisms and clinical implications on obesity. Int.J.Food Sci.Nutr. 7-4-2017; 1-19; PM: 28675945

ABSTRACT: Dietary fat strongly affects human health by modulating gut microbiota composition and low-grade systemic inflammation. High-fat diets have been implicated in reduced gut microbiota richness, increased Firmicutes to Bacteroidetes ratio, and several changes at family, genus and species levels. Saturated (SFA), monounsaturated (MUFA), polyunsaturated (PUFA) and conjugated linolenic fatty acids share important pathways of immune system activation/inhibition with gut microbes, modulating obesogenic and proinflammatory profiles. Mechanisms that link dietary fat, gut microbiota and obesity are mediated by increased intestinal permeability, systemic endotoxemia, and the activity of the endocannabinoid system. Although the probiotic therapy could be a complementary strategy to improve gut microbiota composition, it did not show permanent effects to treat fat-induced dysbiosis. Based upon evidence to date, we believe that high-fat diets and SFA consumption should be avoided, and MUFA and omega-3 PUFA intake should be encouraged in order to regulate gut microbiota and inflammation, promoting body weight/fat control.

Cassard, A. M., Gerard, P., and Perlemuter, G. Microbiota, Liver Diseases, and Alcohol. Microbiol.Spectr. 2017; 5(4); PM: 28840806

ABSTRACT: Being overweight and obesity are the leading causes of liver disease in Western countries. Liver damage induced by being overweight can range from steatosis, harmless in its simple form, to steatohepatitis, fibrosis, cirrhosis, and hepatocellular carcinoma. Alcohol consumption is an additional major cause of liver disease. Not all individuals who are overweight or excessively consume alcohol develop nonalcoholic fatty liver diseases (NAFLD) or alcoholic liver disease (ALD) and advanced liver disease. The role of the intestinal microbiota (IM) in the susceptibility to liver disease in this context has been the subject of recent studies. ALD and NAFLD appear to be influenced by the composition of the IM, and dysbiosis is associated with ALD and NAFLD in rodent models and human patient cohorts. Several microbial metabolites, such as short-chain fatty acids and bile acids, are specifically associated with dysbiosis. Recent studies have highlighted the causal role of the IM in the development of liver diseases, and the use of probiotics or prebiotics improves some parameters associated with liver disease. Several studies have made progress in deciphering the mechanisms associated with the modulation of the IM. These data have demonstrated the intimate relationship between the IM and metabolic liver disease, suggesting that targeting the gut microbiota could be a new preventive or therapeutic strategy for these diseases.

Castro-Bravo, N., Hidalgo-Cantabrana, C., Rodriguez-Carvajal, M. A., Ruas-Madiedo, P., and Margolles, A. Gene Replacement and Fluorescent Labeling to Study the Functional Role of Exopolysaccharides in Bifidobacterium animalis subsp. lactis. Front Microbiol. 2017; 8:1405; PM: 28790996

ABSTRACT: An extracellular layer of exopolysaccharides (EPS) covers the surface of some Bifidobacterium animalis subsp. lactis strains, which could be of relevance for its probiotic performance. In order to understand the functional characteristics of B. animalis subsp. lactis, two isogenic strains that differ in their EPS-producing phenotype, due to a single mutation in the gene Balat_1410, were studied. By means of a double crossover recombination strategy, successfully used for the first time in bifidobacteria, Balat_1410 in the type strain B. animalis subsp. lactis DSM10140 was replaced by a mutated gene containing a non-synonymous mutation previously associated with the appearance of a mucoid-ropy phenotype. Nuclear magnetic resonance and SEC-MALS analyses showed that the novel strain harboring the mutation acquired a ropy phenotype, due to the production of a high molecular weight (HMW)-EPS that is not produced in the wild-type strain. Fluorescence labeling of both strains with two fluorescent proteins, m-Cherry and Green Fluorescent Protein, was achieved by expressing the corresponding genes under the control of a native selected promoter (the elongation factor Tu promoter). Remarkably, qualitative and quantitative fluorescence analyses demonstrated that the ropy strain displays a lower capability to adhere to human intestinal epithelial cells. In addition, the presence of the HMW-EPS reduced the capability of the producing strain to form biofilms upon three different abiotic surfaces. This work also highlights the fact that different EPS confer variable functional characteristics to the bifidobacterial surface, which may be relevant for the performance of B. animalis subsp. lactis as a probiotic. The construction of molecular tools allowing the functional characterization of surface structures in next generation probiotics is still a challenging issue that deserves further attention, given the relevant role that such molecules must play in the interaction with the host.

Ceccarelli, G., Fratino, M., Selvaggi, C., Giustini, N., Serafino, S., Schietroma, I., Corano, Scheri G., Pavone, P., Passavanti, G., Alunni, Fegatelli D., Mezzaroma, I., Antonelli, G., Vullo, V., Scagnolari, C., and d'Ettorre, G. A pilot study on the effects of probiotic supplementation on neuropsychological performance and microRNA-29a-c levels in antiretroviral-treated HIV-1-infected patients. Brain Behav. 2017; 7(8):e00756; PM: 28828217

ABSTRACT: ***INTRODUCTION***: The gut microbiota is involved in the regulation of cognition, mood, anxiety, and pain, and can impact cognitive functions by producing neuroactive substances or releasing bacterial by-products and metabolites. No information is available on the effects of a probiotic supplementation on brain function of HIV+ subjects. In light of the above considerations, we performed a pilot study in cART-treated HIV-1-positive patients with long-term virologic suppression. The aims were to analyze the effect of high-concentration multistrain probiotic supplementation (Vivomixx(R); Visbiome(R)) on several neurocognitive abilities and to evaluate the safety of this supplementation. ***METHODS***: To address those issues, neurocognitive performances were explored by administering neuropsychological tests; moreover, miRNA-29a-c levels were measured in cerebrospinal fluid (CSF) to confirm the persistent undetectable levels of HIV-RNA in the central nervous system after probiotic supplementation. ***RESULTS***: Our results show that the Rey auditory verbal learning test (RAVLT) (immediate and delayed recall), Rey-Osterrieth complex figure test (ROCF) (copy immediate and delayed recall), phonological verbal fluency (PVF) test, Toronto alexithymia scale-20 (Tas-20), State-trait anxiety inventory Y-2 (STAY Y-2), and time and weight estimation test (STEP) scores improved significantly during the study. Moreover, we found unchanged levels, associated to high degree of individual variability, in miRNA-29 levels in CSF collected before and after probiotic supplementation. ***CONCLUSIONS***: In conclusion, we observed that HIV patients treated with 6 months of this probiotic supplementation appear to have an improvement in some neurocognitive functions; moreover, this approach is safe and did not modify significantly the levels of miRNA in CSF. Further studies are needed to better understand the contribution of the probiotics in modulating gut-brain-axis in HIV patients.

Cekici, H. and Sanlier, N. Current nutritional approaches in managing autism spectrum disorder: A review. Nutr.Neurosci. 8-1-2017; 1-11; PM: 28762296

ABSTRACT: The link between nutrition and autism spectrum disorder (ASD), which is a complex developmental disorder manifesting itself in significant delays or deviation in interaction and communication, has provided a fresh point of view and signals that nutrition may have a role in the aetiology of ASD, as well as play an active role in treatment by alleviating symptoms. ***OBJECTIVE***: In this review study aimed at evaluating, with scientific and concrete proof, the current medical nutrition implementations on ASD, existing medical nutrition therapies have been addressed and their effects on ASD symptoms have been discussed in light of current research. ***METHODS***: We reviewed articles regarding the medical nutritional therapy of autism on current nutritional approaches selected from PubMed, Science Direct, EBSCO, and databases about autism and nutrition. ***RESULTS***: The research put forward that in individuals with ASD, while gluten-free/casein-free and ketogenic diets, camel milk, curcumin, probiotics, and fermentable foods can play a role in alleviating ASD symptoms, consumption of sugar, additives, pesticides, genetically modified organisms, inorganic processed foods, and hard-to-digest starches may aggravate symptoms. ***DISCUSSION***: Further prospective controlled trials with large sample sizes are needed before recommendations can be made regarding the ideal ASD diet. This review emphasizes the value of identifying

current nutritional approaches specific to individuals with ASD and integrating their effects on symptoms to the conversation and presents suggestions for future research designed to identify medical nutrition therapies targeting this population to better understand the link between ASD and nutrition.

Chanda, W., Joseph, T. P., Wang, W., Padhiar, A. A., and Zhong, M. The potential management of oral candidiasis using anti-biofilm therapies. Med.Hypotheses. 2017; 106:15-18; PM: 28818264

ABSTRACT: Candida albicans is a minor component of the oral microbiota and an opportunistic pathogen that takes advantage of the immunocompromised host and causes oral mucositis and oral candidiasis. This organism is able to undergo phenotypic modification from a yeast to hyphae growth phase, one of the key arsenals for immune cell evasion, tissue invasion and biofilm formation. The latter property coupled with overgrowth and immune compromising factors such as HIV/AIDS, cancer treatments, organ transplantation, diabetes, corticosteroid use, dentures, and broad-spectrum antibiotic use have modified the fungus from a normal component of the microflora to a foe of an oral cavity and resulting in reduced sensitivity towards commonly utilised antifungal agents. Hence, the need for alternative therapy to curb this plight is of importance. Making use of biomolecules produced by Streptococcus mutans, application of lactoferrin which is a nonspecific host defense factor found in saliva with metal chelating and broader antimicrobial properties, use of probiotics which have the capacity to boost the host immunity through eliciting Immunoglobulin A synthesis, and perturbing the pathogen's environment via competition of space and food, and application of photodynamic therapy can help to manage the burden of oral candidiasis.

Chen, M. and Land, M. The Current State of Food Allergy Therapeutics. Hum.Vaccin.Immunother. 8-28-2017; 0; PM: 28846472

ABSTRACT: The prevalence of IgE mediated food allergy is an increasing public health concern. The current standard of treatment is strict avoidance of the offending food(s). There are no FDA approved treatments for food allergy. This review will provide an overview of strategies currently under investigation for the treatment of food allergy. The main focus of research has been directed at various forms of immunotherapy, including oral, sublingual and epicutaneous delivery routes. While oral immunotherapy (OIT) has shown the greatest promise for efficacy in terms of amount of protein that can be ingested, it has also demonstrated less tolerability and a less favorable safety profile as compared to sublingual immunotherapy (SLIT) and epicutaneous immunotherapy (EPIT), which offers the least protection but has the best safety and tolerability profile. Investigation is also underway for modified antigens that may be used for immunotherapy and for adjuncts that may help facilitate immunotherapy, including biologics such as anti-IgE therapy, and also probiotics. There are also a number of preclinical concepts that are being evaluated to manipulate the antigens and/or the immune system that may one day be translatable to patients.

Chen, Q., Tong, C., Ma, S., Zhou, L., Zhao, L., and Zhao, X. Involvement of MicroRNAs in Probiotics-Induced Reduction of the Cecal Inflammation by Salmonella Typhimurium. Front Immunol. 2017; 8:704; PM: 28659929

ABSTRACT: The microRNAs (miRNAs) have been shown to play important roles in the development of the immune system and in regulation of host inflammation responses. Probiotics can effectively alleviate the inflammation caused by Salmonella in chickens. However, whether and how miRNAs are involved in modulation of the inflammation response in the gut of chickens have not been reported. In this study, the impact of a probiotics, Lactobacillus plantarum Z01 (LPZ01), was investigated on the cecal miRNAs and cytokine secretions in Salmonella Typhimurium (S. Typhimurium)-infected chickens at the age of 3 days. Newly hatched chicks were assigned to four groups (1): NC (basal diet) (2): S (basal diet + S. Typhimurium challenged) (3): SP (basal diet + S. Typhimurium challenged + LPZ01) (4): P (basal diet + LPZ01). In comparison with the S group, chicks in the SP group reduced the number of S. Typhimurium and had lower levels of interferon-gamma and lipopolysaccharide-induced tumor necrosis factor alpha factor (LITAF) in ceca post challenge. Expression of 14 miRNAs was significantly affected by the presence of S. Typhimurium and/or lactobacillus. Five differential expression miRNAs (gga-miR-215-5p, gga-miR-3525, gga-miR-193a-5p, gga-miR-122-5p, and gga-miR-375) were randomly selected for confirmation by the RT-PCR. Predicted target genes of differentially expressed miRNAs were enriched in regulation of cAMP-dependent protein kinase activity, stress-activated MAPK cascade, immune system development and regulation of immune system process as well as in immune related pathways such as MAPK and Wnt signaling pathways. The relationship between changes of miRNAs and changes of cytokines was explored. Finally, 119 novel miRNAs were identified in 36 libraries totally. Identification of novel miRNAs significantly expanded the repertoire of chicken miRNAs and provided the basis for understanding the function of miRNAs in the host. Our results suggest that the probiotics reduce the inflammation of the S. Typhimurium infection in neonatal broiler chicks, at least partially, through regulation of miRNAs expression.

Chen, Z., Zhang, L., Zeng, L., Yang, X., Jiang, L., Gui, G., and Zhang, Z. Probiotics Supplementation Therapy for Pathological Neonatal Jaundice: A Systematic Review and Meta-Analysis. Front Pharmacol. 2017; 8:432;PM: 28713275

ABSTRACT: ***Background***: Neonatal jaundice is a relatively prevalent disease and affects approximately 2.4-15% newborns. Probiotics supplementation therapy could assist to improve the recovery of neonatal jaundice, through enhancing immunity mainly by regulating bacterial colonies. However, there is limited evidence regarding the effect of probiotics on bilirubin level in neonates. Therefore, this study aims at systematically evaluating the efficacy and safety of probiotics supplement therapy for pathological neonatal jaundice. Methods: Databases including PubMed, Embase, Cochrane Library, China National Knowledge Infrastructure (CNKI), Wan Fang Database (Wan Fang), Chinese Biomedical Literature Database (CBM), VIP Database for Chinese Technical Periodicals (VIP) were searched and the deadline is December 2016. Randomized controlled trials (RCTs) of probiotics supplementation for pathological neonatal jaundice in publications were extracted by two reviewers. The cochrane tool was applied to assessing the risk of bias of the trials. The extracted information of RCTs should include efficacy rate, serum total bilirubin level, time of jaundice fading, duration of phototherapy, duration of hospitalization, adverse reactions. The main outcomes of the trials were analyzed by Review Manager 5.3 software. The relative risks (RR) or mean difference (MD) with a 95% confidence interval (CI) was used to measure the effect. ***Results***: 13 RCTs involving 1067 neonatal with jaundice were included in the meta-analysis. Probiotics supplementation treatment showed efficacy [RR: 1.19, 95% CI (1.12, 1.26), P < 0.00001] in neonatal jaundice. It not only decreased the total serum bilirubin

level after 3day [MD: -18.05, 95% CI (-25.51, -10.58), P < 0.00001], 5day [MD: -23.49, 95% CI (-32.80, -14.18), P < 0.00001], 7day [MD: -33.01, 95% CI (-37.31, -28.70), P < 0.00001] treatment, but also decreased time of jaundice fading [MD: -1.91, 95% CI (-2.06, -1.75), P < 0.00001], as well as the duration of phototherapy [MD: -0.64, 95% CI (-0.84, -0.44), P < 0.00001] and hospitalization [MD: -2.68, 95% CI (-3.18, -2.17), P < 0.00001], when compared with the control group. Additionally, no serious adverse reaction was reported. ***Conclusion***: This meta-analysis shows that probiotics supplementation therapy is an effective and safe treatment for pathological neonatal jaundice.

Chey, W. D. SYMPOSIUM REPORT: An Evidence-Based Approach to IBS and CIC: Applying New Advances to Daily Practice: A Review of an Adjunct Clinical Symposium of the American College of Gastroenterology Meeting October 16, 2016 * Las Vegas, Nevada. Gastroenterol.Hepatol.(N.Y.). 2017; 13(2 Suppl 1):1-16; PM: 28729815

ABSTRACT: Many nonpharmacologic and pharmacologic therapies are available to manage irritable bowel syndrome (IBS) and chronic idiopathic constipation (CIC). The American College of Gastroenterology (ACG) regularly publishes reviews on IBS and CIC therapies. The most recent of these reviews was published by the ACG Task Force on the Management of Functional Bowel Disorders in 2014. The key objective of this review was to evaluate the efficacy of therapies for IBS or CIC compared with placebo or no treatment in randomized controlled trials. Evidence-based approaches to managing diarrhea-predominant IBS include dietary measures, such as a diet low in gluten and fermentable oligo-, di-, and monosaccharides and polyols (FODMAPs); loperamide; antispasmodics; peppermint oil; probiotics; tricyclic antidepressants; alosetron; eluxadoline, and rifaximin. Evidence-based approaches to managing constipation-predominant IBS and CIC include fiber, stimulant laxatives, polyethylene glycol, selective serotonin reuptake inhibitors, lubiprostone, and guanylate cyclase agonists. With the growing evidence base for IBS and CIC therapies, it has become increasingly important for clinicians to assess the quality of evidence and understand how to apply it to the care of individual patients.

Chisari, G., Chisari, E. M., Borzi, A. M., Ozyalcin, E., and Chisari, C. G. Aging eye microbiota in Dry Eye Syndrome in patients treated with Enterococcus faecium and Saccharomyces boulardii. Curr.Clin.Pharmacol. 7-4-2017; PM: 28676009

ABSTRACT: Aging seem to have a key role in the onset and progression of ocular surface diseases. Dry Eye Syndrome (DES) is a multifactorial disease of the tears and ocular surface in which symptoms may interfere with the ability to work and carry out daily functions. METHODS: This clinical trial was a pilot study to evaluate the effects of supplementation with mixture (MYA796 and Enterococcus faecium SGEf01) on the tear film. Following the run-in period subjects were randomized in two groups: group A (n.30 subjects) and group B (n.30 subjects). Group A (control) treated only with substitute tear and group B treated with substitute tear + mixture (symbiotic). RESULTS: The data obtained in the two study groups A and B were, respectively the following: Schirmer I: 9.2+/-0.2 Vs 12.8+/-0.4 (p< 0.001); Schirmer II: 3.6+/-0.1 Vs 4.6+/-0.2 (p<0.001); BUT 3.8+/-0.3 Vs 6.2+/-0.2 (p<0.001). Culture test showed initial bacterial growth in group "A" (placebo) 27 out of 60 samples tested, corresponding to 45.0% and "B" after treatment (probiotic) was found positive culture with growth of bacteria in 18 tests equal to 30.0%. The total numbers of isolations of aerobic and anaerobic bacteria were found in both group A and B after treatment. A reduction of 23 to 16 strains of aerobic and anaerobic isolates

from 13 to 7 has been found. CONCLUSIONS: The administration of probiotics strains was effective in reducing DES. In light of these results, we have identified in our probiotic (Saccharomyces boulardii MYA796 and Enterococcus faecium SGEf01) activity integration with the action of tear substitutes, along with standardization of clinical parameters of the tear film and microbiological activity in restoring of the microbiota ocular surface subject with DES.

Chisari, G., Chisari, E. M., Francaviglia, A., and Chisari, C. G. The mixture of bifidobacterium associated with fructo-oligosaccharides reduces the damage of the ocular surface. Clin.Ter. 2017; 168(3):e181-e185; PM: 28612893

ABSTRACT: ***BACKGROUND***: Despite its high prevalence Dry Eye Syndrome (DES) in frequently under-recognized owing to its negative influence on patients visual function. ***METHODS***: This clinical trial was a pilot study to evaluate the effects of supplementation with mixture (Bifidobacterium lactis and Bifidobacterium bifido) on the tear film. Following the run-in period subjects were randomized in two groups: group A (N degrees 20 subjects) and group B (N degrees 20 subjects). Group A (control) treated only with substitute tear and group B treated with substitute tear + mixture (symbiotic). ***RESULTS***: The data obtained in the two study groups A and B were, respectively the following: Schirmer 9.1+/-0.2 vs 12.7+/-0.4 (p< 0.001); Schirmer II 3.5+/-0.1 VS 4.7+/-0.2 (p<0.001); BUT 3.9+/-0.3 vs 6.3+/-0.2 (p<0.001). Culture test showed initial bacterial growth in group "A" (placebo) 18 out of 40 samples tested, corresponding to 45.0% and "B" after treatment ((symbiotic) was found positive culture whit growth of bacteria in 12 tests equal to 30.0%. The total numbers of isolations of aerobic and anaerobic bacteria found group A and B after treatment. A reduction of 15 to 11 strains of aerobic and anaerobic isolates from 9 to 5 has been found. ***CONCLUSIONS***: The present study shows that the administration of bifidobacterium may represent a success full treatment in ameliorating dry eye syndrome (DES). The effect of imbalanced microbiota are not restricted by gastrointestinal abnormalities but could have systemic impact on immunity. Commensal bacteria or probiotics interact with the endogenous enteric microbiota and gut cells therein confereing health benefit to the host.

Collins, F. L., Rios-Arce, N. D., Schepper, J. D., Parameswaran, N., and McCabe, L. R. The Potential of Probiotics as a Therapy for Osteoporosis. Microbiol.Spectr. 2017; 5(4); PM: 28840819

ABSTRACT: Osteoporosis, characterized by low bone mass and micro-architectural deterioration of bone tissue with increased risk of fracture, can be categorized into two forms: primary and secondary, depending on whether it occurs as part of the natural aging process (estrogen deficiency) or as part of disease pathology. In both forms bone loss is due to an imbalance in the bone remodeling process, with resorption/formation skewed more toward bone loss. Recent studies and emerging evidence consistently demonstrate the potential of the intestinal microbiota to modulate bone health. This review discusses the process of bone remodeling and the pathology of osteoporosis and introduces the intestinal microbiota and its potential to influence bone health. In particular, we highlight recent murine studies that examine how probiotic supplementation can both increase bone density in healthy individuals and protect against primary (estrogen deficiency) as well as secondary osteoporosis. Potential mechanisms are described to account for how probiotic treatments could be exerting their beneficial effect on bone health.

Cong, M., Jiang, Q., Xu, X., Huang, L., Su, Y., and Yan, Q. The complete genome sequence of Exiguobacterium arabatum W-01 reveals potential probiotic functions. Microbiologyopen. 6-6-2017; PM: 28589562

ABSTRACT: Shrimp is extensively cultured worldwide. Shrimp farming is suffering from a variety of diseases. Probiotics are considered to be one of the effective methods to prevent and cure shrimp diseases. Exiguobacterium arabatum W-01, a gram-positive and orange-pigmented bacterium, was isolated from the intestine of a healthy Penaeus vannamei specimen. Whole-genome sequencing revealed a genome of 2,914,854 bp, with 48.02% GC content. In total, 3,083 open reading frames (ORFs) were identified, with an average length of 843.98 bp and a mean GC content of 48.11%, accounting for 89.27% of the genome. Among these ORFs, 2,884 (93.5%) genes were classified into Clusters of Orthologous Groups (COG) families comprising 21 functional categories, and 1,650 ORFs were classified into 83 functional Kyoto Encyclopedia of Genes and Genomes (KEGG) pathways. A total of 27 rRNA operons and 68 tRNAs were identified, with all 20 amino acids represented. In addition, 91 genomic islands, 68 potential prophages, and 33 tandem repeats, but no clustered regularly interspaced short palindromic repeats (CRISPRs), were found. No resistance genes and only one virulence gene were identified. Among the 150 secreted proteins of E. arabatum W-01, a variety of transport system substrate-binding proteins, enzymes, and biosynthetic proteins, which play important roles in the uptake and metabolism of nutrients, were found. Two adherence-related protein genes and 31 flagellum-related protein genes were also identified. Taken together, these results indicate potential probiotic functions for E. arabatum W-01.

Corgneau, M., Scher, J., Ritie-Pertusa, L., Le, D. T. L., Petit, J., Nikolova, Y., Banon, S., and Gaiani, C. Recent advances on lactose intolerance: Tolerance thresholds and currently available answers. Crit Rev.Food Sci.Nutr. 10-13-2017; 57(15):3344-3356; PM: 26713460

ABSTRACT: The genetically programmed reduction in lactase activity during adulthood affects 70% of the world adult population and can cause severe digestive disorders, which are the sign of lactose intolerance. Lactose intolerance symptoms vary depending on the residual lactase activity, the small bowel transit time, and especially the amount of ingested lactose. To formulate dairy products suitable for the vast majority of lactose intolerants, it is essential to define lactose intolerance threshold. A recent meta-analysis permitted to show that almost all lactose intolerants tolerate 12 g of lactose in one intake and approximately 18 g of lactose spread over the day. The prevalence and severity of lactose intolerance are probably overestimated by the general public. This misconception usually leads to an unnecessary reduction of dairy foodstuff consumption. Nevertheless, dairy products are essential for health mainly due to their calcium content and the positive influence of probiotic bacteria. The formulation of dairy products suitable for most intolerant and suspicious subjects seems necessary. The use of exogenous enzyme preparations, as well as the consumption of lactose-free products or products rich in probiotic bacteria are proposed as symptom-reducing strategies.

Corsello, G., Carta, M., Marinello, R., Picca, M., De, Marco G., Micillo, M., Ferrara, D., Vigneri, P., Cecere, G., Ferri, P., Roggero, P., Bedogni, G., Mosca, F., Paparo, L., Nocerino, R., and Berni, Canani R. Preventive Effect of Cow's Milk Fermented with Lactobacillus paracasei CBA L74 on Common Infectious Diseases in Children: A Multicenter Randomized Controlled Trial. Nutrients. 6-27-2017; 9(7); PM: 28654019

ABSTRACT: ***Background***: Fermented foods have been proposed to prevent common infectious diseases (CIDs) in children attending day care or preschool. ***OBJECTIVES***: To investigate the efficacy of dietary supplementation with cow's skim milk fermented with the probiotic Lactobacillus paracasei CBA L74 in reducing CIDs in children attending day care or preschool. ***Methods***: Multicenter, randomized, double-blind, placebo-controlled trial on healthy children (aged 12-48 months) consuming daily 7 grams of cow's skim milk fermented with L. paracasei CBA L74 (group A), or placebo (maltodextrins group B) attending day care or preschool during the winter season. The main outcome was the proportion of children who experienced >/=1 episode of CID during a 3-month follow-up. Fecal biomarkers of innate (alpha- and beta-defensins, cathelicidin) and acquired immunity (secretory IgA) were also monitored. ***Results***: A total of 126 children (71 males, 56%) with a mean (SD) age of 33 (9) months completed the study, 66 in group A and 60 in group B. At intention to treat analysis, the proportion of children presenting >/=1 CID was 60% in group A vs. 83% in group B, corresponding to an absolute risk difference (ARD) of -23% (95% CI: -37% to -9%, $p < 0.01$). At per-protocol-analysis (PPA), the proportion of children presenting >/=1 CID was 18% in group A vs. 40% in group B, corresponding to an absolute risk difference (ARD) of -22% (95% CI: -37% to -6%, $p < 0.01$). PPA showed that the proportion of children presenting >/=1 acute gastroenteritis (AGE) was significantly lower in group A (18% vs. 40%, $p < 0.05$). The ARD for the occurrence of >/=1 AGE was -22% (95% CI: -37% to -6%, $p < 0.01$) in group A. Similar findings were obtained at PPA regarding the proportion of children presenting >/=1 upper respiratory tract infection (URTI), which was significantly lower in group A (51% vs. 74%, $p < 0.05$), corresponding to an ARD of -23% (95% CI: -40% to -7%, $p < 0.01$). Significant changes in innate and acquired immunity biomarkers were observed only in subjects in group A. ***Conclusions***: Dietary supplementation with cow's skim milk fermented with L. paracasei CBA L74 is an efficient strategy in preventing CIDs in children.

Cozma-Petrut, A., Loghin, F., Miere, D., and Dumitrascu, D. L. Diet in irritable bowel syndrome: What to recommend, not what to forbid to patients! World J.Gastroenterol. 6-7-2017; 23(21):3771-3783; PM: 28638217

ABSTRACT: A substantial proportion of patients with irritable bowel syndrome (IBS) associate their symptoms with the ingestion of specific foods. Therefore, in recent years, scientific research has increasingly focused on the role of diet in IBS and dietary management is now considered an important tool in IBS treatment. This article reviews the main dietary approaches in IBS emphasizing evidence from experimental and observational studies and summarizing the main diet and lifestyle recommendations provided by dietary guidelines and scientific literature. Despite the limited evidence for a beneficial role, general advice on healthy eating and lifestyle is recommended as the first-line approach in the dietary management of IBS. Standard recommendations include adhering to a regular meal pattern, reducing intake of insoluble fibers, alcohol, caffeine, spicy foods, and fat, as well as performing regular physical activity and ensuring a good hydration. Second-line dietary approach should be considered where IBS symptoms persist and recommendations include following a low FODMAP diet, to be delivered only by a healthcare professional with expertise in dietary management. The efficacy of this diet is supported by a growing body of evidence. In contrast, the role of lactose or gluten dietary restriction in the treatment of IBS remains subject to ongoing research with a lack of high-quality evidence. Likewise, further clinical trials are needed to conclude the efficacy of probiotics on IBS symptoms.

Crovesy, L., Ostrowski, M., Ferreira, D. M. T. P., Rosado, E. L., and Soares-Mota, M. Effect of Lactobacillus on body weight and body fat in overweight subjects: a systematic review of randomized controlled clinical trials. Int.J.Obes.(Lond). 7-10-2017; PM: 28792488

ABSTRACT: Gut microbiota is important for maintaining body weight. Modulation of gut microbiota by probiotics may result in weight loss and thus help in obesity treatment. The aim of this systematic review was to evaluate the effects of Lactobacillus on weight loss and/or fat mass in overweight adults. A search was performed on the Medline (PubMed) and Scopus electronic databases using the search terms: 'probiotics', 'Lactobacillus, 'obesity', 'body weight changes', 'weight loss', 'overweight', 'abdominal obesity', 'body composition', 'body weight', 'body fat' and 'fat mass'. In the total were found 1567 articles, but only 14 were included in this systematic review. Of these nine showed decreased body weight and/or body fat, three did not find effect and two showed weight gain. Results suggest that the beneficial effects are strain dependent. It can highlight that Lactobacillus plantarum and Lactobacillus rhamnosus when combined with a hypocaloric diet, L. plantarum with Lactobacillus curvatus, Lactobacillus gasseri, Lactobacillus amylovorus, Lactobacillus acidophilus and Lactobacillus casei with phenolic compounds, and multiple species of Lactobacillus.International Journal of Obesity advance online publication, 8 August 2017; doi:10.1038/ijo.2017.161.

Cui, J., Xiao, M., Liu, M., Wang, Z., Liu, F., Guo, L., Meng, H., Zhang, H., Yang, J., Deng, D., Huang, S., Ma, Y., and Liu, C. Coupling metagenomics with cultivation to select host-specific probiotic microorganisms for subtropical aquaculture. J.Appl.Microbiol. 8-7-2017; PM: 28783248

ABSTRACT: ***AIMS***: To demonstrate a non-empirical workflow to select host-specific probiotics for aquaculture industry. ***METHODS AND RESULTS***: By using both culture-dependent and -independent methods, we have systematically investigated, for the first time, the gut microbiota of twelve subtropical aquatic animal species. We found that the diversity, abundance, and distribution of gut microorganisms of these animals were host-specific, and that lactic acid bacteria (LAB) were predominant among the indigenous probiotic microbes. By using culturing method, we isolated and characterized ninety-eight LAB strains, however, only a few strains was representative of the dominant LAB OTUs recovered by culture-independent analysis. ***CONCLUSIONS***: Two cultured LAB strains, Enterococcus faecalis LS1-2 and E. faecium Z1-2, capturing the major LAB OTUs in the sequencing dataset of the most animal samples and showing significant antimicrobial activities against shrimp pathogens, were suggested to be the candidates of shrimp probiotics. This article is protected by copyright. All rights reserved.

D'Angelo, C., Reale, M., and Costantini, E. Microbiota and Probiotics in Health and HIV Infection. Nutrients. 6-16-2017; 9(6); PM: 28621726

ABSTRACT: Microbiota play a key role in various body functions, as well as in physiological, metabolic, and immunological processes, through different mechanisms such as the regulation of the development and/or functions of different types of immune cells in the intestines. Evidence indicates that alteration in the gut microbiota can influence infectious and non-infectious diseases. Bacteria that reside on the mucosal surface or within the mucus layer interact with the host immune system, thus, a healthy gut microbiota is essential for the development of mucosal immunity. In patients with human immunodeficiency virus (HIV), including those who control their disease with

antiretroviral drugs (ART), the gut microbiome is very different than the microbiome of those not infected with HIV. Recent data suggests that, for these patients, dysbiosis may lead to a breakdown in the gut's immunologic activity, causing systemic bacteria diffusion and inflammation. Since in HIV-infected patients in this state, including those in ART therapy, the treatment of gastrointestinal tract disorders is frustrating, many studies are in progress to investigate the ability of probiotics to modulate epithelial barrier functions, microbiota composition, and microbial translocation. This mini-review analyzed the use of probiotics to prevent and attenuate several gastrointestinal manifestations and to improve gut-associated lymphoid tissue (GALT) immunity in HIV infection.

D'Souza, B., Slack, T., Wong, S. W., Lam, F., Muhlmann, M., Koestenbauer, J., Dark, J., and Newstead, G. Randomized controlled trial of probiotics after colonoscopy. ANZ.J.Surg. 2017; 87(9):E65-E69; PM: 26183594

ABSTRACT: ***BACKGROUND***: Up to 20% of patients have ongoing abdominal symptoms at day 2 and beyond following colonoscopy. It was hypothesized that some of these symptoms are related to alterations in gut microbiota secondary to bowel preparation and would improve with probiotics compared with placebo. ***METHODS***: Patients were given either a probiotic or placebo capsule in the days following colonoscopy. Colonoscopy was performed with air insufflation. The probiotic capsule contained the strains Lactobacillus acidophilus NCFM and Bifidobacterium lactis Bi-07. Patients recorded their symptoms at 1 h, 1, 2, 4, 7 and 14 days post colonoscopy and returned results once their symptoms had resolved. The primary outcomes used were the length of days to resolution of bloating, abdominal pain and altered bowel function post colonoscopy. ***RESULTS***: A total of 320 patients were randomized. After loss to follow-up and withdrawal, 133 patients were analysed in the probiotic group and 126 in the placebo group. Patients having probiotic had a lower number of pain days following colonoscopy, 1.99 versus 2.78 days ($P < 0.033$). There was no significant difference in bloating or return to normal bowel habit days ($P = 0.139$ and 0.265 respectively). Subgroup analysis revealed that patients with pre-existing abdominal pain benefited from probiotics in number of pain days, 2.16 versus 4.08 ($P = 0.0498$). ***CONCLUSION***: Our study has shown a significant reduction in the duration of pain days post colonoscopy in patients taking probiotic compared with placebo. No significant effect was seen in terms of return to normal bowel function or bloating post colonoscopy.

Dahlberg, C. J., Ou, J. J., Babish, J. G., Lamb, J. J., Eliason, S., Brabazon, H., Gao, W., Kaadige, M. R., and Tripp, M. L. A 13-week, randomized, pilot trial of a low glycemic load diet and lifestyle modification program combining low glycemic load protein shakes and targeted nutraceuticals improved weight loss and cardio-metabolic risk factors over a low glycemic load diet alone in subjects with cardiovascular risk factors. Can.J.Physiol Pharmacol. 8-11-2017; PM: 28800398

ABSTRACT: An open label, randomized, exploratory study comprising 44 healthy, overweight subjects with cardio-metabolic syndrome (CMS) risk factors was conducted to assess the safety, tolerability and efficacy of a proprietary lifestyle modification program without (DIET) and with (PROG) targeted nutraceutical supplementation including soy, pea and whey proteins, phytosterols, antioxidants, probiotics, fish oil and berberine over 13-weeks. Key metrics were recorded at baseline, weeks 9 and 13. For DIET and PROG compliance was 85% and 86%, respectively, with no adverse events related to the diet or supplements. Twelve subjects discontinued prior to week 9 for

reasons unrelated to the study. PROG subjects experienced greater decreases (P<0.05) than DIET in body weight, fat mass, total cholesterol, LDL cholesterol, TG, cholesterol/HDL, TG/HDL, ApoB/ApoA, and hs-CRP. The Framingham 10-year cardiovascular disease risk score decreased by 40% (P<0.01) in the PROG arm versus no change for the DIET arm. As a pilot study, it was not possible to state whether the observed effects were a result of nutraceutical supplementation alone or the result of additive or synergistic interactions among diet, lifestyle modifications and nutraceutical supplementation. Moreover, individuals with CMS risk factors following a lifestyle modification program received additional health benefits from targeted nutraceutical supplementation. NCT03097965.

Das, G., Patra, J. K., Lee, S. Y., Kim, C., Park, J. G., and Baek, K. H. Analysis of metabolomic profile of fermented Orostachys japonicus A. Berger by capillary electrophoresis time of flight mass spectrometry. PLoS.One. 2017; 12(7):e0181280; PM: 28704842

ABSTRACT: Microbial cell performance in food biotechnological processes has become an important concern for improving human health worldwide. Lactobacillus plantarum, which is widely distributed in nature, is a lactic acid bacterium with many industrial applications for fermented foods or functional foods (e.g., probiotics). In the present study, using capillary electrophoresis time of flight mass spectrometry, the metabolomic profile of dried Orostachys japonicus A. Berger, a perennial medicinal herb with L. plantarum was compared with that of O. japonicus fermented with L. plantarum to elucidate the metabolomic changes induced by the fermentation process. The levels of several metabolites were changed by the fermentation process, indicating their involvement in microbial performance. For example, glycolysis, the pentose phosphate pathway, the TCA cycle, the urea cycle-related metabolism, nucleotide metabolism, and lipid and amino acid metabolism were altered significantly by the fermentation process. Although the fermented metabolites were not tested using in vivo studies to increase human health benefits, our findings provide an insight into the alteration of metabolites induced by fermentation, and indicated that the metabolomic analysis for the process should be accompanied by fermenting strains and conditions.

Daskalakis, G. J. and Karambelas, A. K. Vaginal Probiotic Administration in the Management of Preterm Premature Rupture of Membranes. Fetal Diagn.Ther. 2017; 42(2):92-98; PM: 27744438

ABSTRACT: ***OBJECTIVE***: To examine the influence of vaginal probiotic administration as an adjunct to standard antibiotic treatment on perinatal outcome in women with preterm premature rupture of membranes (PPROM). ***MATERIALS AND METHODS***: This was a prospective randomized trial of cases with PPROM (24-34 weeks) that were admitted to our department between 2011 and 2015. Forty-nine cases received vaginal probiotics for 10 days in combination with antibiotic prophylaxis and were compared to 57 others that received only antibiotics for the same time period. ***RESULTS***: The mean gestational age at birth (35.49 vs. 32.53 weeks), the mean duration of the latency period (5.60 vs. 2.48 weeks), and the mean birth weight (2,439.08 vs. 2,004.81 g) were significantly higher in the study group in comparison to the controls. Moreover, the neonates of the study group had a lower chance to enter the neonatal intensive care unit or the neonatal special care unit, shorter total hospitalization time, and lower need for oxygen administration and mechanical ventilation, as well as lower length of oxygen administration. ***CONCLUSIONS***: Vaginal probiotics as an adjunct to antibiotic prophylaxis

in women with PPROM prolonged the latency period and improved the perinatal outcome.

de Albuquerque, T. M. R., Garcia, E. F., de Oliveira, Araujo A., Magnani, M., Saarela, M., and de Souza, E. L. In Vitro Characterization of Lactobacillus Strains Isolated from Fruit Processing By-Products as Potential Probiotics. Probiotics.Antimicrob.Proteins. 8-23-2017; PM: 28836171

ABSTRACT: Nine wild Lactobacillus strains, namely Lactobacillus plantarum 53, Lactobacillus fermentum 56, L. fermentum 60, Lactobacillus paracasei 106, L. fermentum 250, L. fermentum 263, L. fermentum 139, L. fermentum 141, and L. fermentum 296, isolated from fruit processing by-products were evaluated in vitro for a series of safety, physiological functionality, and technological properties that could enable their use as probiotics. Considering the safety aspects, the resistance to antibiotics varied among the examined strains, and none of the strains presented hemolytic and mucinolytic activity. Regarding the physiological functionality properties, none of the strains were able to deconjugate bile salts; all of them presented low to moderate cell hydrophobicity and were able to autoaggregate, coaggregate with Listeria monocytogenes and Escherichia coli, and antagonize pathogenic bacteria. Exposure to pH 2 sharply decreased the survival of the examined strains after 1- or 2-h exposure; variable decreases were noted after 3-h exposure to pH 3. Overall, exposure to pH 5 and to bile salts (0.15, 0.3, and 1%) did not decrease the strains' survival. Examined strains presented better ability to survive from the exposure to simulated gastrointestinal conditions in laboratorial media and milk than in grape juice. Considering the technological properties, all the strains were positive for proteolytic activity and EPS and diacetyl production, and most of them had good tolerance to 1-4% NaCl. These results indicate that wild Lactobacillus strains isolated from fruit processing by-products could present performance compatible with probiotic properties and technological features that enable the development of probiotic foods with distinct characteristics.

de Andrade Calaca, P. R., Bezerra, R. P., Albuquerque, W. W. C., Porto, A. L. F., and Cavalcanti, M. T. H. Probiotics as a preventive strategy for surgical infection in colorectal cancer patients: a systematic review and meta-analysis of randomized trials. Transl.Gastroenterol.Hepatol. 2017; 2:67; PM: 28905008

ABSTRACT: ***BACKGROUND***: Infection following abdominal surgery remains a major factor in morbidity among colorectal cancer (CRC) patients. Probiotic therapy has been suggested to improve the clinical and laboratory outcome of patients undergoing gastrointestinal surgery. The aim of this study was to investigate the efficacy of probiotic lactic acid bacteria in patients with CRC in the pre- and postoperative phases. ***METHODS***: Systematic database searches identified 1,080 related articles. However, only seven articles were selected according to the eligibility criteria for qualitative and quantitative evaluation. ***RESULTS***: Most of the reviewed articles presented satisfactory results related to the prevention of surgical inflammation in patients undergoing resection of CRC when using strains of Lactobacillus genus, predominantly. ***CONCLUSIONS***: Probiotics are suggested to prevent surgical inflammation of CRC, at the same time that the combination of particular microorganisms administered is beneficial to the treatment and surgical recovery.

de Moura, M. Q., da Silva Terto, W. D., Jeske, S. T., de Castro, L. M., Pinto, N. B., da Costa Avila, L. F., Leite, F. P. L., and Berne, M. E. A. Evaluation of the transcription of interleukin-12 in the intestinal mucosa of mice subjected to experimental toxocariasis and supplemented with Saccharomyces boulardii. Vet.Parasitol. 8-15-2017; 242:59-62; PM: 28606326

No Abstract Available.

de Muinck, E. J., Lundin, K. E. A., and Trosvik, P. Linking Spatial Structure and Community-Level Biotic Interactions through Cooccurrence and Time Series Modeling of the Human Intestinal Microbiota. mSystems. 2017; 2(5); PM: 28904999

ABSTRACT: The gastrointestinal (GI) microbiome is a densely populated ecosystem where dynamics are determined by interactions between microbial community members, as well as host factors. The spatial organization of this system is thought to be important in human health, yet this aspect of our resident microbiome is still poorly understood. In this study, we report significant spatial structure of the GI microbiota, and we identify general categories of spatial patterning in the distribution of microbial taxa along a healthy human GI tract. We further estimate the biotic interaction structure in the GI microbiota, both through time series and cooccurrence modeling of microbial community data derived from a large number of sequentially collected fecal samples. Comparison of these two approaches showed that species pairs involved in significant negative interactions had strong positive contemporaneous correlations and vice versa, while for species pairs without significant interactions, contemporaneous correlations were distributed around zero. We observed similar patterns when comparing these models to the spatial correlations between taxa identified in the adherent microbiota. This suggests that colocalization of microbial taxon pairs, and thus the spatial organization of the GI microbiota, is driven, at least in part, by direct or indirect biotic interactions. Thus, our study can provide a basis for an ecological interpretation of the biogeography of the human gut. IMPORTANCE The human gut microbiome is the subject of intense study due to its importance in health and disease. The majority of these studies have been based on the analysis of feces. However, little is known about how the microbial composition in fecal samples relates to the spatial distribution of microbial taxa along the gastrointestinal tract. By characterizing the microbial content both in intestinal tissue samples and in fecal samples obtained daily, we provide a conceptual framework for how the spatial structure relates to biotic interactions on the community level. We further describe general categories of spatial distribution patterns and identify taxa conforming to these categories. To our knowledge, this is the first study combining spatial and temporal analyses of the human gut microbiome. This type of analysis can be used for identifying candidate probiotics and designing strategies for clinical intervention.

de Oliveira, G. L. V., Leite, A. Z., Higuchi, B. S., Gonzaga, M. I., and Mariano, V. S. Intestinal dysbiosis and probiotic applications in autoimmune diseases. Immunology. 2017; 152(1):1-12; PM: 28556916

ABSTRACT: In humans, a complex interaction between the host immune system and commensal microbiota is required to maintain gut homeostasis. In this symbiotic relationship, the microbiota provides carbohydrate fermentation and digestion, vitamin synthesis and gut-associated lymphoid tissue development, as well as preventing colonization by pathobionts, whereas the host offers a niche and nutrients for the survival of the microbiota. However, when this mutualistic relationship is compromised and an

altered interaction between immune cells and microorganisms occurs, the gut microbiota may cause or contribute to the establishment of infectious diseases and trigger autoimmune diseases. Researchers have made efforts to clarify the role of the microbiota in autoimmune disease development and find new therapeutic approaches to treat immune-mediated diseases. However, the exact mechanisms involved in the dysbiosis and breakdown of the gut epithelial barrier are currently unknown. Here, we provide a general overview of studies describing gut microbiota perturbations in animal models of autoimmune diseases, such as type 1 diabetes, multiple sclerosis, rheumatoid arthritis and systemic lupus erythematosus. Moreover, we include the main studies concerning dysbiosis in humans and a critical discussion of the existing data on the use of probiotics in these autoimmune diseases.

de Roos, N. M., van, Hemert S., Rovers, J. M. P., Smits, M. G., and Witteman, B. J. M. The effects of a multispecies probiotic on migraine and markers of intestinal permeability-results of a randomized placebo-controlled study. Eur.J.Clin.Nutr. 5-24-2017; PM: 28537581

ABSTRACT: ***BACKGROUND/OBJECTIVES***: Migraine, associated with several gastrointestinal disorders, may result from increased intestinal permeability, allowing endotoxins to enter the bloodstream. We tested whether probiotics could reduce migraine through an effect on intestinal permeability and inflammation. ***SUBJECTS/METHODS***: In total, 63 patients were randomly allocated to the probiotic (n=31) or the placebo group (n=32). Participants ingested a multispecies probiotic (5x109 colony-forming units) or placebo daily for 12 weeks. Migraine was assessed with the Migraine Disability Assessment Scale (MIDAS), the Headache Disability Inventory (HDI) and headache diaries. At baseline and 12 weeks, intestinal permeability was measured with the urinary lactulose/mannitol test and fecal and serum zonulin; inflammation was measured from interleukin (IL) -6, IL-10, tumor necrosis factor-alpha and C-reactive protein in serum. ***RESULTS***: The MIDAS migraine intensity score significantly decreased in both groups (P<0.001) and the HDI score significantly decreased in the probiotic group (P=0.032) and borderline in the placebo group (P=0.053). In the probiotics group, patients had a median of 6 migraine days in the first month, 4 in the second month (P=0.002) and 5 in the last month, which was not significantly different from the 5, 4, and 4 days in the placebo group. A 2day reduction in migraine days was seen in 12/31 patients in the probiotics group versus 7/29 in the placebo group (ns). Probiotic use did not significantly affect medication use, intestinal permeability or inflammation compared to placebo. ***CONCLUSIONS***: In this study, we could not confirm significant benefit from a multispecies probiotic compared to a placebo on the outcome parameters of migraine and intestinal integrity.European Journal of Clinical Nutrition advance online publication, 24 May 2017; doi:10.1038/ejcn.2017.57.

De, Lorenzo A., Costacurta, M., Merra, G., Gualtieri, P., Cioccoloni, G., Marchetti, M., Varvaras, D., Docimo, R., and Di, Renzo L. Can psychobiotics intake modulate psychological profile and body composition of women affected by normal weight obese syndrome and obesity? A double blind randomized clinical trial. J.Transl.Med. 6-10-2017; 15(1):135; PM: 28601084

ABSTRACT: ***BACKGROUND***: Evidence of probiotics effects on gut function, brain activity and emotional behaviour were provided. Probiotics can have dramatic effects on behaviour through the microbiome-gut-brain axis, through vagus nerve. We investigated whether chronic probiotic intake could modulate psychological state, eating behaviour

and body composition of normal weight obese (NWO) and preobese-obese (PreOB/OB) compared to normal weight lean women (NWL). ***METHODS***: 60 women were enrolled. At baseline and after a 3-week probiotic oral suspension (POS) intake, all subjects underwent evaluation of body composition by anthropometry and dual X-ray absorptiometry, and psychological profile assessment by self-report questionnaires (i.e. EDI-2, SCL90R and BUT). Statistical analysis was carried out using paired t test or a non-parametric Wilcoxon test to evaluate differences between baseline and after POS intake, one-way ANOVA to compare all three groups and, where applicable, Chi square or t test were used to assess symptoms. ***RESULTS***: Of the 48 women that concluded the study, 24% were NWO, 26% were NWL and 50% were PreOB/OB. Significant differences in body composition were highlighted among groups both at baseline and after a POS ($p < 0.05$). After POS intake, a significant reduction of BMI, resistance, FM (kg and %) ($p < 0.05$), and a significant increase of FFM (kg and %) ($p < 0.05$) were observed in all subjects in NOW and PreOB/OB. After POS intake, reduction of bacterial overgrowth syndrome ($p < 0.05$) and lower psychopathological scores ($p < 0.05$) were observed in NWO and PreOB/OB women. At baseline and after POS intake, all subjects tested were negative to SCL90R_GSI scale, but after treatment subjects positive to BUT_GSI scale were significantly reduced (8.33%) ($p < 0.05$) compared to the baseline (33.30%). In NWO and PreOB/OB groups significant differences ($p < 0.05$) in response to the subscales of the EDI-2 were observed. Significant improvement of the orocecal transit time was observed ($p < 0.05$) after POS intake. Furthermore, significant differences were observed for meteorism ($p < 0.05$) and defecation frequency ($p < 0.05$). ***CONCLUSIONS***: A 3-week intake of selected psychobiotics modulated body composition, bacterial contamination, psychopathological scores of NWO and PreOB/OB women. Further research is needed on a larger population and for a longer period of treatment before definitive conclusions can be made. Trial registration ClinicalTrials.gov Id: NCT01890070.

de, Vos P., Mujagic, Z., de Haan, B. J., Siezen, R. J., Bron, P. A., Meijerink, M., Wells, J. M., Masclee, A. A. M., Boekschoten, M. V., Faas, M. M., and Troost, F. J. Lactobacillus plantarum Strains Can Enhance Human Mucosal and Systemic Immunity and Prevent Non-steroidal Anti-inflammatory Drug Induced Reduction in T Regulatory Cells. Front Immunol. 2017; 8:1000; PM: 28878772

ABSTRACT: Orally ingested bacteria interact with intestinal mucosa and may impact immunity. However, insights in mechanisms involved are limited. In this randomized placebo-controlled cross-over trial, healthy human subjects were given Lactobacillus plantarum supplementation (strain TIFN101, CIP104448, or WCFS1) or placebo for 7 days. To determine whether L. plantarum can enhance immune response, we compared the effects of three stains on systemic and gut mucosal immunity, by among others assessing memory responses against tetanus toxoid (TT)-antigen, and mucosal gene transcription, in human volunteers during induction of mild immune stressor in the intestine, by giving a commonly used enteropathic drug, indomethacin [non-steroidal anti-inflammatory drug (NSAID)]. Systemic effects of the interventions were studies in peripheral blood samples. NSAID was found to induce a reduction in serum CD4+/Foxp3 regulatory cells, which was prevented by L. plantarum TIFN101. T-cell polarization experiments showed L. plantarum TIFN101 to enhance responses against TT-antigen, which indicates stimulation of memory responses by this strain. Cell extracts of the specific L. plantarum strains provoked responses after WCFS1 and TIFN101 consumption, indicating stimulation of immune responses against the specific bacteria. Mucosal immunomodulatory effects were studied in duodenal biopsies. In small intestinal mucosa, TIFN101 upregulated genes associated with maintenance of T- and B-cell function and antigen presentation.

Furthermore, L. plantarum TIFN101 and WCFS1 downregulated immunological pathways involved in antigen presentation and shared downregulation of snoRNAs, which may suggest cellular destabilization, but may also be an indicator of tissue repair. Full sequencing of the L. plantarum strains revealed possible gene clusters that might be responsible for the differential biological effects of the bacteria on host immunity. In conclusion, the impact of oral consumption L. plantarum on host immunity is strain dependent and involves responses against bacterial cell components. Some strains may enhance specific responses against pathogens by enhancing antigen presentation and leukocyte maintenance in mucosa. In future studies and clinical settings, caution should be taken in selecting beneficial bacteria as closely related strains can have different effects. Our data show that specific bacterial strains can prevent immune stress induced by commonly consumed painkillers such as NSAID and can have enhancing beneficial effects on immunity of consumers by stimulating antigen presentation and memory responses.

de, Weerth C. Do Bacteria Shape our Development? Crosstalk between Intestinal Microbiota and HPA Axis. Neurosci.Biobehav.Rev. 9-13-2017; PM: 28918360

ABSTRACT: The human body contains as many bacteria in the intestine as the total number of human body cells. These bacteria have a central position in human health and disease, and would also play a role in the regulation of emotions, behavior, and even higher cognitive functions. The Hypothalamic-Pituitary-Adrenal axis (HPA axis) is a major physiological stress system that produces cortisol. This hormone is involved in responding to environmental stress and also shapes many aspects of brain development. Both the HPA axis and the intestinal microbiota show rapid and profound developmental changes during the first years of life. Early environmental disturbances can affect the development of both systems. Early adversity, for example, is known to lead to later unbalances in both, as well as to psychopathological behavior and emotions. The goal of this theoretical review is to summarize current knowledge on the developmental crosstalk between the intestinal microbiota and the HPA axis, providing a basis for understanding the development and bidirectional communication between these two essential systems in human functioning.

Debre, P. [Challenges set by the microbiota]. Biol.Aujourdhui. 2017; 211(1):19-28; PM: 28682224

ABSTRACT: The microbiota designates the various flora of commensal microbes of living species. Most research in human focusing mainly on the intestinal microbiota, we will limit ourselves to its description and role in physiology and pathology. The intestinal microbiota acts on digestion and the immune system. It seems responsible, at least in part, for obesity, digestive cancers, several autoimmune and allergic pathologies, and pathologies of the nervous system. The role of prebiotics, probiotics, xenobiotics and stool transplantations will be discussed.

Deng, B., Wu, J., Li, X., Men, X., and Xu, Z. Probiotics and Probiotic Metabolic Product Improved Intestinal Function and Ameliorated LPS-Induced Injury in Rats. Curr.Microbiol. 7-31-2017; PM: 28761979

ABSTRACT: In the present study, we sought to determine the effects of Bacillus subtilis (BAS) and Bacillus licheniformis (BAL) in rats after lipopolysaccharide (LPS)-induced acute

intestinal inflammation. We also determined whether the B. subtilis metabolic product (BASM) is as effective as the live-cell probiotic. 60 male SD rats were randomly assigned to five groups and administered a diet containing 0.05% B. licheniformis (BAL group), 0.05% B. subtilis (BAS group), 0.5% B. subtilis metabolic product (BASM group), or a basic diet (PC group and NC group) for 40 days. On day 40, BAL, BAS, BASM, and NC groups were injected with 4 mg/kg body weight LPS. 4 h later, all rats were anesthetized and sacrificed. The results showed that the administration of B. licheniformis and B. subtilis improved intestinal function as evidenced by histology, increased enzyme activity, and mucosal thickness. They also increased the number of intraepithelial lymphocytes and decreased mucosal myeloperoxidase activity and plasma TNF-alpha. In addition, the cecal content of B. subtilis-treated rats had significantly increased microbial diversity, decreased numbers of Firmicutes, and increased numbers of Bacteroidetes as compared to rats fed basic diets. Similar to BAS group, the cecal content of B. licheniformis-treated rats decreased the number of Firmicutes. Administration of B. subtilis metabolic product had similar effects on intestinal function, inflammation response, and microbial diversity as B. subtilis but these effects were attenuated. In conclusion, administration of probiotic strains B. licheniformis or B. subtilis improved intestinal function, ameliorated the inflammation response, and modulated microflora after LPS-induced acute inflammation in rats. Non-living cells also exerted probiotic properties but live cells tended to function better.

Derwa, Y., Gracie, D. J., Hamlin, P. J., and Ford, A. C. Systematic review with meta-analysis: the efficacy of probiotics in inflammatory bowel disease. Aliment.Pharmacol.Ther. 2017; 46(4):389-400; PM: 28653751

ABSTRACT: ***BACKGROUND***: Ulcerative colitis (UC) and Crohn's disease (CD) are inflammatory bowel diseases (IBD). Evidence implicates disturbances of the gastrointestinal microbiota in their pathogenesis. AIM: To perform a systematic review and meta-analysis to examine the efficacy of probiotics in IBD. ***METHODS***: MEDLINE, EMBASE, and the Cochrane Controlled Trials Register were searched (until November 2016). Eligible randomised controlled trials (RCTs) recruited adults with UC or CD, and compared probiotics with 5-aminosalicylates (5-ASAs) or placebo. Dichotomous symptom data were pooled to obtain a relative risk (RR) of failure to achieve remission in active IBD, or RR of relapse of disease activity in quiescent IBD, with 95% confidence intervals (CIs). ***RESULTS***: The search identified 12 253 citations. Twenty-two RCTs were eligible. There was no benefit of probiotics over placebo in inducing remission in active UC (RR of failure to achieve remission=0.86; 95% CI=0.68-1.08). However, when only trials of VSL#3 were considered there appeared to be a benefit (RR=0.74; 95% CI=0.63-0.87). Probiotics appeared equivalent to 5-ASAs in preventing UC relapse (RR=1.02; 95% CI=0.85-1.23). There was no benefit of probiotics in inducing remission of active CD, in preventing relapse of quiescent CD, or in preventing relapse of CD after surgically induced remission. ***CONCLUSIONS***: VSL#3 may be effective in inducing remission in active UC. Probiotics may be as effective as 5-ASAs in preventing relapse of quiescent UC. The efficacy of probiotics in CD remains uncertain, and more evidence from RCTs is required before their utility is known.

Deshmukh, J., Deshmukh, M., and Patole, S. Probiotics for the management of neonatal hyperbilirubinemia: a systematic review of randomized controlled trials. J.Matern.Fetal Neonatal Med. 8-31-2017; 1-10; PM: 28823200

ABSTRACT: ***BACKGROUND***: Neonatal jaundice requiring phototherapy is associated with significant socioeconomic burden including hospital readmission, prolonged hospital stay, and separation of the baby from mother. ***OBJECTIVES***: To assess the efficacy and safety of probiotics in reducing the need for phototherapy and its duration in neonatal hyperbilirubinemia. ***METHODS***: A systematic review of randomized controlled trials (RCTs) of probiotic supplementation for prevention or treatment of jaundice in neonates (any gestation or weight) using the Cochrane methodology. Primary outcome was the duration of phototherapy. Secondary outcomes included incidence of jaundice, total serum bilirubin (TSB) level at 24, 48, 72, 96 h, and day 7, duration of hospital stay, and adverse effects (e.g. probiotic sepsis). Results were summarized as per GRADE guidelines. ***RESULTS***: Nine RCTs (prophylactic: six trials, N = 1761; therapeutic: three trials, N = 279) with low to high risk of bias were included. Meta-analysis (random-effects model) showed probiotic supplementation reduced duration of phototherapy [N = 415, mean difference (MD): -11.80 (-17.47, -6.13); p < .0001; level of evidence (LOE): low]. TSB was significantly reduced at 96 h [MD: -1.74 (-2.92, -0.57); p = .004] and 7 d [MD: -1.71 (-2.25, -1.17); p < .00001; LOE: low] after probiotic treatment. Prophylactic probiotics did not reduce the incidence of jaundice significantly [N = 1582, relative risk (RR): 0.56 (0.25, 1.27); p = .16; LOE: low]. There were no probiotic-related adverse effects. ***CONCLUSION***: Limited low-quality evidence indicates that probiotic supplementation may reduce the duration of phototherapy in neonates with jaundice. Routine use of probiotics to prevent or treat neonatal jaundice cannot be recommended. Large well-designed trials are essential to confirm these findings.

Dimidi, E., Rossi, M., and Whelan, K. Irritable bowel syndrome and diet: where are we in 2018? Curr.Opin.Clin.Nutr.Metab Care. 9-1-2017; PM: 28872467

ABSTRACT: ***PURPOSE OF REVIEW***: The aim is to review the most recent advances in the evidence supporting the use of various dietary interventions for the management of irritable bowel syndrome (IBS). ***RECENT FINDINGS***: There is insufficient evidence of the effect of fibres other than psyllium in IBS, whereas the recent studies on prebiotics suggest a limited effect in IBS. Recent probiotic trials continue to provide varying results, with some probiotic strains exhibiting beneficial effects, whereas others show no effect. Recent trials have also confirmed the clinical effectiveness of a diet low in fermentable oligosaccharides, disaccharides, monosaccharides and polyols (i.e. low FODMAP diet) in IBS. Although gluten sensitivity has also been recently investigated, its presence cannot be confirmed yet because of the presence of other potential contributing compounds in wheat. Studies also suggest a potential beneficial effect of peppermint oil, which warrants further research. ***SUMMARY***: It is clear that a low FODMAP diet has a beneficial effect in a majority of patients with IBS. Probiotics also have great potential in the management of IBS; however, it is still unclear which strains and doses are the most beneficial. Further research is needed on the effect of different fibres, or combinations of fibres, in IBS.

Dinan, T. G. and Cryan, J. F. Brain-gut-microbiota axis and mental health. Psychosom.Med. 8-11-2017; PM: 28806201

ABSTRACT: ***OBJECTIVE***: The brain-gut-microbiota axis has been put forward as a new paradigm in neuroscience, which may be of relevance to mental illness. The mechanisms of signal transmission in the brain-gut-microbiota axis are complex and involve bidirectional communications which enables gut microbes to communicate with

the brain, and the brain to communicate with the microbes. This review assesses the potential usefulness and limitations of the paradigm. ***METHODS***: A selective literature review was conducted to evaluate the current knowledge in clinical and pre-clinical brain-gut-microbiota interactions as related to psychiatric disorders. ***RESULTS***: The overwhelming majority of published studies in the field are preclinical and there is so far a lack of clinical studies. Preliminary studies in psychiatric populations, support the view of a dysbiosis in some conditions, but studies are often small-scale and marred by potential confounding variables. Preclinical studies support the view that psychobiotics ('bacteria which when ingested in adequate amounts have a positive mental health benefit') might be of use in treating some patients with mental health difficulties. To date we have no well conducted studies in clinical populations, though there are some studies in healthy volunteers. A cocktail of probiotics has been shown to alter brain activity as monitored by functional MRI and Bifidobacterium longum was reported to alter brain electrical activity. ***CONCLUSION***: It has yet to be convincingly demonstrated that the exciting findings of psychobiotic efficacy demonstrated in preclinical models of psychiatric illness will translate to patients.

do Carmo, F. L. R., Rabah, H., Huang, S., Gaucher, F., Deplanche, M., Dutertre, S., Jardin, J., Le, Loir Y., Azevedo, V., and Jan, G. Propionibacterium freudenreichii Surface Protein SlpB Is Involved in Adhesion to Intestinal HT-29 Cells. Front Microbiol. 2017; 8:1033; PM: 28642747

ABSTRACT: Propionibacterium freudenreichii is a beneficial bacterium traditionally used as a cheese ripening starter and more recently for its probiotic abilities based on the release of beneficial metabolites. In addition to these metabolites (short-chain fatty acids, vitamins, and bifidogenic factor), P. freudenreichii revealed an immunomodulatory effect confirmed in vivo by the ability to protect mice from induced acute colitis. This effect is, however, highly strain-dependent. Local action of metabolites and of immunomodulatory molecules is favored by the ability of probiotics to adhere to the host cells. This property depends on key surface compounds, still poorly characterized in propionibacteria. In the present study, we showed different adhesion rates to cultured human intestinal cells, among strains of P. freudenreichii. The most adhesive one was P. freudenreichii CIRM-BIA 129, which is known to expose surface-layer proteins. We evidenced here the involvement of these proteins in adhesion to cultured human colon cells. We then aimed at deciphering the mechanisms involved in adhesion. Adhesion was inhibited by antibodies raised against SlpB, one of the surface-layer proteins in P. freudenreichii CIRM-BIA 129. Inactivation of the corresponding gene suppressed adhesion, further evidencing the key role of slpB product in cell adhesion. This work confirms the various functions fulfilled by surface-layer proteins, including probiotic/host interactions. It opens new perspectives for the understanding of probiotic determinants in propionibacteria, and for the selection of the most efficient strains within the P. freudenreichii species.

do Vale, Pereira G., da Cunha, D. G., Pedreira Mourino, J. L., Rodiles, A., Jaramillo-Torres, A., and Merrifield, D. L. Characterization of microbiota in Arapaima gigas intestine and isolation of potential probiotic bacteria. J.Appl.Microbiol. 8-18-2017; PM: 28833934

ABSTRACT: ***AIM***: The aim of this study was to determine the intestinal microbiota of pirarucu (A. gigas) in different growth stages (adult and fingerlings), and to isolate and identify potential probiotic bacteria. ***METHODS AND RESULTS***: High-throughput sequencing (HTS) analysis of the intestinal contents revealed that the majority of

sequences belonged to the Proteobacteria, Fusobacteria and Firmicutes phyla. At the genus level, the greatest number of sequences belonged to Bradyrhizobium in adult fish, while Cetobacterium was the most abundant in juvenile fish. Twenty-three lactic acid bacteria (LAB) were isolated on MRS agar from healthy juvenile fish. The isolates were tested in vitro for probiotic properties. Two isolates (identified as strains of Lactococcus lactis subsp. lactis and Enterococcus faecium) displayed antagonism against all ten pathogens tested, were non-hemolytic and maintained good viability for at least 3 weeks when supplemented to fish diets. The presence of a number of antibiotic resistance genes (ARGs), conferring resistance to erythromycin, tetracycline and chloramphenicol, was investigated by PCR. ***CONCLUSIONS***: The absence of ARGs investigated, the potential to antagonize pathogens and favorable growth and survival characteristics indicates that these autochthonous isolates have the potential to be considered probiotics, which will be studied in future in vivo experiments. ***SIGNIFICANCE AND IMPACT OF STUDY***: The present study has demonstrated, for the first time, the normal microbiota in the A. gigas intestine during different life stages and the presence of LAB strains. It also demonstrated LAB antibiotic resistance and antagonistic behavior against pathogens isolated from the same fish. This article is protected by copyright. All rights reserved.

Dodoo, C. C., Wang, J., Basit, A. W., Stapleton, P., and Gaisford, S. Targeted delivery of probiotics to enhance gastrointestinal stability and intestinal colonisation. Int.J.Pharm. 9-15-2017; 530(1-2):224-229; PM: 28764983

ABSTRACT: The aim of this work was to assess the viability of some commercial probiotics after exposure to gastric acid and the possibility of modifying these formulations for delivery into the distal parts of the intestines. Gastrointestinal tolerance testing was conducted for three commercial probiotics and an in-house freeze-dried Lactobacillus acidophilus strain. The contents of the commercial products and the in-house freeze-dried strain were then loaded into capsules for site-specific delivery into the colon using the Phloral(R) coating technology; the viability upon release was then ascertained. An assessment of the potential of these products to adhere to intestinal cells was also conducted. The results showed that all the commercial products contained the minimum number of probiotic strains as indicated on their respective packages. When gastric acid tolerance tests were performed on these products, all the commercial probiotics and the prepared freeze-dried strain demonstrated over 106 CFU reductions within 5min. When these were encapsulated for site-specific delivery into the distal parts of the gut, viabilities of approximately 90% were obtained after these capsules had been initially deposited in gastric acid for 2h. An evaluation of the ability of the probiotic formulations to adhere to intestinal cells demonstrated adhesion in the range 64-76% for the products evaluated. The need to target the delivery of probiotics into the intestines has been demonstrated here as this offers a greater potential for colonisation of the intestines once the harshness of the stomach has been overcome.

Dong, B., Yi, Y., Liang, L., and Shi, Q. High Throughput Identification of Antimicrobial Peptides from Fish Gastrointestinal Microbiota. Toxins.(Basel). 8-30-2017; 9(9); PM: 28867788

ABSTRACT: Antimicrobial peptides (AMPs) are a group of small peptides, which are secreted by almost all creatures in nature. They have been explored in therapeutic and agricultural aspects as they are toxic to many bacteria. A considerable amount of work

has been conducted in analyzing 16S and metagenomics of the gastrointestinal (GI) microbiome of grass carp (Ctenopharyngodon idellus). However, these datasets are still untapped resources. In this present study, a homologous search was performed to predict AMPs from our newly generated metagenome of grass carp. We identified five AMPs with high similarities to previously reported bacterial toxins, such as lantibiotic and class II bacteriocins. In addition, we observed that the top abundant genus in the GI microbiota of the grass carp was generally consistent with the putative AMP-producing strains, which are mainly from Lactobacillales. Furthermore, we constructed the phylogenetic relationship of these putative AMP-producing bacteria existing in the GI of grass carp and some popular commercial probiotics (commonly used for microecologics), demonstrating that they are closely related. Thus, these strains have the potential to be developed into novel microecologics. In a word, we provide a high-throughput way to discover AMPs from fish GI microbiota, which can be developed as alternative pathogen antagonists (toxins) for microecologics or probiotic supplements.

Douglas, G. L. and Voorhies, A. A. Evidence based selection of probiotic strains to promote astronaut health or alleviate symptoms of illness on long duration spaceflight missions. Benef.Microbes. 8-1-2017; 1-12; PM: 28760005

ABSTRACT: Spaceflight impacts multiple aspects of human physiology, which will require non-invasive countermeasures as mission length and distance from Earth increases and the capability for external medical intervention decreases. Studies on Earth have shown that probiotics have the potential to improve some of the conditions that have manifested during spaceflight, such as gastrointestinal distress, dermatitis, and respiratory infections. The constraints and risks of spaceflight make it imperative that probiotics are carefully selected based on their strain-specific benefits, doses, delivery mechanisms, and relevance to likely crew conditions prior to evaluation in astronauts. This review focuses on probiotics that have been incorporated into healthy human gastrointestinal microbiomes and associated clinically with improvements in inflammatory state or alleviation of symptoms of crew-relevant illness. These studies provide an evidence base for probiotic selection with the greatest potential to support crew health and well-being in spaceflight.

Draper, K., Ley, C., and Parsonnet, J. Probiotic guidelines and physician practice: a cross-sectional survey and overview of the literature. Benef.Microbes. 8-24-2017; 8(4):507-519; PM: 28618862

ABSTRACT: Probiotic use by patients and physicians has dramatically increased over the last decade, although definitive evidence is often lacking for their use. We examined probiotic-prescribing practices among health care providers (HCP) at a tertiary medical centre and compared these practices to clinical guidelines. HCP at the Stanford Medical Center received a survey on probiotic prescribing practices including choice of probiotic and primary indications. A broad overview of the literature was performed. Among 2,331 HCP surveyed, 632 responded. Of the 582 of these who routinely prescribed medications, 61% had recommended probiotic foods or supplements to their patients. Women and gastroenterologists were more likely to prescribe probiotics (odds ratio (OR): 1.5, 95% confidence interval (CI): 1.0-2.1; OR: 3.9, 95% CI: 1.5-10.1, respectively). Among probiotic prescribers, 50% prescribed inconsistently or upon patient request, and 40% left probiotic choice to the patient. Common indications for probiotics, particularly Lactobacillus GG, were prevention and treatment of antibiotic-associated diarrhoea (79

and 66%, respectively). Probiotics were often prescribed for 'general bowel health' or at patient request (27 and 39% of responders, respectively). Most respondents (63%) thought an electronic medical record (EMR) pop-up would change probiotic prescribing patterns. However, a review of published guidelines and large trials found inconsistencies in probiotic indications, dosages and strain selection. Probiotic prescribing is common but lacks consistency, with choice of probiotic frequently left to the patient, even for indications with some strain-specific evidence. Implementation of EMR pop-ups/pocket guides may increase consistency in probiotic prescribing, although the lack of clear and consistent guidelines must first be addressed with large, well-designed clinical trials.

Du, X., Zhai, Y., Deng, Q., Tan, H., and Cao, L. Illumina-Based Sequencing Analysis Directed Selection for Actinobacterial Probiotic Candidates for Banana Plants. Probiotics.Antimicrob.Proteins. 5-30-2017; PM: 28560514

ABSTRACT: As potential probiotic candidates, plant vertically transmitted actinobacteria are beneficial to growth and health of host plants. New methods to isolate the actinobacterial taxa with low growth rates should be developed. Based on the actinobacterial population information, the probiotic actinobacterial taxa could be directly isolated from healthy banana shoot tips. However, actinobacterial DNAs with high GC contents could bias estimates of actinobacteria by PCR. In the study, two amplicon sequencing strategies were adopted to elucidate the endophytic actinobacterial community of banana plants. More than 92.5% bacterial OTUs were affiliated with actinobacteria by these two strategies, and total 14,289 actinobacterial OTUs with above 97% similarity were detected in banana shoot tips. Although the libraries generated by the two strategies differed in the abundance of some genera, Mycobacterium and Nocardia dominated both libraries and most actinobacterial taxa were overlapped. Higher phylogenetic resolution actinobacteriome of banana plants was successfully established. Based on the endophytic actinobacterial community information, the streptomycetes were isolated from shoot tips. Pot experiments illustrated that the strain could promote banana plantlet growth and elevate resistance to Fusarium oxysporum f. sp. cubense (FOC) under FOC infested soils. The results suggested that the selection for probiotic agents based on actinobacteriome analysis is reliable and feasible compared with present greenhouse selection.

Duar, R. M., Frese, S. A., Lin, X. B., Fernando, S. C., Burkey, T. E., Tasseva, G., Peterson, D. A., Blom, J., Wenzel, C. Q., Szymanski, C. M., and Walter, J. Experimental Evaluation of Host Adaptation of Lactobacillus reuteri to Different Vertebrate Species. Appl.Environ.Microbiol. 6-15-2017; 83(12); PM: 28389535

ABSTRACT: The species Lactobacillus reuteri has diversified into host-specific lineages, implying a long-term association with different vertebrates. Strains from rodent lineages show specific adaptations to mice, but the processes underlying the evolution of L. reuteri in other hosts remain unknown. We administered three standardized inocula composed of strains from different host-confined lineages to mice, pigs, chickens, and humans. The ecological performance of each strain in the gastrointestinal tract of each host was determined by typing random colonies recovered from fecal samples collected over five consecutive days postadministration. Results revealed that rodent strains were predominant in mice, confirming previous findings of host adaptation. In chickens, poultry strains of the lineage VI (poultry VI) and human isolates from the same lineage (human VI) were recovered at the highest and second highest rates, respectively.

Interestingly, human VI strains were virtually undetected in human feces. These findings, together with ancestral state reconstructions, indicate poultry VI and human VI strains share an evolutionary history with chickens. Genomic analysis revealed that poultry VI strains possess a large and variable accessory genome, whereas human VI strains display low genetic diversity and possess genes encoding antibiotic resistance and capsular polysaccharide synthesis, which might have allowed temporal colonization of humans. Experiments in pigs and humans did not provide evidence of host adaptation of L. reuteri to these hosts. Overall, our findings demonstrate host adaptation of L. reuteri to rodents and chickens, supporting a joint evolution of this bacterial species with several vertebrate hosts, although questions remain about its natural history in humans and pigs. ***IMPORTANCE***: Gut microbes are often hypothesized to have coevolved with their vertebrate hosts. However, the evidence is sparse and the evolutionary mechanisms have not been identified. We developed and applied an experimental approach to determine host adaptation of L. reuteri to different hosts. Our findings confirmed adaptation to rodents and provided evidence of adaptation to poultry, suggesting that L. reuteri evolved via natural selection in different hosts. By complementing phylogenetic analyses with experimental evidence, this study provides novel information about the mechanisms driving host-microbe coevolution with vertebrates and serve as a basis to inform the application of L. reuteri as a probiotic for different host species.

Dubreuil, J. D. Enterotoxigenic Escherichia coli and probiotics in swine: what the bleep do we know? Biosci.Microbiota.Food Health. 2017; 36(3):75-90; PM: 28785529

ABSTRACT: The concept of certain microorganisms conferring direct benefits to the host relates to the term "probiotic". Probiotics are microorganisms, bacteria, or yeast that when administered orally in sufficient quantity can counteract the effect of pathogenic microorganisms. The gastrointestinal (GI) tract is the site where probiotics are believed to play the most important role. The proposed effects of probiotics include antagonism of pathogens, interference with adherence, competition for nutrients, enterotoxin inactivation, modulation of the immune response, and strengthening of the intestinal barrier. From birth to postweaning, piglets are very sensitive to gut colonisation by pathogens. Enterotoxigenic Escherichia coli represents one of the most common agents of swine diarrhoea. The enterotoxins produced by this E. coli virotype are responsible for the loss of electrolytes and water observed following infection. This review addresses more specifically the studies done during the last 10 years deciphering the molecular mechanisms at play between host cell and probiotic interactions in the swine GI tract.

Dunner, B., Birrer, S., Nathues, C., Hassig, M., Stephan, R., and Sidler, X. [Influence of probiotics on the establishment of a competitive flora, as well as on antibiotic use and performance parameters in pig breeding farms]. Schweiz.Arch.Tierheilkd. 2017; 159(8):429-435; PM: 28791949

ABSTRACT: ***INTRODUCTION***: The aim of the present study was to investigate the effect of Probiotics in Progress (PIP) on the establishment of a competitive flora as well as on antibiotic use and losses of suckling piglets in pig breeding farms. The tested products were PIP AHC(R) and PIP AHS(R) produced by "Chrisal AG" in Lommel, Belgium. PIP`s are cleaning products containing Bacillus spores. According to the manufacturer's specifications, they are able to establish a steady non-pathogenic stable flora. In a field trial in 19 pig breeding farms, the use of PIP-products did not lead to any reduction of antibiotic use or improvement of fertility parameters, especially in relation to losses of

suckling piglets. In addition, we compared the bacterial flora using PIP products with the flora under conventional management conditions in a farrowing pen by means of swab samples. The use of PIP-products did not lead to any significant effect on the pen flora. Only very few swab samples contained a majority of probiotic Bacillus spp.

Duranti, S., Ferrario, C., van, Sinderen D., Ventura, M., and Turroni, F. Obesity and microbiota: an example of an intricate relationship. Genes Nutr. 2017; 12:18; PM: 28638490

ABSTRACT: It is widely accepted that metabolic disorders, such as obesity, are closely linked to lifestyle and diet. Recently, the central role played by the intestinal microbiota in human metabolism and in progression of metabolic disorders has become evident. In this context, animal studies and human trials have demonstrated that alterations of the intestinal microbiota towards enhanced energy harvest is a characteristic of the obese phenotype. Many publications, involving both animal studies and clinical trials, have reported on the successful exploitation of probiotics and prebiotics to treat obesity. However, the molecular mechanisms underlying these observed anti-obesity effects of probiotics and prebiotic therapies are still obscure. The aim of this mini-review is to discuss the intricate relationship of various factors, including diet, gut microbiota, and host genetics, that are believed to impact on the development of obesity, and to understand how modulation of the gut microbiota with dietary intervention may alleviate obesity-associated symptoms.

Ebrahimi, Z. S., Nasli-Esfahani, E., Nadjarzade, A., and Mozaffari-Khosravi, H. Effect of symbiotic supplementation on glycemic control, lipid profiles and microalbuminuria in patients with non-obese type 2 diabetes: a randomized, double-blind, clinical trial. J.Diabetes Metab Disord. 2017; 16:23; PM: 28589103

ABSTRACT: ***BACKGROUND***: The prevalent raise of type 2 diabetes (T2D) around the globe, are creating higher risk for cardiovascular diseases (CVDs) and increasing strain on each country's health care budget in the world. Microalbuminuria has appeared as a key parameter in diabetic patients. Microalbuminuria is also related to increased cardiovascular morbidity in people who are non-obese diabetic. Some studies have suggested that consumption of symbiotic foods might help improve the metabolic profile, inflammatory factors and biomarkers of oxidative stress. The aim of trial was to determine the effect of symbiotic supplementation on glycemic control, lipid profiles and microalbuminuria in non-obese T2D. ***METHODS***: In this randomized, double-blind, clinically controlled trial, 70 patients with T2D (28 females, 42 males) were randomly divided into two groups (n = 35 for each group). The symbiotic group (SG) consumed 500 mg/d of symbiotic supplementations containing probiotics (Lactobacillus family, Bifidobacterium family, Streptococus thermophilus), Prebiotics (Fructo oligosaccharide) and B group vitamins (1 mg), lactose (0.5 mg), malt-dextrin, magnesium saturate and the placebo group (PG) consumed capsules filled with row starch and also B group vitamins (1 mg), lactose (0.5 mg), malt-dextrin, magnesium saturate for 9 weeks. Fasting blood glucose (FBG), hemoglobin A1c (HbA1c), blood lipid profiles, 24-h dietary recalls, and anthropometric measurements were measured at the baseline and at the end of trial. SPSS software, version 16 was used to test the data and the results were expressed as mean +/- standard deviation. Paired samples T-Test were used to compare continuous variables within groups. Comparison between different groups was performed through two independent samples T-Test. In the absence of normal distribution, the comparison between the groups was made using non-parametric Wilcoxon on signed ranks and

Mann-Whitney tests. P values <0.05 was considered significant. ***RESULTS***: Symbiotic supplementation decreased significantly, FBG (P = 0.05) and HbA1c (P < 0.01). There were no significant differences in lipid profiles within and between the groups at the end of study (P > 0.05). Microalbuminuria (P < 0.05) and HbA1c (P < 0.05) are increased significantly in PG at the end of the study. Furthermore, the mean changes of microalbuminuria and HbA1c experienced significant between the two groups. There was significant reduction in urea between two groups from baseline (P = 0.051). No significant changes in baseline were shown in creatinine among the two groups or within either groups (P > 0.05). ***CONCLUSION***: The consumption of 500 mg/d symbiotic supplementation for 9 weeks could improve the HbA1c, BMI and Microalbuminuria in T2D. Although, No effect has been indicated on FBS, lipid profiles, urea and creatinine. ***TRIAL REGISTRATION***: The trial has been registered in the Iranian Registry of Clinical Trials IRCT2015072223284N1, identifier. Registered 21 May 2016 "retrospectively registered".

Ekmekciu, I., von, Klitzing E., Fiebiger, U., Neumann, C., Bacher, P., Scheffold, A., Bereswill, S., and Heimesaat, M. M. The Probiotic Compound VSL#3 Modulates Mucosal, Peripheral, and Systemic Immunity Following Murine Broad-Spectrum Antibiotic Treatment. Front Cell Infect.Microbiol. 2017; 7:167; PM: 28529928

ABSTRACT: There is compelling evidence linking the commensal intestinal microbiota with host health and, in turn, antibiotic induced perturbations of microbiota composition with distinct pathologies. Despite the attractiveness of probiotic therapy as a tool to beneficially alter the intestinal microbiota, its immunological effects are still incompletely understood. The aim of the present study was to assess the efficacy of the probiotic formulation VSL#3 consisting of eight distinct bacterial species (including Streptococcus thermophilus, Bifidobacterium breve, B. longum, B. infantis, Lactobacillus acidophilus, L. plantarum, L. paracasei, and L. delbrueckii subsp. Bulgaricus) in reversing immunological effects of microbiota depletion as compared to reassociation with a complex murine microbiota. To address this, conventional mice were subjected to broad-spectrum antibiotic therapy for 8 weeks and perorally reassociated with either VSL#3 bacteria or a complex murine microbiota. VSL#3 recolonization resulted in restored CD4+ and CD8+ cell numbers in the small and large intestinal lamina propria as well as in B220+ cell numbers in the former, whereas probiotic intervention was not sufficient to reverse the antibiotic induced changes of respective cell populations in the spleen. However, VSL#3 application was as efficient as complex microbiota reassociation to attenuate the frequencies of regulatory T cells, activated dendritic cells and memory/effector T cells in the small intestine, colon, mesenteric lymph nodes, and spleen. Whereas broad-spectrum antibiotic treatment resulted in decreased production of cytokines such as IFN-gamma, IL-17, IL-22, and IL-10 by CD4+ cells in respective immunological compartments, VSL#3 recolonization was sufficient to completely recover the expression of the anti-inflammatory cytokine IL-10 without affecting pro-inflammatory mediators. In summary, the probiotic compound VSL#3 has an extensive impact on mucosal, peripheral, and systemic innate as well as adaptive immunity, exerting beneficial anti-inflammatory effects in intestinal as well as systemic compartments. Hence, VSL#3 might be considered a therapeutic immunomodulatory tool following antibiotic therapy.

Elbanna, K., Sarhan, O. M., Khider, M., Elmogy, M., Abulreesh, H. H., and Shaaban, M. R. Microbiological, histological, and biochemical evidence for the adverse effects of food azo dyes on rats. J.Food Drug Anal. 2017; 25(3):667-680; PM: 28911652

ABSTRACT: In this study, 120 lactic acid bacterial strains from different fermented dairy products as well as 10 bacterial intestinal isolates were evaluated for in vitro and in vivo degradation of various food azo dyes. Of these isolates, lactic acid bacteria (LAB) strains 13 and 100 and the intestinal isolates Ent2 and Eco5 exhibited 96-98% degradation of the tested food azo dyes within 5-6 hours. High performance liquid chromatography mass spectra of sunset yellow (E110) and carmoisine (E122) anaerobic degradation products by the intestinal isolates showed that they were structurally related to toxic aromatic amines. For an in vivo study, eight groups of rats were treated for 90 days with either the food azo dyes or their degradation products. All groups were kept for a further 30 days as recovery period and then dissected at 120 days. Hematological, histopathological, and protein markers were assessed. Rats treated with either E110/E122 or their degradation products exhibited highly significant changes in red blood cell count, hemoglobin, hematocrit, mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, and white blood cell count. In addition, alanine and aspartate aminotransferases, amylase, total bilirubin, blood urea nitrogen, creatinine, glucose, total protein, and globulins were significantly increased. Furthermore, marked histopathological alterations in the liver, kidney, spleen, and small intestine were observed. Significant decreases in inflammation and a noticeable improvement in the liver, kidney, spleen, and small intestine of rats treated with LAB and food azo dyes simultaneously were observed. Finally, these results provide a reliable basis for not only a better understanding of the histological and biochemical effects of food additives, but also for early diagnostics. In addition, LAB strains 13 and 100 may play an important role as potential probiotics in food and dairy technology as a probiotic lactic acid starter.

Elshaghabee, F. M. F., Rokana, N., Gulhane, R. D., Sharma, C., and Panwar, H. Bacillus As Potential Probiotics: Status, Concerns, and Future Perspectives. Front Microbiol. 2017; 8:1490; PM: 28848511

ABSTRACT: Spore-forming bacilli are being explored for the production and preservation of food for many centuries. The inherent ability of production of large number of secretory proteins, enzymes, antimicrobial compounds, vitamins, and carotenoids specifies the importance of bacilli in food chain. Additionally, Bacillus spp. are gaining interest in human health related functional food research coupled with their enhanced tolerance and survivability under hostile environment of gastrointestinal tract. Besides, bacilli are more stable during processing and storage of food and pharmaceutical preparations, making them more suitable candidate for health promoting formulations. Further, Bacillus strains also possess biotherapeutic potential which is connected with their ability to interact with the internal milieu of the host by producing variety of antimicrobial peptides and small extracellular effector molecules. Nonetheless, with proposed scientific evidences, commercial probiotic supplements, and functional foods comprising of Bacillus spp. had not gained much credential in general population, since the debate over probiotic vs pathogen tag of Bacillus in the research and production terrains is confusing consumers. Hence, it's important to clearly understand the phenotypic and genotypic characteristics of selective beneficial Bacillus spp. and their substantiation with those having GRAS status, to reach a consensus over the same. This review highlights the probiotic candidature of spore forming Bacillus spp. and presents an overview of the proposed health benefits, including application in food and pharmaceutical industry. Moreover, the growing need to evaluate the safety of individual Bacillus strains as well as species on a case by case basis and necessity of more profound analysis for the

selection and identification of Bacillus probiotic candidates are also taken into consideration.

Eren, Kuru B., Laleman, I., Yalnizoglu, T., Kuru, L., and Teughels, W. The Influence of a Bifidobacterium Animalis Probiotic on Gingival Health: a Randomized Controlled Clinical Trial. J.Periodontol. 7-28-2017; 1-14; PM: 28753102

ABSTRACT: ***BACKGROUND***: There is a growing interest for probiotics in periodontal therapy, however, until to date, most research is focused on lactobacilli probiotics. The aim of this study was to evaluate the effect of the 4-week usage of a Bifidobacterium animalis subsp. lactis DN-173010 supplemented yoghurt versus a placebo yoghurt, followed by a 5-day non-brushing period. ***METHODS***: Individuals were included in this single-blind, randomized controlled study if probing depth was (PD) </= 3 mm and attachment loss </= 2 mm. After professional prophylaxis, they were randomized into two groups receiving a placebo or Bifidobacterium containing yoghurt for 28 days, followed by a 5-day non-brushing period. The outcome measures were plaque and gingival indices, bleeding on probing, probing depth, gingival crevicular fluid (GCF) volume, total amount and concentration of interleukin-1beta in GCF. These were measured at baseline, after 28 days of the study product usage and subsequently after the 5 days of plaque accumulation. ***RESULTS***: 51 patients were analyzed. No intergroup differences could be detected before and after the intake of the study products. However, after plaque accumulation, significant better results for all parameters could be seen in the probiotic group compared to the control group ($p<0.001$): lower plaque and gingivitis scores, less bleeding on probing, less increase in GCF volume and lower total interleukin-1beta amount/ concentration. ***CONCLUSION***: The use of a probiotic yoghurt supplemented with Bifidobacterium animalis can have a positive effect on plaque accumulation and gingival inflammatory parameters after refraining oral hygiene practices.

Esaiassen, E., Hjerde, E., Cavanagh, J. P., Simonsen, G. S., and Klingenberg, C. Bifidobacterium Bacteremia: Clinical Characteristics and a Genomic Approach To Assess Pathogenicity. J.Clin.Microbiol. 2017; 55(7):2234-2248; PM: 28490487

ABSTRACT: Bifidobacteria are commensals that colonize the orogastrointestinal tract and rarely cause invasive human infections. However, an increasing number of bifidobacterial blood culture isolates has lately been observed in Norway. In order to investigate the pathogenicity of the Bifidobacterium species responsible for bacteremia, we studied Bifidobacterium isolates from 15 patients for whom cultures of blood obtained from 2013 to 2015 were positive. We collected clinical data and analyzed phenotypic and genotypic antibiotic susceptibility. All isolates (11 Bifidobacterium longum, 2 B. breve, and 2 B. animalis isolates) were subjected to whole-genome sequencing. The 15 patients were predominantly in the extreme lower or upper age spectrum, many were severely immunocompromised, and 11 of 15 had gastrointestinal tract-related conditions. In two elderly patients, the Bifidobacterium bacteremia caused a sepsis-like picture, interpreted as the cause of death. Most bifidobacterial isolates had low MICs (</=0.5 mg/liter) to beta-lactam antibiotics, vancomycin, and clindamycin and relatively high MICs to ciprofloxacin and metronidazole. We performed a pangenomic comparison of invasive and noninvasive B. longum isolates based on 65 sequences available from GenBank and the sequences of 11 blood culture isolates from this study. Functional annotation identified unique genes among both invasive and noninvasive isolates of Bifidobacterium

Phylogenetic clusters of invasive isolates were identified for a subset of the B. longum subsp. longum isolates. However, there was no difference in the number of putative virulence genes between invasive and noninvasive isolates. In conclusion, Bifidobacterium has an invasive potential in the immunocompromised host and may cause a sepsis-like picture. Using comparative genomics, we could not delineate specific pathogenicity traits characterizing invasive isolates.

Esposito, C., Roberti, A., Turra, F., Cerulo, M., Severino, G., Settimi, A., and Escolino, M. Frequency of Antibiotic-Associated Diarrhea and Related Complications in Pediatric Patients Who Underwent Hypospadias Repair: a Comparative Study Using Probiotics vs Placebo. Probiotics.Antimicrob.Proteins. 9-4-2017; PM: 28871492

ABSTRACT: This study aimed to evaluate the effectiveness of probiotics (Lactobacillus rhamnosus GG), as a preventive measure of antibiotic-associated diarrhea (AAD) in children who underwent hypospadias repair and its clinical consequences on postoperative outcome, comparing the group treated with probiotics + antibiotics with two control groups (only antibiotics and antibiotics + placebo). We performed a prospective, randomized, placebo-controlled study with three groups of patients (30 boys for each group) who underwent hypospadias repair in our unit from March 2016 to December 2016. G1 received antibiotics + probiotics (L. rhamnosus GG), while G2 and G3 respectively received only antibiotics or antibiotics + placebo (glucose solution at 5%) for the same period. The patients were evaluated in regard to the number of evacuations/day, stool consistency, and the number of dressings/day. The overall incidence of postoperative AAD was 33.3% (30/90), and it was statistically lower in G1 patients compared to G2 and G3 ones (p = 0.002). The duration of AAD was significantly longer in G2 and G3 compared to G1 (p = 0.001). In G1, the frequency of dressing change was significantly lower compared to G2 and G3 (p = 0.001).The incidence of postoperative complications (fistula and dehiscence) was significantly higher in G2 and G3 compared to G1 (p = 0.001). Our study confirmed that the use of probiotic L. rhamnosus GG associated with antibiotics significantly reduced the incidence and the duration of postoperative AAD. In addition, the use of probiotics LGG reduced the frequency of dressing changes and the incidence of postoperative complications, such as urethral fistula and foreskin dehiscence.

Esposito, S. and Principi, N. Impact of nasopharyngeal microbiota on the development of respiratory tract diseases. Eur.J.Clin.Microbiol.Infect.Dis. 8-9-2017; PM: 28795339

ABSTRACT: Knowledge of whether and how respiratory microbiota composition can prime the immune system and provide colonisation resistance, limiting consecutive pathobiont overgrowth and infections, is essential to improving the prevention and therapy of respiratory disorders. Modulation of dysbiotic ecosystems or reconstitution of missing microbes might be a possible measure to reduce respiratory diseases. The aim of this review is to analyse the role of nasopharyngeal microbiota in the development of respiratory tract disease in paediatric-age subjects. PubMed was used to search for all studies published over the last 15 years using the following key words: "microbiota" or "microbioma" and "nasopharyngeal" or "respiratory" or "nasal" and "children" or "paediatric" or "infant". Analysis of the literature showed that respiratory microbiota can regulate health and disease development in the respiratory tract. Like the gut microbiota, the respiratory microbiota is established at birth, and early respiratory microbiota composition determines bacterial succession patterns and respiratory health

in children. Protective and dangerous bacteria have been identified, and this can be considered the base for developing new approaches to diseases that respond poorly to traditional interventions. Reconstitution of missing microbes can be achieved by the administration of pre- and probiotics. Modulation of respiratory microbiota by favouring colonisation of the upper respiratory tract by beneficial commensals can interfere with the proliferation and activity of resident pathobionts and is a possible new measure to reduce the risk of disease. However, further studies are needed because a deeper understanding of these and related issues can be transferred to clinical practice.

Evivie, S. E., Huo, G. C., Igene, J. O., and Bian, X. Some current applications, limitations and future perspectives of lactic acid bacteria as probiotics. Food Nutr.Res. 2017; 61(1):1318034; PM: 28659729

ABSTRACT: Several mechanism and non-mechanism-based studies supporting the claim that lactic acid bacteria (LAB) strains confer health benefits and play immune-modulatory roles were examined in this review. Probiotic applications of LAB on global burdens such as obesity and type-2 diabetes were discussed as well as the use of yoghurt and ice cream as important vehicles to convey several beneficial LAB strains. Probiotic and symbiotic dairy products may be used in the nearest future to treat a variety of health disorders. Current studies suggest that lactic acid bacteria possess anti-obesity and anti-diabetic propensities on their hosts and thus can play a crucial role in human health care. Research in the rheological and physicochemical properties of ice cream as well as its applications are also on the increase. These applications face certain hurdles including technological (for less developed countries), consumer acceptability of new functional foods may be influenced by culture, ethics or religion. There is need for more studies on the genetic basis for probiotic properties which will give further understanding regarding novel manipulation skills and applicability in nutrition and health sectors. More studies confirming the direct effects of probiotic LABs in lowering the spread of food-borne and other pathogens are also anticipated.

Fabrega, M. J., Rodriguez-Nogales, A., Garrido-Mesa, J., Algieri, F., Badia, J., Gimenez, R., Galvez, J., and Baldoma, L. Intestinal Anti-inflammatory Effects of Outer Membrane Vesicles from Escherichia coli Nissle 1917 in DSS-Experimental Colitis in Mice. Front Microbiol. 2017; 8:1274; PM: 28744268

ABSTRACT: Escherichia coli Nissle 1917 (EcN) is a probiotic strain with proven efficacy in inducing and maintaining remission of ulcerative colitis. However, the microbial factors that mediate these beneficial effects are not fully known. Gram-negative bacteria release outer membrane vesicles (OMVs) as a direct pathway for delivering selected bacterial proteins and active compounds to the host. In fact, vesicles released by gut microbiota are emerging as key players in signaling processes in the intestinal mucosa. In the present study, the dextran sodium sulfate (DSS)-induced colitis mouse model was used to investigate the potential of EcN OMVs to ameliorate mucosal injury and inflammation in the gut. The experimental protocol involved pre-treatment with OMVs for 10 days before DSS intake, and a 5-day recovery period. Oral administration of purified EcN OMVs (5 mug/day) significantly reduced DSS-induced weight loss and ameliorated clinical symptoms and histological scores. OMVs treatment counteracted altered expression of cytokines and markers of intestinal barrier function. This study shows for the first time that EcN OMVs can mediate the anti-inflammatory and barrier protection effects previously reported for this probiotic in experimental colitis. Remarkably,

translation of probiotics to human healthcare requires knowledge of the molecular mechanisms involved in probiotic-host interactions. Thus, OMVs, as a non-replicative bacterial form, could be explored as a new probiotic-derived therapeutic approach, with even lower risk of adverse events than probiotic administration.

Faghfoori, Z., Pourghassem, Gargari B., Saber, A., Seyyedi, M., Fazelian, S., and Yari, Khosroushahi A. Prophylactic effects of secretion metabolites of dairy lactobacilli through downregulation of ErbB-2 and ErbB-3 genes on colon cancer cells. Eur.J.Cancer Prev. 7-4-2017; PM: 28683007

ABSTRACT: Colon cancer is one of the most prevalent cancers, and intestinal microbial community plays a pivotal role in colorectal tumor genesis. Probiotics as live microorganisms may be able to exert an anticancer effect in colon cancer. The aim of this study was to isolate and identify Lactobacillus spp. from traditional dairy products with probiotic properties and to investigate their anticancer effects through ErbB-2 and ErbB-3 gene expression in colon cancer cells. The isolated lactobacilli from yogurt and cheese samples were molecularly identified by blasting of 16-23s rDNA region PCR sequenced products. The probiotic properties, including acid and bile tolerance, antimicrobial activity, and antibiotic susceptibility, were assayed. The proliferation inhibition effects of lactobacilli secretion metabolites with probiotic potential on colon cancer cell lines (HT-29 and caco-2) were analyzed using MTT assay. The real-time PCR was used for assessment of ErbB-2 and ErbB-3 gene expression after being treated with probiotics. Four species of bacteria with the most probiotic properties, including Lactobacillus casei, Lactobacillus paracasei, Lactobacillus rhamnosus, and Lactobacillus plantarum, were characterized and their effects on different human cell lines were taken into consideration. Total bacterial secretions significantly reduced the viability of HT-29 and caco-2 cancer cells compared with untreated controls. The metabolites secreted by bacteria downregulated the expression of ErbB-2 and ErbB-3 genes in colon cancer cells. The present study indicated that probiotic bacteria isolated from traditional dairy products exert anticancer effect on colon cancer cells through the downregulation of ErbB-2 and ErbB-3 gene expression.

Falcinelli, S., Rodiles, A., Hatef, A., Picchietti, S., Cossignani, L., Merrifield, D. L., Unniappan, S., and Carnevali, O. Dietary lipid content reorganizes gut microbiota and probiotic L. rhamnosus attenuates obesity and enhances catabolic hormonal milieu in zebrafish. Sci.Rep. 7-17-2017; 7(1):5512; PM: 28717234

ABSTRACT: In the present study, we explored whether dietary lipid content influences the gut microbiome in adult zebrafish. Diets containing three different lipid levels (high [HFD], medium [MFD], and low [LFD]) were administered with or without the supplementation of Lactobacillus rhamnosus (P) to zebrafish in order to explore how the dietary lipid content may influence the gut microbiome. Dietary lipid content shifted the gut microbiome structure. The addition of L. rhamnosus in the diets, induced transcriptional reduction of orexigenic genes, upregulation of anorexigenic genes, and transcriptional decrease of genes involved in cholesterol and triglyceride (TAG) metabolism, concomitantly with lower content of cholesterol and TAG. Probiotic feeding also decreased nesfatin-1 peptide in HFD-P and attenuated weight gain in HFD-P and MFD-P fed zebrafish, but not in LFD-P group. Intestinal ultrastructure was not affected by dietary fat level or probiotic inclusion. In conclusion, these findings underline the role of fat content in the diet in altering gut microbiota community by shifting phylotype composition and highlight the potential of probiotics to attenuate high-fat diet-related metabolic disorder.

Fan, W. T., Ding, C., Xu, N. N., Zong, S., Ma, P., and Gu, B. Close association between intestinal microbiota and irritable bowel syndrome. Eur.J.Clin.Microbiol.Infect.Dis. 8-7-2017; PM: 28785822

ABSTRACT: Trillions of microbes inhabiting the intestine form a complex ecological community, affecting the normal physiology and pathological susceptibility through their collective metabolic activities and interactions with the host. Increased numbers of diseases have been found to be associated with disturbances in this ecosystem. There is evidence that intestinal microflora undergoes alterations in patients with irritable bowel syndrome (IBS). IBS is a frequent functional gut disease with negative impact on the patient's quality of life. Although the etiology and pathology of IBS remain largely unknown, it is generally accepted that the interaction between the microbiota and the host is associated with IBS. However, there are no specific or effective therapies for the treatment of IBS at present. In recent years, researchers have shown a growing interest in seeking safer and more effective alternatives for the treatment of IBS by focusing their attention on the potential role of probiotics and prebiotics. In this review, we will discuss alterations in intestinal microbiota and how these alterations may exacerbate IBS, and introduce several new IBS treatment options aiming at re-establishing a healthy and beneficial ecosystem.

Fang, D., Shi, D., Lv, L., Gu, S., Wu, W., Chen, Y., Guo, J., Li, A., Hu, X., Guo, F., Ye, J., Li, Y., and Li, L. Bifidobacterium pseudocatenulatum LI09 and Bifidobacterium catenulatum LI10 attenuate D-galactosamine-induced liver injury by modifying the gut microbiota. Sci.Rep. 8-18-2017; 7(1):8770; PM: 28821814

ABSTRACT: The gut microbiota is altered in liver diseases, and several probiotics have been shown to reduce the degree of liver damage. We hypothesized that oral administration of specific Bifidobacterium strains isolated from healthy guts could attenuate liver injury. Five strains were tested in this study. Acute liver injury was induced by D-galactosamine after pretreating Sprague-Dawley rats with the Bifidobacterium strains, and liver function, liver and ileum histology, plasma cytokines, bacterial translocation and the gut microbiome were assessed. Two strains, Bifidobacterium pseudocatenulatum LI09 and Bifidobacterium catenulatum LI10, conferred liver protection, as well as alleviated the increase in plasma M-CSF, MIP-1alpha and MCP-1 and bacterial translocation. They also ameliorated ileal mucosal injury and gut flora dysbiosis, especially the enrichment of the opportunistic pathogen Parasutterella and the depletion of the SCFA-producing bacteria Anaerostipes, Coprococcus and Clostridium XI. Negative correlations were found between MIP-1alpha / MCP-1 and Odoribacter (LI09 group) and MIP-1alpha / M-CSF and Flavonifractor (LI10 group). Our results indicate that the liver protection effects might be mediated through gut microbiota modification, which thus affect the host immune profile. The desirable characteristics of these two strains may enable them to serve as potential probiotics for the prevention or adjuvant treatment of liver injury.

Farhat-Khemakhem, A., Blibech, M., Boukhris, I., Makni, M., and Chouayekh, H. Assessment of the potential of the multi-enzyme producer Bacillus amyloliquefaciens US573 as alternative feed additive. J.Sci.Food Agric. 7-25-2017; PM: 28741666

ABSTRACT: ***BACKGROUND***: Recently, probiotics have increasingly been used as feed additives in poultry diets as an alternative to antibiotic growth promoters fostering

resistance development. ***RESULTS***: This study was aimed at assessing the potential of Bacillus amyloliquefaciens US573 as a direct-fed microbial. The US573 strain was found to be free of harmful enzymatic activities and sensitive to antibiotics. In addition, it showed a good acid and bovine bile tolerance, high adhesion efficacy to chicken enterocytes, and an ability to form biofilms, which may favor its survival and persistence in the animal gastrointestinal tract. Moreover, beside the previously described extremely salt-tolerant and highly thermostable phytase, the US573 strain secretes xylanase, beta-glucanase and amylase activities useful in neutralizing the anti-nutritional factors and maximizing the absorption of nutrients. The secretion of such enzymes may be responsible for the good performance of the US573 isolate in the digestibility of wheat in vitro. Indeed, using the vegetative cells, a yield of wheat dry matter digestibility of approximately 48% was achieved, which is slightly lower than the commercial feed additive Rovabio used as a reference (56.73% digestibility). ***CONCLUSION***: The obtained results illustrate the potential of US573 strain as a promising direct-fed microbial candidate for application in poultry industry.

Fathi, M., Abdelsalam, M., Al-Homidan, I., Ebeid, T., El-Zarei, M., and bou-Emera, O. Effect of probiotic supplementation and genotype on growth performance, carcass traits, hematological parameters and immunity of growing rabbits under hot environmental conditions. Anim Sci.J. 5-22-2017; PM: 28544086

ABSTRACT: The effect of dietary inclusion of probiotics and genetic groups on rabbit performance under hot environmental conditions was studied. A total of 80 rabbits aged 8 weeks were distributed into a completely randomized design in a 4 x 3 factorial arrangement, including four genetic groups and three concentrations of dietary probiotic (0, 200 and 400 g/t feed). The utilized probiotic contained 4 x 109 colony-forming units/g of Bacillus subtilis. Jabali local breed (J), imported Spanish V-line (V) and their crossbreds ((1/4)J(3/4)V and (3/4)J(1/4)V) were included in the current study. Final weight and body weight gain were not significantly affected by dietary probiotic levels or genetic group. The feed conversion ratio was better for purebreds than that of crossbreds. A significant improvement in percentage of dressed carcass, mid and hind parts was recorded for rabbits fed a diet containing 400 g probiotic/t feed compared with those fed a basal diet or low probiotic level. Probiotic supplementation had a significant decrease in serum cholesterol. Rabbits given 400 g probiotic/t feed had higher hemoglobin, red blood cells and platelets. Adding 400 g probiotic/t feed to rabbit's diet significantly (P </= 0.05) improved cell-mediated immunity compared to the other treatments 48 h post-injection.

Fathi, M. M., Ebeid, T. A., Al-Homidan, I., Soliman, N. K., and bou-Emera, O. K. Influence of probiotic supplementation on immune response in broilers raised under hot climate. Br.Poult.Sci. 6-6-2017; 1-5; PM: 28521530

ABSTRACT: 1. The objective of the study was to evaluate the potential effects of dietary probiotic supplementation and stocking density and their interaction on growth performance, humoral and cellular immune responses of broiler chickens raised under hot climate conditions. 2. A total of 1800 1-d-old unsexed broiler chicks (Ross 308) were allocated in a completely randomised 3 x 2 factorial design, with three concentrations of dietary probiotic (0, 200 and 400 mg/kg) containing 4 x 109 cfu/g of Bacillus subtilis and two stocking densities (12 or 18 birds/m2) in a total of 6 treatment subgroups. 3. Dietary probiotic and stocking density had no significant effect on live body weight, feed

consumption and feed conversion ratio. 4. Dietary probiotic supplementation had a positive effect on serum immunoglobulin M (IgM) and cell-mediated immunity when compared to the control at 6 weeks of age, whereas serum immunoglobulin A (IgA) and immunoglobulin Y (IgY) were improved, but not significantly so. Dietary probiotic and stocking density had no effect on relative weights of the bursa of Fabricius and spleen. 5. Dietary probiotic supplementation had a positive significant effect on serum IgM concentration and cell-mediated immunity without penalising growth performance in broilers raised under high ambient temperature.

Fdhila, K., Haddaji, N., Chakroun, I., Dhiaf, A., Macherki, M. E. E., Khouildi, B., Lamari, F., Chaieb, K., Abid, N., Marzougui, H., Khouadja, S., and Missaoui, H. Culture conditions improvement of Crassostrea gigas using a potential probiotic Bacillus sp strain. Microb.Pathog. 2017; 110:654-658; PM: 28710014

ABSTRACT: It is well demonstrated that some probiotics improve rearing water quality and thereby have beneficial effects on reared organisms. We conducted this study to determine the effect of Bacillus consortium on Crassostrea gigas reared in contemned seawater with indigo dye priory treated with Bacillus or no treated. This effect was studied by assessing hemocytes death using flow cytometry analysis. We found that the percentage of decolorization of indigo dye in polluted seawater in presence of C. gigas increased from 41% to 90% when using Bacillus consortium. In these conditions, the hemocytes mortality of reared C. gigas decreased from 87% to 56%. We have demonstrated also that seawater contemned with priory treated indigo with Bacillus consortium is less toxic than seawater contemned with the no treated indigo. The percentage of hemocytes death is 81% for the contemned seawater with indigo and 56% for no contemned seawater. This consortium shows a protector effect of C. gigas against Vibrio harveyi contemning reared seawater.

Feng, J. R., Wang, F., Qiu, X., McFarland, L. V., Chen, P. F., Zhou, R., Liu, J., Zhao, Q., and Li, J. Efficacy and safety of probiotic-supplemented triple therapy for eradication of Helicobacter pylori in children: a systematic review and network meta-analysis. Eur.J.Clin.Pharmacol. 7-5-2017; PM: 28681177

ABSTRACT: ***AIM***: The aim of this study was to identify the best probiotic supplementation in triple therapy for pediatric population with Helicobacter pylori infection. ***METHODS***: Eligible trials were identified by comprehensive searches. Relative risks with 95% confidence intervals and relative ranks with P scores were assessed. ***RESULTS***: Twenty-nine trials (3122 participants) involving 17 probiotic regimens were identified. Compared with placebo, probiotic-supplemented triple therapy significantly increased H. pylori eradication rates (relative ratio (RR) 1.19, 95% CI 1.13-1.25) and reduced the incidence of total side effects (RR 0.49, 95% CI 0.38-0.65). Furthermore, to supplemented triple therapy, Lactobacillus casei was identified the best for H. pylori eradication rates (P score = 0.84), and multi-strain of Lactobacillus acidophilus and Lactobacillus rhamnosus for total side effects (P score = 0.93). As for the subtypes of side effects, multi-strain of Bifidobacterium infantis, Bifidobacterium longum, L. acidophilus, L. casei, Lactobacillus plantarum, Lactobacillus reuteri, L. rhamnosus, Lactobacillus salivarius, Lactobacillus sporogenes, and Streptococcus thermophilus was the best to reduce the incidence of diarrhea; multi-strain of Bacillus mesentericus, Clostridium butyricum, and Streptococcus faecalis for loss of appetite; multi-strain of B. longum, Lactobacillus bulgaricus, and S. thermophilus for constipation; multi-strain of Bifidobacterium bifidum, B. infantis, L. acidophilus, L.

bulgaricus, L. casei, L. reuteri, and Streptococcus for taste disturbance; Saccharomyces boulardii for bloating; and multi-strain of Bifidobacterium breve, B. infantis, L. acidophilus, L. bulgaricus, L. casei, L. rhamnosus, and S. thermophilus for nausea/vomiting. ***CONCLUSIONS***: Probiotics are recommended to supplement triple therapy in pediatrics, and the effectiveness of triple therapy is associated with specific probiotic supplementation.

Fernando, W. M. A. D., Flint, S. H., Ranaweera, K. K. D. S., Bamunuarachchi, A., Johnson, S. K., and Brennan, C. S. The potential synergistic behaviour of inter- and intra-genus probiotic combinations in the pattern and rate of short chain fatty acids formation during fibre fermentation. Int.J.Food Sci.Nutr. 6-28-2017; 1-11; PM: 28659066

ABSTRACT: This study compared the rate of short chain fatty acid (SCFA) production by different probiotic combinations of Lactobacillus and Bifidobacterium to determine any synergistic effects. Six different fibre fractions were fermented with nine combinations of Lactobacillus rhamnosus (LR), Lactobacillus acidophilus (LA), Bifidobacterium longum (BL) and Bifidobacterium breve (BB) for 0, 6, 24 and 48 h. SCFAs were quantified by gas chromatography. Inter-genus combinations of bacteria produced more SCFA, especially BB + BL + LR, compared to intra-genus that yielded the lowest SCFA production. Acetate was the most abundant, while propionate and butyrate were the most utilised. The SCFA formation was as acetate > propionate > butyrate and the total dietary fibre produced most of the SCFA. Most combinations utilised 60-80% of the fibre; BB + BL + LR digested the fibre completely. The quantity, pattern and the time of release of SCFA depends on the genus, but the combination of pre and probiotics is of great importance for the outcome.

Ferreira, A. A., Huang, S., Perrone, I. T., Schuck, P., Jan, G., and Carvalho, A. F. Tracking Amazonian cheese microbial diversity: Development of an original, sustainable, and robust starter by freeze drying/spray drying. J.Dairy Sci. 2017; 100(9):6997-7006; PM: 28734600

ABSTRACT: Marajo cheese made with raw buffalo milk in the Amazon region of Brazil can be considered a good source of wild lactic acid bacteria strains with unexplored and promising characteristics. The aim of this study was to develop a potential probiotic starter culture for industrial applications using freeze drying and spray drying. A decrease in the survival rates of freeze-dried samples compared with spray-dried samples was noted. The spray-dried cultures remained approximately 109 cfu.g-1, whereas the freeze-dried samples showed 107 cfu.g-1 after 60 d of storage at 4 degrees C. All of the spray-dried samples showed a greater ability to decrease the pH in 10% skim milk over 24 h compared with the freeze-dried samples. The spray-dried samples showed a greater resistance to acidic conditions and to the presence of bile salts. In addition, under heat stress conditions, reduction was under 2 log cycles in all samples. Although the survival rate was similar among the evaluated samples after drying, the technological performance for skim milk showed some differences. This study may direct further investigations into how to preserve lactic acid bacteria probiotics to produce spray-dried starters that have a high number of viable cells that can then be used for industrial applications in a cost-effective way.

Firouzi, S., Majid, H. A., Ismail, A., Kamaruddin, N. A., and Barakatun-Nisak, M. Y. Effect of multi-strain probiotics (multi-strain microbial cell preparation) on glycemic control and other diabetes-related outcomes in people with type 2 diabetes: a randomized controlled trial. Eur.J.Nutr. 2017; 56(4):1535-1550; PM: 26988693

ABSTRACT: ***AIM***: Evidence of a possible connection between gut microbiota and several physiological processes linked to type 2 diabetes is increasing. However, the effect of multi-strain probiotics in people with type 2 diabetes remains unclear. This study investigated the effect of multi-strain microbial cell preparation-also refers to multi-strain probiotics-on glycemic control and other diabetes-related outcomes in people with type 2 diabetes. ***DESIGN***: A randomized, double-blind, parallel-group, controlled clinical trial. ***SETTING***: Diabetes clinic of a teaching hospital in Kuala Lumpur, Malaysia. ***PARTICIPANTS***: A total of 136 participants with type 2 diabetes, aged 30-70 years, were recruited and randomly assigned to receive either probiotics (n = 68) or placebo (n = 68) for 12 weeks. ***OUTCOMES***: Primary outcomes were glycemic control-related parameters, and secondary outcomes were anthropomorphic variables, lipid profile, blood pressure and high-sensitivity C-reactive protein. The Lactobacillus and Bifidobacterium quantities were measured before and after intervention as an indicator of successful passage of the supplement through gastrointestinal tract. ***STATISTICAL ANALYSIS***: Intention-to-treat (ITT) analysis was performed on all participants, while per-protocol (PP) analysis was performed on those participants who had successfully completed the trial with good compliance rate. ***RESULTS***: With respect to primary outcomes, glycated hemoglobin decreased by 0.14 % in the probiotics and increased by 0.02 % in the placebo group in PP analysis ($p < 0.05$, small effect size of 0.050), while these changes were not significant in ITT analysis. Fasting insulin increased by 1.8 microU/mL in placebo group and decreased by 2.9 microU/mL in probiotics group in PP analysis. These changes were significant between groups at both analyses ($p < 0.05$, medium effect size of 0.062 in PP analysis and small effect size of 0.033 in ITT analysis). Secondary outcomes did not change significantly. Probiotics successfully passed through the gastrointestinal tract. ***CONCLUSION***: Probiotics modestly improved HbA1c and fasting insulin in people with type 2 diabetes.

Flach, J., van der Waal, M. B., van den, Nieuwboer M., Claassen, E., and Larsen, O. F. A. The underexposed role of food matrices in probiotic products: Reviewing the relationship between carrier matrices and product parameters. Crit Rev.Food Sci.Nutr. 6-13-2017; 1-15; PM: 28609116

ABSTRACT: Probiotic microorganisms are increasingly incorporated into food matrices in order to confer proposed health benefits on the consumer. It is important that the health benefits, sensory properties, shelf-life and probiotic gastrointestinal tract (GIT) survival of these products are carefully balanced as they determine functionality and drive consumer acceptance. The strain-specific effects of probiotic species are imperative in this process but carrier matrices may play a pivotal role as well. This study therefore recapitulates the wealth of knowledge on carrier matrices and their interaction with probiotic strains. The most substantiated carrier matrices, factors that influence probiotic functionality and matrix effects on shelf-life, GIT survival and clinical efficacy are reviewed. Results indicate that carrier matrices have a significant impact on the quality of probiotic products. Matrix components, such as proteins, carbohydrates and flavoring agents are shown to alter probiotic efficacy and viability. In vivo studies furthermore revealed strain-dependent matrix effects on the GIT survival of probiotic bacteria. However, only a limited number of studies have specifically addressed the effects of

carrier matrices on the aforementioned product-parameters; most studies seem to focus solely on the strain-specific effects of probiotic microorganisms. This hampers the innovation of probiotic products. More human studies, comparing not only different probiotic strains but different carrier matrices as well, are needed to drive the innovation cycle.

Francoz, D., Wellemans, V., Dupre, J. P., Karreman, H. J., Roy, J. P., Labelle, F., Lacasse, P., and Dufour, S. Invited review: A systematic review and qualitative analysis of treatments other than conventional antimicrobials for clinical mastitis in dairy cows. J.Dairy Sci. 7-26-2017; PM: 28755947

ABSTRACT: Clinical mastitis is an important disease in dairies. Its treatment is mainly based on the use of antimicrobial drugs. Numerous non-antimicrobial drugs and treatment strategies have already been reported for clinical mastitis treatment, but data on their efficacy have never been collated in a systematic way. The objective of this systematic review was to identify treatments other than conventional antimicrobials for the treatment of clinical mastitis in lactating dairy cows. A systematic review was performed with studies written in English or French selected from CAB Abstracts, PubMed, and Web of Science from January 1970 to June 2014. Controlled clinical trials, observational studies, and experimental challenges were retained. Lactating dairy cows with clinical mastitis were the participant of interest. All treatments other than conventional antimicrobials for clinical mastitis during lactation were retained. Only studies comparing the treatment under investigation to a negative or positive control, or both, were included. Outcomes evaluated were clinical and bacteriological cure rates and milk production. Selection of the study, data extraction, and assessment of risk of bias was performed by 3 reviewers. Assessment of risk of bias was evaluated using the Cochrane Collaboration tool for systematic review of interventions. A total of 2,451 manuscripts were first identified and 39 manuscripts corresponding to 41 studies were included. Among these, 22 were clinical trials, 18 were experimental studies, and 1 was an observational study. The treatments evaluated were conventional anti-inflammatory drugs (n = 14), oxytocin with or without frequent milk out (n = 5), biologics (n = 9), homeopathy (n = 5), botanicals (n = 4), probiotics (n = 2), and other alternative products (n = 2). All trials had at least one unclear or high risk of bias. Most trials (n = 13) did not observe significant differences in clinical or bacteriological cure rates in comparison with negative or positive controls. Few studies evaluated the effect of treatment on milk yield. In general, the power of the different studies was very low, thus precluding conclusions on noninferiority or nonsuperiority of the treatments investigated. No evidence-based recommendations could be given for the use of an alternative or non-antimicrobial conventional treatment for clinical mastitis. However, probiotics and oxytocin with or without frequent milk out should not be recommended. We concluded that homeopathic treatments are not efficient for management of clinical mastitis.

Freire, F. C., Adorno, M. A. T., Sakamoto, I. K., Antoniassi, R., Chaves, A. C. S. D., Dos Santos, K. M. O., and Sivieri, K. Impact of multi-functional fermented goat milk beverage on gut microbiota in a dynamic colon model. Food Res.Int. 2017; 99(Pt 1):315-327; PM: 28784489

ABSTRACT: The aim of this research was to evaluate the effect of grape probiotic fermented beverages made of goat milk, with or without added grape pomace on gut microbiota in a Simulator of Human Intestinal Microbial Ecosystem (SHIME(R)). SHIME(R) model was used to investigate to assess changes in microbial composition and

fermentation metabolites (short- and branched-chain fatty acids and ammonium), as well as under the antioxidant capacity. The results demonstrated that the beverages formulated, with or without grape pomace extract, exhibited high dietary fiber, oleic acid, phenolic compounds content and antioxidant activity. Both beverages also kept L. rhamnosus and S. thermophilus viable during their passage through the intestinal tract and had a positive effect on gut microbiota metabolism, increasing the antioxidant capacity and the production of short-chain fatty acids, and decreasing the ammonium concentration. Therefore, the multifunctional beverages formulated in this study can offer a new perspective for the production of foods with positive potential effects on human health.

Friedrich, A. D., Paz, M. L., Leoni, J., and Gonzalez Maglio, D. H. Message in a Bottle: Dialog between Intestine and Skin Modulated by Probiotics. Int.J.Mol.Sci. 6-9-2017; 18(6); PM: 28598354

ABSTRACT: At the beginning, probiotics were used exclusively for gastrointestinal conditions. However, over the years, evidence has shown that probiotics exert systemic effects. In this review article, we will summarize recent reports that postulate probiotic treatment as an efficient one against skin pathologies, such as cancer, allergy, photoaging and skin infections. The focus will be restricted to oral probiotics that could potentially counteract the ultraviolet irradiation-induced skin alterations. Moreover, the possible underlying mechanisms by which probiotics can impact on the gut and exert their skin effects will be reviewed. Furthermore, how the local and systemic immune system is involved in the intestine-cutaneous crosstalk will be analyzed. In conclusion, this article will be divided into three core ideas: (a) probiotics regulate gut homeostasis; (b) gut and skin homeostasis are connected.

Fujimoto, M., Lovett, B., Angoshtari, R., Nirenberg, P., Loch, T. P., Scribner, K. T., and Marsh, T. L. Antagonistic Interactions and Biofilm Forming Capabilities Among Bacterial Strains Isolated from the Egg Surfaces of Lake Sturgeon (Acipenser fulvescens). Microb.Ecol. 7-3-2017; PM: 28674774

ABSTRACT: Characterization of interactions within a host-associated microbiome can help elucidate the mechanisms of microbial community formation on hosts and can be used to identify potential probiotics that protect hosts from pathogens. Microbes employ various modes of antagonism when interacting with other members of the community. The formation of biofilm by some strains can be a defense against antimicrobial compounds produced by other taxa. We characterized the magnitude of antagonistic interactions and biofilm formation of 25 phylogenetically diverse taxa that are representative of isolates obtained from egg surfaces of the threatened fish species lake sturgeon (Acipenser fulvescens) at two ecologically relevant temperature regimes. Eight isolates exhibited aggression to at least one other isolate. Pseudomonas sp. C22 was found to be the most aggressive strain, while Flavobacterium spp. were found to be one of the least aggressive and the most susceptible genera. Temperature affected the prevalence and intensity of antagonism. The aggressive strains identified also inhibited growth of known fish pathogens. Biofilm formations were observed for nine isolates and were dependent on temperature and growth medium. The most aggressive of the isolates disrupted biofilm formation of two well-characterized isolates but enhanced biofilm formation of a fish pathogen. Our results revealed the complex nature of

interactions among members of an egg associated microbial community yet underscored the potential of specific microbial populations as host probiotics.

Fuochi, V., Volti, G. L., and Furneri, P. M. Probiotic Properties of Lactobacillus fermentum Strains Isolated from Human Oral Samples and Description of their Antibacterial Activity. Curr.Pharm.Biotechnol. 2017; 18(2):138-149; PM: 28034294

ABSTRACT: ***BACKGROUND***: Gram positive bacteria produce peptides, defined bacteriocins which exhibit good antibacterial activity. ***OBJECTIVE***: We evaluated the ability of L. fermentum to produce bacteriocins having therefore, good probiotic features and finally, be safe towards microglial cells. ***METHOD***: Eight wild strains, identified using molecular techniques, were investigated for the evaluation of resistance to bile salts, low pH, H2O2 production, biofilm formation, antibacterial activity and safety on microglia cells (BV2). ***RESULTS***: The determination of the susceptibility/resistance profile showed that the strains are sensitive to the antibiotics tested. All strains showed a good tolerability to extremely low pH as well as resisting in presence of bile salts. In addition, the strains showed excellent activity against pathogens and one of them (LAC 42) showed activity also against Pseudomonas aeruginosa and Klebsiella pneumoniae. Finally, LAC 42 and its active compound did not change microglia cell viability following 24h exposure. Our data on this antibacterial molecule suggest that it is a compound with low molecular weight and with highly hydrophilic component. ***CONCLUSION***: These results describe the characteristics of Lactobacillus strains and provide evidences for their possible use as new potential probiotic. In addition, other studies are now warranted to exploit the antibacterial activity of the supernatant LAC 42 and for its complete chemical characterization.

Gani, A., Shah, A., Ahmad, M., Ashwar, B. A., and Masoodi, F. A. beta-d-glucan as an enteric delivery vehicle for probiotics. Int.J.Biol.Macromol. 8-26-2017; PM: 28842198

ABSTRACT: Three strains of probiotics L. casei, L. acidophilus and B. bifidum were encapsulated in beta-d-glucan matrix using freeze drying technique in order to increase survivability during their journey through GI tract. The encapsulation efficiency (%) of beta-d-glucan varied significantly with Bifidobacteria showing low survival rate than Lactobacilli. SEM images revealed a partially collapsed structure with bacterial cells distributed randomly in the matrix. Further absorption band between 1300 and 900cm-1 in FTIR spectra shows the presence of bacterial proteins and nucleic acids. For encapsulated beta-d-glucan maximum degree of swelling was observed at pH 3 and 4, whereas when the pH value was increased to 6.5 the encapsulated beta-d-glucan started their disintegration. In vitro release studies revealed that the microcapsules start to dissolve upon entry to the small intestine where it is needed most.

Gao, P., Ma, C., Sun, Z., Wang, L., Huang, S., Su, X., Xu, J., and Zhang, H. Feed-additive probiotics accelerate yet antibiotics delay intestinal microbiota maturation in broiler chicken. Microbiome. 8-3-2017; 5(1):91; PM: 28768551

ABSTRACT: ***BACKGROUND***: Reducing antibiotics overuse in animal agriculture is one key in combat against the spread of antibiotic resistance. Probiotics are a potential replacement of antibiotics in animal feed; however, it is not clear whether and how probiotics and antibiotics differ in impact on physiology and microbial ecology of host

animals. ***RESULTS***: Host phenotype and fecal microbiota of broilers with either antibiotics or probiotics as feed additive were simultaneously sampled at four time points from birth to slaughter and then compared. Probiotic feeding resulted in a lower feed conversion ratio (FCR) and induced the highest level of immunity response, suggesting greater economic benefits in broiler farming. Probiotic use but not antibiotic use recapitulated the characteristics of age-dependent development of gut microbiota in the control group. The maturation of intestinal microbiota was greatly accelerated by probiotic feeding, yet significantly retarded and eventually delayed by antibiotic feeding. LP-8 stimulated the growth of many intestinal Lactobacillus spp. and led to an altered bacterial correlation network where Lactobacillus spp. are negatively correlated with 14 genera and positively linked with none, yet from the start antibiotic feeding featured a less-organized network where such inter-genera interactions were fewer and weaker. Consistently, microbiota-encoded functions as revealed by metagenome sequencing were highly distinct between the two groups. Thus, "intestinal microbiota maturation index" was proposed to quantitatively compare impact of feed additives on animal microecology. ***CONCLUSIONS***: Our results reveal a tremendous potential of probiotics as antibiotics' substitute in poultry farming.

Gerhard, D., Sousa, F. J. D. S., Andraus, R. A. C., Pardo, P. E., Nai, G. A., Neto, H. B., Messora, M. R., and Maia, L. P. Probiotic therapy reduces inflammation and improves intestinal morphology in rats with induced oral mucositis. Braz.Oral Res. 7-3-2017; 31:e71; PM: 28678976

ABSTRACT: The aim of the present study was to evaluate the effect of systemic administration of probiotics (PROB) on the progression of experimentally induced oral and intestinal mucositis in rats immunosuppressed by chemotherapy (5-fluorouracil: 5-FU). Twenty-four rats were divided into the following groups (n=6): GC (control), GPROB, G5FU and G5-FU/PROB. Groups GPROB and G5-FU/PROB received 1 g of probiotic incorporated into each 100 g of feed (Bacillus subtilis, Bifidobacterium bifidum, Enterococcus faecium and Lactobacilllus acidophilus), beginning 30 days before oral mucositis induction. Groups G5FU and G5-FU/PROB received 60 mg/kg of 5-FU on days 0 and 2. The left oral mucosa of each animal was irritated by mechanical trauma (days 1 and 2). On days 3 and 7, three animals from each group were sacrificed, and their oral mucosa and small intestine were biopsied and processed for histopathological analysis. Groups G5-FU and G5-FU/PROB showed ulcerated oral lesions at day 3, with progression in group G5-FU and regression in group G5-FU/PROB at day 7. Histologically, less severe signs of inflammation in the oral mucosa were observed in group G5-FU/PROB than in group G5-FU. Regarding the intestine, villus-related defects of lesser magnitude were observed in group G5-FU/PROB, compared with group G5-FU. Group GPROB showed greater villus height than group GC. It can be concluded that probiotic supplementation reduced oral and intestinal inflammation in immunosuppressed rats with experimentally induced mucositis, and may protect the intestine from changes induced by chemotherapy, thus contributing to overall health.

Ghasemi, E., Mazaheri, R., and Tahmourespour, A. Effect of Probiotic Yogurt and Xylitol-Containing Chewing Gums on Salivary S Mutans Count. J.Clin.Pediatr.Dent. 2017; 41(4):257-263; PM: 28650782

ABSTRACT: ***BACKGROUND AND AIMS***: In addition to improving gastrointestinal health and intestinal microflora, probiotic bacteria have been recently suggested to decrease

cariogenic agents in the oral cavity. The aim of this study was to investigate the effects of probiotic yogurt and xylitol-containing chewing gums on reducing salivary Streptococcus mutans levels. ***STUDY DESIGN***: This randomized clinical trial recruited 50 female students with over 105 colony forming units S. mutans per milliliter of their saliva. The participants were randomly allocated to two equal groups to receive either probiotic yogurt containing Lactobacillus acidophilus ATCC 4356 andBifidobacteriumbifidum ATCC 29521 (200 g daily) or xylitol-containing chewing gums (two gums three times daily after each meal; total xylitol content: 5.58 g daily) for three weeks. At baseline and one day, two weeks, and four weeks after the interventions, saliva samples were cultured on mitis-salivarius-bacitracin agar and salivary S. mutans counts were determined. Data were analyzed with independent t-tests, analysis of variance, and Fisher's least significant difference test. ***RESULTS***: In both groups, S. mutans counts on the first day, second week, and fourth weeks after the intervention were significantly lower than baseline values ($P < 0.05$). The greatest level of reduction in both groups was observed in the second week after the intervention. Moreover, although the reduction was greater in probiotic yogurt consumers, the difference between the two groups was not statistically significant. ***CONCLUSION***: Probiotic yogurt and xylitol-containing chewing gums seem to be as effective in reduction of salivary S. mutans levels. Their constant long-term consumption is thus recommended to prevent caries.

Ghosh, S., Malik, Y. S., and Kobayashi, N. Therapeutics and Immunoprophylaxis against Noroviruses and Rotaviruses. Curr.Drug Metab. 9-12-2017; PM: 28901254

ABSTRACT: Noroviruses and rotaviruses are important viral etiologies of severe gastroenteritis. Noroviruses are the primary cause of non-bacterial diarrheal outbreaks in humans, whilst rotaviruses are a major cause of childhood diarrhea. Although both enteric pathogens substantially impact human health and economies, there are no approved drugs against noroviruses and rotaviruses, so far. On the other hand, whilst the currently licensed rotavirus vaccines have been successfully implemented in over 100 countries, the most advanced norovirus vaccine has recently completed phase-I and II trials. Technological advances coupled with proper understanding of viral morphology and replication over the past decade has facilitated pioneering research on therapeutics and immunoprophylaxis against noroviruses and rotaviruses, with promising outcomes in human clinical trials of some of the drugs and vaccines. Herein, we focus on the developments in the field of norovirus and rotavirus therapeutics and immunoprophylaxis, such as potential antiviral drug molecules, passive immunotherapies (oral human immunoglobulins, egg yolk and bovine colostral antibodies, llama-derived nanobodies, and antibodies expressed in probiotics, plants, rice grains and insect larvae), immune system modulators, probiotics, phytochemicals and other biological substances such as bovine milk proteins, therapeutic nanoparticles, hydrogels and viscogens, conventional viral vaccines (live and inactivated whole virus vaccines), and genetically engineered viral vaccines (reassortant viral particles, virus-like particles (VLPs) and other subunit recombinant vaccines including multi-valent viral vaccines, edible plant vaccines, and encapsulated viral particles).

Ghoshal, U. C., Gwee, K. A., Holtmann, G., Li, Y., Park, S. J., Simadibrata, M., Sugano, K., Wu, K., Quigley, E. M. M., and Cohen, H. The Role of the Microbiome and the use Of Probiotics in Gastrointestinal Disorders in Adults in the Asia-Pacific Region. J.Gastroenterol.Hepatol. 6-6-2017; PM: 28589613

ABSTRACT: The Asia-Pacific region is diverse, with regard to ethnicity, culture and economic development incorporating some of the world's least and most developed nations. Gastrointestinal diseases are common in the Asia-Pacific region and their prevalence, presentation, and management vary considerably within the region. There is growing evidence for an important role for the human gut microbiota in gastrointestinal health. As a consequence, geographic variations in the composition of the gut microbiota may contribute to variations in both the prevalence and response to therapy of specific diseases. Probiotics have been proposed as a valuable option in the prevention and treatment of a number of gastrointestinal illnesses, but the quality of available evidence to support their efficacy is variable. A meeting of international experts in adult and pediatric gastroenterology was held at the Sorbonne University, Paris, France on April 11th and 12th , 2016 to discuss current evidence supporting the use of probiotics in gastrointestinal disorders in the Asia-Pacific region. This article provides an overview of the discussions held at this meeting and recommends the formation of an Asia-Pacific Consortium on Gut Microbiota similar to those established in Europe and North America.

Gibson, G. R., Hutkins, R., Sanders, M. E., Prescott, S. L., Reimer, R. A., Salminen, S. J., Scott, K., Stanton, C., Swanson, K. S., Cani, P. D., Verbeke, K., and Reid, G. Expert consensus document: The International Scientific Association for Probiotics and Prebiotics (ISAPP) consensus statement on the definition and scope of prebiotics. Nat.Rev.Gastroenterol.Hepatol. 2017; 14(8):491-502; PM: 28611480

ABSTRACT: In December 2016, a panel of experts in microbiology, nutrition and clinical research was convened by the International Scientific Association for Probiotics and Prebiotics to review the definition and scope of prebiotics. Consistent with the original embodiment of prebiotics, but aware of the latest scientific and clinical developments, the panel updated the definition of a prebiotic: a substrate that is selectively utilized by host microorganisms conferring a health benefit. This definition expands the concept of prebiotics to possibly include non-carbohydrate substances, applications to body sites other than the gastrointestinal tract, and diverse categories other than food. The requirement for selective microbiota-mediated mechanisms was retained. Beneficial health effects must be documented for a substance to be considered a prebiotic. The consensus definition applies also to prebiotics for use by animals, in which microbiota-focused strategies to maintain health and prevent disease is as relevant as for humans. Ultimately, the goal of this Consensus Statement is to engender appropriate use of the term 'prebiotic' by relevant stakeholders so that consistency and clarity can be achieved in research reports, product marketing and regulatory oversight of the category. To this end, we have reviewed several aspects of prebiotic science including its development, health benefits and legislation.

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.

Gohil, P., Patel, V., Deshpande, S., Chorawala, M., and Shah, G. Anti-arthritic activity of cell wall content of Lactobacillus plantarum in freund's adjuvant-induced arthritic rats: involvement of cellular inflammatory mediators and other biomarkers. Inflammopharmacology. 7-6-2017; PM: 28685302

ABSTRACT: Alteration of microbiota is related with rheumatoid arthritis (RA) and administration of certain probiotics showed an improvement in RA. The present study was designed to find out the anti-arthritic activity of cell wall content of Lactobacillus plantarum in complete Freund's adjuvant (CFA)-induced arthritis in rats. Freund's adjuvant was injected into the left footpad in female rats on day 0 and dexamethasone (1 mg kg-1, s.c.) & cell wall content of L. plantarum (105, 107, and 109 cfu/animal, s.c.) treatment were given from day 7 to 21. The change in body weight, paw volume and arthritic index, joint stiffness, gait test, mobility test, erythrocyte sedimentation rate (ESR), serum C-reactive protein (CRP) level, serum rheumatoid factor (RF), and serum TNF-alpha was measured on day 21. Cell wall content of L. plantarum treated animals showed improvement in all the parameters as compared to that in CFA-treated animals and exert anti-arthritic activity.

Goldstein, E. J. C., Johnson, S. J., Maziade, P. J., Evans, C. T., Sniffen, J. C., Millette, M., and McFarland, L. V. Probiotics and prevention of Clostridium difficile infection. Anaerobe. 2017; 45:114-119; PM: 27988389

ABSTRACT: The role of probiotics as adjunctive measures in the prevention of Clostridium difficile infection (CDI) has been controversial. However, a growing body of evidence has suggested that they have a role in primary prevention of CDI. Elements of this controversy are reviewed and the proposed mechanisms of action, the value and cost effectiveness of probiotics are addressed with a focus on three agents, Saccharomyces boulardii, Lactobacillus rhamnosus GG and the combination of Lactobacillus acidophilus CL1285, Lactobacillus casei LBC80R, Lactobacillus rhamnosus CLR2 (Bio-K+).

Gong, Z. Y., Yuan, Z. Q., Dong, Z. W., and Peng, Y. Z. Glutamine with probiotics attenuates intestinal inflammation and oxidative stress in a rat burn injury model through altered iNOS gene aberrant methylation. Am.J.Transl.Res. 2017; 9(5):2535-2547; PM: 28560003

ABSTRACT: Severe burns may lead to intestinal inflammation and oxidative stress resulting in intestinal barrier damage and gut dysfunction. In the management of severe burns, therapies are needed to attenuate whole-body inflammatory responses and control the burden of oxidative stress. In this study, we evaluated the effects of oral glutamine (Gln) with probiotics on burn-induced intestinal inflammation and oxidative stress using a Wistar rat burn injury model. We then explored potential molecular mechanisms for the effects of glutamine and probiotics on intestinal tissue inflammation and oxidative stress. We found that glutamine and probiotics together significantly inhibited nitric oxide (NO) content; reduced levels of the inflammatory factors TNF-alpha, IL-6, and IL-8; and altered expression of oxidative stress factors including reactive oxygen species and superoxide dismutase. We found that the apoptotic proportion of intestinal epithelial cells in severely burned subjects was notably decreased following treatment with glutamine plus probiotics. We also found that glutamine and probiotics given together markedly reduced NO content by down-regulating the expression of iNOS in blood and intestinal tissue. These findings indicate that regulation of the iNOS gene plays a pivotal role in inflammation and oxidative stress in the response to severe burns in the Wistar rat. We then further investigated the mechanism by which combined therapy with glutamine and probiotics might reduce expression of iNOS and found that this treatment resulted in increased methylation of the iNOS gene. The methylation level of the iNOS gene was found to be regulated via differential expression of DNMT1 and Tet1. Collectively, our results suggest that combined therapy with glutamine and probiotics can markedly reduce the synthesis of NO, suppressing intestinal inflammation and oxidative stress in the Wistar rat burn injury model.

Gonzalez-Ferrero, C., Irache, J. M., and Gonzalez-Navarro, C. J. Soybean protein-based microparticles for oral delivery of probiotics with improved stability during storage and gut resistance. Food Chem. 1-15-2018; 239:879-888; PM: 28873648

ABSTRACT: The present work describes the encapsulation of probiotics using a by-product as wall material and a process feasible to be scaled-up: coacervation of soybean protein concentrate (SPC) by using calcium salts and spray-drying. SPC was extracted from soybean flour, produced during the processing of soybean milk, by alkaline extraction following isoelectric precipitation. Two probiotic strains were selected for encapsulation (Lactobacillus plantarum CECT 220 and Lactobacillus casei CECT 475) in order to evaluate the ability of SPC to encapsulate and protect bacteria from stress conditions. The viability of these encapsulated strains under in vitro gastrointestinal conditions and shelf-life during storage were compared with the most common forms commercialized nowadays. Results show that SPC is a feasible material for the development of probiotic microparticles with adequate physicochemical properties and enhanced significantly both probiotic viability and tolerance against simulated gastrointestinal fluids when compared to current available commercial forms.

Gonzalez-Ochoa, G., Flores-Mendoza, L. K., Icedo-Garcia, R., Gomez-Flores, R., and Tamez-Guerra, P. Modulation of rotavirus severe gastroenteritis by the combination of probiotics and prebiotics. Arch.Microbiol. 6-20-2017; PM: 28634691

ABSTRACT: Annual mortality rates due to infectious diarrhea are about 2.2 million; children are the most vulnerable age group to severe gastroenteritis, representing group A rotaviruses as the main cause of disease. One of the main factors of rotavirus pathogenesis is the NSP4 protein, which has been characterized as a viral toxin involved in triggering several cellular responses leading to diarrhea. Furthermore, the rotavirus protein NSP1 has been associated with interferon production inhibition by inducing the degradation of interferon regulatory factors IRF3, IRF5, and IRF7. On the other hand, probiotics such as Bifidobacterium and Lactobacillus species in combination with prebiotics such as inulin, HMO, scGOS, lcFOS have been associated with improved generalized antiviral response and anti-rotavirus effect by the reduction of rotavirus infectivity and viral shedding, decreased expression of NSP4 and increased levels of specific anti-rotavirus IgAs. Moreover, these probiotics and prebiotics have been related to shorter duration and severity of rotavirus diarrhea, to the prevention of infection and reduced incidence of reinfections. In this review we will discuss in detail about the rotavirus pathogenesis and immunity, and how probiotics such as Lactobacillus and Bifidobacterium species in combination with prebiotics have been associated with the prevention or modulation of rotavirus severe gastroenteritis.

Gopel, W., Drese, J., Rausch, T. K., Twisselmann, N., Bohnhorst, B., Muller, A., Franz, A., Ziegler, A., Hartel, C., and Herting, E. Necrotizing enterocolitis and high intestinal iron uptake due to genetic variants. Pediatr.Res. 9-13-2017; PM: 28820869

ABSTRACT: BackgroundIntestinal iron is a nutritional compound, which is essential for enteric microbiota. We evaluated the hypothesis that polymorphisms, which are known modifiers of intestinal iron uptake in adults, are associated with necrotizing enterocolitis (NEC) in preterm infants.MethodsPreterm infants (birth weight below 1,500 g) were studied. Single-nucleotide polymorphisms with known effects on serum iron levels (rs1800562, rs1799945, and rs855791) were determined using PCR. The effects of polymorphisms on NEC surgery were tested by Mendelian randomization. Outcome data were compared with chi2-test, Fisher's exact test, t-test, and Cochran-Armitage test for trend and multiple logistic regression analysis.ResultsComplete genotyping data were available for 11,166 infants. High serum iron levels due to rs855791 genotype were associated with a significantly reduced risk of NEC surgery (odds ratio (OR) 0.265; 95% confidence interval (CI) 0.11-0.65; adjusted P=0.011). Carriers of the rs855791 A-allele not receiving prophylactic probiotics had a higher risk of NEC surgery (OR 1.12, 95% CI 1.08-1.70, nominal P=0.002). Prophylactic treatment with probiotics was associated with a reduced risk of NEC surgery in carriers of the rs855791 A-Allele. No differences were found with regard to other short- or long-term outcome data.ConclusionPolymorphisms inducing lower intestinal iron uptake like the rs855791 A-allele might be an underestimated risk factor for NEC.Pediatric Research advance online publication, 13 September 2017; doi:10.1038/pr.2017.195.

Gracie, D. J., Derwa, Y., Hamlin, P. J., and Ford, A. C. Editorial: probiotics in inflammatory bowel disease-wrong organisms, wrong disease, or flawed concepts? Authors' reply. Aliment.Pharmacol.Ther. 2017; 46(6):633-634; PM: 28805328

No Abstract Available.

Granath, A. Recurrent Acute Otitis Media: What Are the Options for Treatment and Prevention? Curr.Otorhinolaryngol.Rep. 2017; 5(2):93-100; PM: 28616364

ABSTRACT: ***PURPOSE OF REVIEW***: To survey current strategies for treatment and prevention of recurrent acute otitis media (rAOM). ***RECENT FINDINGS***: Treatment with systemic antibiotics is required in recurrent episodes of acute otitis media. A cautious attitude is recommended due to antibiotic resistance. Antibiotics also provide effective prophylaxis for rAOM. Topical treatment with ear drops is recommended in rAOM with otorrhea from tympanostomy tubes. Pneumococcal conjugated vaccines seem to have a moderate reductive effect on overall otitis media. The effect on rAOM is still unclear. Different administrations of immunoglobulins have not been effective against rAOM. Breastfeeding had a protective effect against rAOM. A recommendation against cigarette smoke exposure as a measure to prevent otitis seems warranted. An effect for adenoidectomy in children <2 years old with rAOM has been suggested. There is a strong genetic connection with rAOM. Probiotics and nasal spray with Streptococci might offer future opportunities as prophylaxis. Too little is known about complimentary treatments to give any recommendations. ***SUMMARY***: Systemic antibiotics are still needed as treatment against episodes of AOM in rAOM children. There are several preventive measures that can be taken to reduce the burden of AOM but they all have a small-moderate effect. Systemic antibiotics provide effective prophylaxis in rAOM, but must be used with extreme caution due to the emerging antibiotic resistance.

Grande, R., Celia, C., Mincione, G., Stringaro, A., Di, Marzio L., Colone, M., Di Marcantonio, M. C., Savino, L., Puca, V., Santoliquido, R., Locatelli, M., Muraro, R., Hall-Stoodley, L., and Stoodley, P. Detection and Physicochemical Characterization of Membrane Vesicles (MVs) of Lactobacillus reuteri DSM 17938. Front Microbiol. 2017; 8:1040; PM: 28659878

ABSTRACT: Membrane vesicles (MVs) are bilayer structures which bleb from bacteria, and are important in trafficking biomolecules to other bacteria or host cells. There are few data about MVs produced by the Gram-positive commensal-derived probiotic Lactobacillus reuteri; however, MVs from this species may have potential therapeutic benefit. The aim of this study was to detect and characterize MVs produced from biofilm (bMVs), and planktonic (pMVs) phenotypes of L. reuteri DSM 17938. MVs were analyzed for structure and physicochemical characterization by Scanning Electron Microscope (SEM) and Dynamic Light Scattering (DLS). Their composition was interrogated using various digestive enzyme treatments and subsequent Transmission Electron Microscopy (TEM) analysis. eDNA (extracellular DNA) was detected and quantified using PicoGreen. We found that planktonic and biofilm of L. reuteri cultures generated MVs with a broad size distribution. Our data also showed that eDNA was associated with pMVs and bMVs (eMVsDNA). DNase I treatment demonstrated no modifications of MVs, suggesting that an eDNA-MVs complex protected the eMVsDNA. Proteinase K and Phospholipase C treatments modified the structure of MVs, showing that lipids and proteins are important structural components of L. reuteri MVs. The biological composition and the physicochemical characterization of MVs generated by the probiotic L. reuteri may represent a starting point for future applications in the development of vesicles-based therapeutic systems.

Grau, T., Vilcinskas, A., and Joop, G. Probiotic Enterococcus mundtii Isolate Protects the Model Insect Tribolium castaneum against Bacillus thuringiensis. Front Microbiol. 2017; 8:1261; PM: 28736550

ABSTRACT: Enterococcus mundtii strains isolated from the larval feces of the Mediterranean flour moth Ephestia kuehniella show antimicrobial activity against a broad spectrum of Gram-positive and Gram-negative bacteria. The in vitro probiotic characterization of one isolate revealed a high auto-aggregation score, a hydrophilic cell surface, tolerance for low pH, no hemolytic activity, and susceptibility to all tested antibiotics. We used the red flour beetle Tribolium castaneum, an established model organism, for the in vivo characterization of one probiotic E. mundtii isolate from E. kuehniella larvae. Tribolium castaneum larvae were fed orally with the probiotic isolate or the corresponding supernatant and then infected with either the entomopathogen Bacillus thuringiensis or Pseudomonas entomophila. Larvae exposed to the isolate or the supernatant showed increased survival following infection with B. thuringiensis but not P. entomophila. Heat treatment or treatment with proteinase K reduced the probiotic effect of the supernatant. However, the increased resistance attracts a fitness penalty manifested as a shorter lifespan and reduced fertility. T. castaneum has, pending on further research, the potential as an alternative model for the pre-screening of probiotics.

Gresse, R., Chaucheyras-Durand, F., Fleury, M. A., Van de, Wiele T., Forano, E., and Blanquet-Diot, S. Gut Microbiota Dysbiosis in Postweaning Piglets: Understanding the Keys to Health. Trends Microbiol. 6-8-2017; PM: 28602521

ABSTRACT: Weaning is a critical event in the pig's life cycle, frequently associated with severe enteric infections and overuse of antibiotics; this raises serious economic and public health concerns. In this review, we explain why gut microbiota dysbiosis, induced by abrupt changes in the diet and environment of piglets, emerges as a leading cause of post-weaning diarrhea, even if the exact underlying mechanisms remain unclear. Then, we focus on nonantimicrobial alternatives, such as zinc oxide, essential oils, and prebiotics or probiotics, which are currently evaluated to restore intestinal balance and allow a better management of the crucial weaning transition. Finally, we discuss how in vitro models of the piglet gut could be advantageously used as a complement to ex vivo and in vivo studies for the development and testing of new feed additives.

Grigoryan, E. G. and Serobyan, N. S. [Dynamics of the intestinal biocenosis, indicators of the blood lipid profile, antioxidant system, and energy metabolism in the patients presenting with chronic non-calculous cholecystitis under the influence of the therapeutic physical factors in the combination with probiotics]. Vopr.Kurortol.Fizioter.Lech.Fiz Kult. 2017; 94(2):42-46; PM: 28665381

ABSTRACT: The present study included 60 patients presenting with chronic non-calculous cholecystitis and intestinal dysbiosis. It has been demonstrated that the application of the 'Nor Narine' probiotic in the combination with 'Djermuk' hydrocarbon sodium sulfate mineral water and the pre-formed physical factors, in the first place the magnetic laser radiation, increases the effectiveness of the rehabilitative treatment of the patients. Such treatment resulted not only in the positive dynamics of the clinical picture of disease but also in the well apparent marked tendency toward normalization of the intestinal biocenosis, the lipid blood spectrum, the antioxidant system, and the energetic exchange.

Guadamuro, L., Florez, A. B., Alegria, A., Vazquez, L., and Mayo, B. Characterization of four beta-glucosidases acting on isoflavone-glycosides from Bifidobacterium pseudocatenulatum IPLA 36007. Food Res.Int. 2017; 100(Pt 1):522-528; PM: 28873716

ABSTRACT: Bifidobacterium pseudocatenulatum IPLA 36007 acts on isoflavone glycosides, releasing their corresponding aglycones. This strain-specific activity might be a key step in making isoflavones bioavailable and harnessing their oestrogenic activity. To investigate the molecular mechanisms involved in this activity, four glycosyl hydrolase-encoding genes in the IPLA 36007 genome (AW18_01575, AW18_09810, AW18_08145, and AW18_08090) were selected, synthesized with heterologous promoter and terminator signals (r-beta-gluA, r-beta-gluB, r-beta-gluD and r-beta-gluE, respectively), cloned into Escherichia coli, overexpressed as His-tagged proteins, and the enzymes purified and characterized. All four enzymes - GluAHis, GluBHis, GluDHis and GluEHis - proved to have beta-glucosidase activity and deglycosylated (although at different rates) the isoflavone glycosides daidzin and genistin, releasing the aglycone moieties daidzein and genistein, respectively. GluDHis and GluEHis were also shown to hydrolyse beta-glucosyl disaccharides such as cellobiose and gentiobiose, while GluAHis and GluBHis did not. Differences in activity were recorded for all four beta-glucosidases at different pHs and temperatures under otherwise similar assay conditions, suggesting they have complementary activities under different environmental conditions. Two of the recombinant genes, r-beta-gluA, and r-beta-gluD, were cloned and expressed in the model lactic acid bacterium Lactococcus lactis, suggesting starter and probiotic organisms could be endowed with beta-glucosidase activity. B. pseudocatenulatum IPLA 36007 contains additional beta-glucosidases to those studied in this work, indicating a high level of redundancy for this enzymatic activity. Knowledge of glycoside-degrading enzymes should facilitate the development of novel, more effective or more selective prebiotics or functional foods for the promotion of bifidobacterial numbers in the human gut. It might also be of interest in the development of novel probiotics with specific health-promoting activities.

Gupta, M. and Bajaj, B. K. Functional Characterization of Potential Probiotic Lactic Acid Bacteria Isolated from Kalarei and Development of Probiotic Fermented Oat Flour. Probiotics.Antimicrob.Proteins. 7-20-2017; PM:28730403¶

ABSTRACT: Considerable variations among probiotics with respect to their health benefitting attributes fuel the research on bioprospecting of proficient probiotic strains from various ecological niches especially the poorly unexplored ones. In the current study, kalarei, an indigenous cheese-like fermented milk product, and other dairy-based sources like curd and raw milk were used for isolation of lactic acid bacteria (LAB). Among 34 LAB isolates, 7 that could withstand simulated gastrointestinal (GI) conditions were characterized for functional probiotic attributes, viz. adhesion ability, aggregation and coaggregation, extracellular enzyme producing capability, antibacterial activity against pathogens and antibiotic resistance. The isolate M-13 (from kalarei) which exhibited most of the desirable probiotic functional properties was identified as Lactobacillus plantarum based on 16S ribosomal DNA sequence analysis and designated as L. plantarum M-13. The sequence was submitted to GenBank (accession number KT592509). The study presents the first ever report of isolation of potential probiotic LAB, i.e. L. plantarum M-13 from indigenous food kalarei, and its application for development of potential probiotic fermented oat flour (PFOF). PFOF was analysed for parameters like viability of L. plantarum M-13, acidity and pH. Results show that PFOF serves as a good matrix for potential probiotic L. plantarum M-13 as it supported

adequate growth of the organism (14.4 log cfu/ml after 72 h of fermentation). In addition, appreciable acid production by L. plantarum M-13 and consequential pH reduction indicates the vigorous and active metabolic status of the potential probiotic organism in the food matrix. Thus, study shows that fermented oat flour may possibly be developed as a potential probiotic carrier especially in view of the problems associated with dairy products as probiotic vehicles.

Gupta, M. and Sicherer, S. H. Timing of food introduction and atopy prevention. Clin.Dermatol. 2017; 35(4):398-405; PM: 28709571

ABSTRACT: The apparent increase in atopic disease, particularly food allergy, over the past 2 decades has resulted in reconsideration of prevention strategies aimed at the infant's diet. Early advice to have atopy-prone infants delay ingestion of potential food allergens, such as egg, cow's milk, and peanut, was rescinded, as new evidence emerged that did not support these approaches. More recently, randomized controlled trials have provided data to support an opposite strategy, promoting early ingestion of allergens as a means of food allergy prevention. Specifically, new guidelines suggest early ingestion of peanut as a means to prevent peanut allergy. Additional dietary approaches regarding breastfeeding, early introduction of other types of food allergens, formula feeding, dietary nutrients, and probiotics are also under scrutiny as potential preventative strategies. This review focuses on the timing of food introduction as a preventative strategy for food allergy and also discusses other aspects of the infant diet that may provide opportunities for prevention of atopic disease.

Gurry, T. Synbiotic approaches to human health and well-being. Microb.Biotechnol. 8-3-2017; PM: 28771949

ABSTRACT: Synbiotics refer to combinations of probiotics and prebiotics that act synergistically to confer health benefits to the host. As a therapeutic strategy, they provide a gentle yet powerful method for modulating the composition and metabolic output of the human gut microbiota. In the context of achieving the UN Sustainable Development Goals, synbiotics have the potential to act as cost-effective prophylactic measures against a variety of human ailments, ranging from infant diarrhoea to metabolic and inflammatory diseases in adults, by maintaining commensal microbial communities and metabolic networks that are conducive to human health.

Haddaji, N., Mahdhi, A. K., Ismaiil, M. B., and Bakhrouf, A. Effect of environmental stress on cell surface and membrane fatty acids of Lactobacillus plantarum. Arch.Microbiol. 6-8-2017; PM: 28597197

ABSTRACT: Adhesion has been regarded as one of the basic features of probiotics. We undertake this study in the aim to give new insight about the change in cellular physiological state under heat and acid treatments of Lactobacillus plantarum. Different cell properties have been investigated such as adhesive ability to abiotic surfaces, the cell surface hydrophobicity and the fatty acids profiles. The results of cell surface properties and Gas chromatography analysis demonstrated a modification in term adhesive ability and fatty acid (FA) composition of the tested strain under stressful conditions. In fact, after the exposure of the strain to heat and acid treatments, an

increase in the hydrophobicity level and the adhesion capacity on HeLa cells was shown. Our findings revealed that high temperature and low pH change the fatty acids profiles of the treated cells, especially the proportions of unsaturated and saturated fatty acid. In this context, our data revealed that the unsaturated FA-to-saturated FA ratio was increased significantly ($P < 0.05$) for stressed strains compared with control cells. The results of the present finding suggest that the tested strain have suffered changes like the modifications on bacterial membrane as a cellular response to survive the hard environmental conditions, allowing them to withstand harsh conditions and sudden environmental changes to survive under.

Hajare, S. T. and Bekele, G. Effect of Probiotic strain Lactobacillus acidophilus (LBKV-3) on fecal residual lactase activity in undernourished children below 10 year. J.Immunoassay Immunochem. 8-30-2017; PM: 28853996

ABSTRACT: Clinically proven Lactobacillus acidophilus strain LBKV-3 intended as probiotc for human was used to test its effect on fecal residual lactase activity in undernourished children below 10 years. The children were selected from malnutrition declared area of Maharashtra (India). One of the major causes of malnutrition is lactose intolerance which leads to diarrhea. The basic consideration in selecting the probiotic strain of Lactobacillus acidophilus-LBKV3 in this investigation was the fact that the organism is isolated from human vaginal surface swab and it was found extensively studied for probiotic characteristic. LBKB3 tested by several workers as probiotic for hypocholesterolaemic activity, implantation ability, therapeutic effects on GI and related ailments. The results of present investigation shown that the fecal residual lactase activity significantly increased than the initial value (which was almost zero). It appeared that the fecal residual beta-galactosidase activity is an indication of positive implementation abilities of the cultures under investigation. These trends were compared with the control and blank group of children receiving Dahi and Buffalo milk (BM). It was observed that both these product failed to exert any significant impact on increase in residual lactase activity.

Halder, D., Mandal, M., Chatterjee, S. S., Pal, N. K., and Mandal, S. Indigenous Probiotic Lactobacillus Isolates Presenting Antibiotic like Activity against Human Pathogenic Bacteria. Biomedicines. 6-16-2017; 5(2); PM: 28621711

ABSTRACT: ***BACKGROUND***: Indigenous lactic acid bacteria are well known probiotics having antibacterial activity against potentially pathogenic bacteria. This study aims to characterize the curd lactobacilli for their probiotic potentiality and antagonistic activity against clinical bacteria. ***METHODS***: Four curd samples were processed microbiologically for the isolation of lactic acid bacteria (LAB). The LAB strains obtained were identified by conventional methods: cultural aspect, gram-staining, biochemical and sugar fermentation tests. The probiotic properties were justified with tolerance to low-pH, bile salt and sodium chloride, and the antagonistic activity of the lactobacilli against human pathogenic bacteria (Escherichia coli, Proteus vulgaris, Acinetobacter baumannii and Salmonella enterica serovar Typhi) was assessed. Hemolytic activity and antibiotic susceptibility were determined for the lactobacilli isolates, and the cumulative probiotic potential (CPP) values were recorded. ***RESULT***: Four lactobacilli isolates, L. animalis LMEM6, L. plantarum LMEM7, L. acidophilus LMEM8 and L. rhamnosus LMEM9, procured from the curd samples, survived in low-pH and high bile salt conditions, and showed growth inhibitory activity against the indicator bacteria by agar-well (zone diameter of

inhibition; ZDIs: 13.67 +/- 0.58-29.50 +/- 2.10 mm) and agar overlay (ZDIs: 11.33 +/- 0.58-35.67 +/- 2.52 mm) methods; the average growth inhibitory activity of lactobacilli ranged 233.34 +/- 45.54-280.56 +/- 83.67 AU/mL, against the test bacterial pathogens. All the lactobacilli were non-hemolytic and sensitive to most of the test antibiotics. The CPP values of the isolated LAB were recorded as 80-100%. *CONCLUSION*: The curd lactobacilli procured might be used as the valid candidates of probiotics, and bio-therapeutics against bacterial infection to humans.

Hammes, T. O., Leke, R., Escobar, T. D. C., Fracasso, L. B., Meyer, F. S., Andrades, M. E., and Silveira, T. R. D. Lactobacillus rhamnosusGG reduces hepatic fibrosis in a model of chronic liver disease in rats. Nutr.Hosp. 6-5-2017; 34(3):702-709; PM: 28627210

ABSTRACT: ***BACKGROUND***: The intestinal dysbiosis is common in chronic liver disease and can induce to inflammatory responses and mediate the collagen deposition in the liver. AIM: To evaluate the probiotic Lactobacillus rhamnosus GG (LGG) for the treatment of liver fibrosis in a model of chronic cholestatic liver disease in rats. METHODS: Male adult Wistar rats (n = 29) were submitted to common bile duct ligation (BDL groups) or manipulation of common bile duct without ligation (Ctrl groups).Two weeks after surgery, each group was randomly divided to receive 1 ml of PBS (Ctrl and BDL) or PBS containing 2.5 x 107 CFU of LGG (Ctrl-P and BDL-P) through gavages for 14 days. Euthanasia occurred 33 days after surgery when samples of blood and liver tissue were collected. ***RESULTS***: The hepatic gene expression of Tlr4, Tnfalpha, IL-6, Tgfbeta, and metalloproteinase-2 and -9 were higher in the BDL groups in comparison to Ctrl. The ductular reaction evaluated by immunocontent of cytokeratin-7 (CK7) and the content of collagen were increased in BDL groups. Also, there was an imbalance in the antioxidant defenses (superoxide dismutase and catalase) and an increase in the oxidative stress marker sulfhydryl in BDL groups. The treatment with LGG significantly reduced gene expression of IL-6, collagen deposition, and ductular reaction in hepatic tissue of animals from BDL-P groups. ***CONCLUSION***: The treatment with the probiotic LGG was able to reduce liver fibrosis, ductular reaction, and hepatic gene expression of IL-6 in a model of cholestatic liver disease in rats.

Han, B., Sivaramakrishnan, P., Lin, C. J., Neve, I. A. A., He, J., Tay, L. W. R., Sowa, J. N., Sizovs, A., Du, G., Wang, J., Herman, C., and Wang, M. C. Microbial Genetic Composition Tunes Host Longevity. Cell. 6-15-2017; 169(7):1249-1262 PM: 28622510

ABSTRACT: Homeostasis of the gut microbiota critically influences host health and aging. Developing genetically engineered probiotics holds great promise as a new therapeutic paradigm to promote healthy aging. Here, through screening 3,983 Escherichia coli mutants, we discovered that 29 bacterial genes, when deleted, increase longevity in the host Caenorhabditis elegans. A dozen of these bacterial mutants also protect the host from age-related progression of tumor growth and amyloid-beta accumulation. Mechanistically, we discovered that five bacterial mutants promote longevity through increased secretion of the polysaccharide colanic acid (CA), which regulates mitochondrial dynamics and unfolded protein response (UPRmt) in the host. Purified CA polymers are sufficient to promote longevity via ATFS-1, the host UPRmt-responsive transcription factor. Furthermore, the mitochondrial changes and longevity effects induced by CA are conserved across different species. Together, our results identified molecular targets for developing pro-longevity microbes and a bacterial metabolite acting on host mitochondria to promote longevity.

Han, W. B., Liu, Y. L., Wan, Y. G., Sun, W., Tu, Y., Yang, J. J., Wu, W., He, W. M., and Yao, J. [Pathomechanism and treatment of gut microbiota dysbiosis in chronic kidney disease and interventional effects of Chinese herbal medicine]. Zhongguo Zhong.Yao Za Zhi. 2017; 42(13):2425-2432; PM: 28840678

ABSTRACT: The gut microbiota dysbiosis is one of the risk factors in the progression from the advanced chronic kidney diseaseCKDto uremia, characterized by the reduction of probiotics and the increase of opportunistic pathogens including urease-related microbes, endotoxin-related microbes and toxin-related microbes, which can produce uremic toxins. According to the core point of "the gut-kidney axis" theory and "the chronic kidney disease-colonic axis" concept, the gut microbiota dysbiosis aggravates renal damage by accumulating uremic toxins and inducing the systemic micro-inflammation. The preliminary clinical trials and animal experiments show that the probiotics biologicals from Lactobacillus acidophilus or Bifidobacterium, and the prebiotics including inulin and galactooligosaccharides, as well as lubiprostone and activated carbon adsorbents can be used for improving dysfunction of CKD patients with the gut microbiota dysbiosis via reducing uremic toxins and inhibiting the systemic micro-inflammation. But not only that, it is reported that, to some extent, a number of the single Chinese herbal medicineCHM, the CHM prescriptions and the CHM extractsemodin, etc.with oral or enema administration can also regulate the gut microbiota dysbiosis, protect the intestinal epithelial barrier, reduce uremic toxins accumulation and delay CKD progression. Thereinto, Dahuang Gancao Decoctionthe concentrated granule TJ-84, a classical CHM prescription of rhubarb, can ameliorate uremic toxins accumulation in the animal models with renal failure probably through targeting the gut-kidney axis triggered from gut microbiota, but not targeting the kidney. Based on these results, the interventional studies targeting the gut microbiota-related pathological factors such as tight junction proteins, helper T cells and regulatory T cells in the intestinal tract of the advanced CKD patients will become one of the key development directions in the future.

Hanaway, P. J. Which Probiotics Should I Take? A Practical Guide for Family Physicians. Am.Fam.Physician. 8-1-2017; 96(3):156; PM: 28762695

No Abstract Available.

Harris, V. C., Haak, B. W., Boele van, Hensbroek M., and Wiersinga, W. J. The Intestinal Microbiome in Infectious Diseases: The Clinical Relevance of a Rapidly Emerging Field. Open.Forum Infect.Dis. 2017; 4(3):ofx144; PM: 28852682

ABSTRACT: The field of infectious disease is undergoing a paradigm shift as the intestinal microbiome is becoming understood. The aim of this review is to inform infectious disease physicians of the potential relevance of the intestinal microbiome to their practice. We searched Medline using both index and text words relating to infectious diseases, microbiome, and probiotics. Relevant articles published up through 2017 were reviewed within Rayyan. The review illustrates pathophysiologic concepts linking the microbiome and infectious diseases; specifically, the intestinal microbiome's relevance to early immune development, the microbiome and enteric infections, the microbiome's relevance in compromised hosts, and antimicrobial resistance. Within each subject, there are specific examples of diseases and at-risk patient populations where a role for

the microbiome has been strongly established. This provides an overview of the significance of the intestinal microbiome to microbiology, pediatric and adult infectious diseases with an underpinning of concepts useful for the practicing clinician.

Hartel, C., Pagel, J., Spiegler, J., Buma, J., Henneke, P., Zemlin, M., Viemann, D., Gille, C., Gehring, S., Frommhold, D., Rupp, J., Herting, E., and Gopel, W. Lactobacillus acidophilus/Bifidobacterium infantis probiotics are associated with increased growth of VLBWI among those exposed to antibiotics. Sci.Rep. 7-17-2017; 7(1):5633; PM: 28717131

ABSTRACT: We performed an observational study with very-low-birth weight infants (VLBWI) </=33 weeks of gestation born in centers of the German Neonatal Network (GNN; (total n = 8534, n = 6229 received probiotics). The primary objectives of our study were (a) to assess the effect of Lactobacillus acidophilus/Bifidobacterium infantis probiotics on growth in VLBWI during primary stay in hospital and (b) to determine whether this effect is modified by antibiotic exposure. In linear regression models the administration of probiotics was independently associated with improved weight gain [g/d; effect size B = 0.62 (95% CI: 0.37-0.87), p < 0.001], and higher growth rates for body length [(mm/d; B = 0.06 (95% CI: 0.04-0.08), p < 0.001] and head circumference [mm/d; B = 0.03, 95% CI: 0.02-0.04, p < 0.001]. This effect was pronounced in infants with postnatal exposure to antibiotics; i.e. weight gain [g/d; B = 0.66 (95% CI: 0.32-1), p < 0.001], growth rate body length [(mm/d; B = 0.09 (95% CI: 0.06-0.12), p < 0.001] and head circumference [mm/d; B = 0.04, 95% CI: 0.02-0.06, p < 0.001]. In the small subgroup that was available for analysis at 5-year-follow-up (with probiotics: n = 120 vs. without probiotics: n = 54) we noted a sustained effect of probiotics in infants who received postnatal antibiotics. Probiotics may improve growth in antibiotic-treated infants which needs to be confirmed in randomized-controlled trials.

Heeney, D. D., Gareau, M. G., and Marco, M. L. Intestinal Lactobacillus in health and disease, a driver or just along for the ride? Curr.Opin.Biotechnol. 8-31-2017; 49:140-147; PM: 28866243

ABSTRACT: Metagenomics and related methods have led to significant advances in our understanding of the human microbiome. Members of the genus Lactobacillus, although best understood for essential roles in food fermentations and applications as probiotics, have also come to the fore in a number of untargeted gut microbiome studies in humans and animals. Even though Lactobacillus is only a minor member of the human colonic microbiota, the proportions of those bacteria are frequently either positively or negatively correlated with human disease and chronic conditions. Recent findings on Lactobacillus species in human and animal microbiome research, together with the increased knowledge on probiotic and other ingested lactobacilli, have resulted in new perspectives on the importance of this genus to human health.

Hemalatha, R., Ouwehand, A. C., Saarinen, M. T., Prasad, U. V., Swetha, K., and Bhaskar, V. Effect of probiotic supplementation on total lactobacilli, bifidobacteria and short chain fatty acids in 2-5-year-old children. Microb.Ecol.Health Dis. 2017; 28(1):1298340; PM: 28572751

ABSTRACT: ***Background***: Consumption of Lactobacillus paracasei Lpc-37 or Bifidobacterium lactis HN019 by 2-5-year-old children was found to reduce risk for diarrhoea and fever during the rainy season. Objective: Can changes in faecal short

chain fatty acids (SCFAs) or branched chain fatty acids (BCFAs) explain the observed positive influence of probiotics and their role on nutritional status and diarrhoea risk? ***Design***: Faecal samples were analysed for SCFAs and BCFAs and correlated to Bifidobacterium and Lactobacillus levels; both at the start and after nine months' consumption of either of the two probiotic strains, or placebo. ***Results***: No differences in SCFAs, BCFAs, Lactobacillus or Bifidobacterium levels were found between boys and girls. Severely underweight children were observed to have the highest Lactobacillus levels. Probiotic intervention was found to be associated with higher levels of selected SCFAs and BCFAs in subjects who had experienced diarrhoea. Treatment with either of the probiotics led to changes in SCFAs and BCFAs. SCFAs, acetate, propionate and butyrate, were found to correlate with each other. Likewise, BCFAs isobutyrate, 2-methylbutyrate and isovalerate correlated with each other. After the intervention, L. paracasei Lpc-37 correlated positively with total Bifidobacterium counts and isovalerate levels. B. lactis HN019 counts were found to correlate positively with total bacterial counts and negatively with propionate levels. Conclusions: Nutritional status was associated with higher levels of faecal lactobacilli; the meaning of this requires further investigation. The intervention with the two probiotics was observed to influence the levels of faecal SCFAs and BCFAs and there is a differential response in those who developed diarrhoea and those who did not. It is, however, not clear to what extent this is a mechanism that explains the earlier observed effect the strains had on diarrhoea risk.

Hidalgo-Cantabrana, C., O'Flaherty, S., and Barrangou, R. CRISPR-based engineering of next-generation lactic acid bacteria. Curr.Opin.Microbiol. 6-13-2017; 37:79-87; PM: 28622636

ABSTRACT: The advent of CRISPR-based technologies has opened new avenues for the development of next-generation food microorganisms and probiotics with enhanced functionalities. Building off two decades of functional genomics studies unraveling the genetic basis for food fermentations and host-probiotic interactions, CRISPR technologies offer a wide range of opportunities to engineer commercially-relevant Lactobacillus and Bifidobacteria. Endogenous CRISPR-Cas systems can be repurposed to enhance gene expression or provide new features to improve host colonization and promote human health. Alternatively, engineered CRISPR-Cas systems can be harnessed to genetically modify probiotics and enhance their therapeutic potential to deliver vaccines or modulate the host immune response.

Hidalgo-Cantabrana, C., Delgado, S., Ruiz, L., Ruas-Madiedo, P., Sanchez, B., and Margolles, A. Bifidobacteria and Their Health-Promoting Effects. Microbiol.Spectr. 2017; 5(3); PM: 28643627

ABSTRACT: Bifidobacteria are members of the intestinal microbiota of mammals and other animals, and some strains are able to exert health-promoting effects. The genus Bifidobacterium belongs to the Actinobacteria phylum. Firmicutes, Bacteroidetes, and Actinobacteria constitute the most abundant phyla in the human intestinal microbiota, Firmicutes and Bacteroidetes being predominant in adults, and Actinobacteria in breast-fed infants, where bifidobacteria can reach levels higher than 90% of the total bacterial population. They are among the first microbial colonizers of the intestines of newborns, and play key roles in the development of their physiology, including maturation of the immune system and use of dietary components. Indeed, some nutrients, such as human milk oligosaccharides, are important drivers of bifidobacterial development. Some Bifidobacterium strains are considered probiotic microorganisms because of their

beneficial effects, and they have been included as bioactive ingredients in functional foods, mainly dairy products, as well as in food supplements and pharma products, alone, or together with, other microbes or microbial substrates. Well-documented scientific evidence of their activities is currently available for bifidobacteria-containing preparations in some intestinal and extraintestinal pathologies. In this review, we focus on the role of bifidobacteria as members of the human intestinal microbiota and their use as probiotics in the prevention and treatment of disease.

Hill, D., Sugrue, I., Arendt, E., Hill, C., Stanton, C., and Ross, R. P. Recent advances in microbial fermentation for dairy and health. F1000Res. 2017; 6:751; PM: 28649371

ABSTRACT: Microbial fermentation has been used historically for the preservation of foods, the health benefits of which have since come to light. Early dairy fermentations depended on the spontaneous activity of the indigenous microbiota of the milk. Modern fermentations rely on defined starter cultures with desirable characteristics to ensure consistency and commercial viability. The selection of defined starters depends on specific phenotypes that benefit the product by guaranteeing shelf life and ensuring safety, texture, and flavour. Lactic acid bacteria can produce a number of bioactive metabolites during fermentation, such as bacteriocins, biogenic amines, exopolysaccharides, and proteolytically released peptides, among others. Prebiotics are added to food fermentations to improve the performance of probiotics. It has also been found that prebiotics fermented in the gut can have benefits that go beyond helping probiotic growth. Studies are now looking at how the fermentation of prebiotics such as fructo-oligosaccharides can help in the prevention of diseases such as osteoporosis, obesity, and colorectal cancer. The potential to prevent or even treat disease through the fermentation of food is a medically and commercially attractive goal and is showing increasing promise. However, the stringent regulation of probiotics is beginning to detrimentally affect the field and limit their application.

Ho, Y. Y., Lin, C. M., and Wu, M. C. Evaluation of the prebiotic effects of citrus pectin hydrolysate. J.Food Drug Anal. 2017; 25(3):550-558; PM: 28911641

ABSTRACT: Citrus pectin enzyme hydrolysate (PEH) of different hydrolysis time intervals (6 hours, PEH-6; 12 hours, PEH-12; 24 hours, PEH-24; or 48 hours, PEH-48) or concentrations (1%, 2%, and 4%) was tested for its growth stimulation effect on two probiotics, Bifidobacterium bifidum and Lactobacillus acidophilus. Higher monosaccharide concentrations and smaller molecular weights of PEHs were obtained by prolonging the hydrolysis time. In addition, higher PEH concentrations resulted in significantly higher ($p < 0.05$) probiotic populations, pH reduction, and increase in total titratable acidity than the glucose-free MRS negative control. Furthermore, significantly higher populations in the low pH environment and longer survival time in nonfat milk ($p < 0.05$) were observed when the two probiotics were incubated in media supplemented with 2% PEH-24, than in glucose and the negative control. In comparison with other prebiotics, addition of 2% PEH-24 resulted in a more significant increase in the probiotic population ($p < 0.05$) than in the commercial prebiotics. This study demonstrated that PEH derived from citrus pectin could be an effective prebiotic to enhance the growth, fermentation, acid tolerance, and survival in nonfat milk for the tested probiotics.

Hojsak, I., Szajewska, H., Canani, R. B., Guarino, A., Indrio, F., Kolacek, S., Orel, R., Shamir, R., Vandenplas, Y., van Goudoever, J. B., and Weizman, Z. Probiotics for the Prevention of Nosocomial Diarrhea in Children. J.Pediatr.Gastroenterol.Nutr. 6-2-2017; PM: 28574970

ABSTRACT: This document provides recommendations developed by the ESPGHAN Working Group (WG) on Probiotics and Prebiotics on the role of probiotics in the prevention of nosocomial diarrhea in children based on a systematic review of previously completed systematic reviews and of subsequently published randomized controlled trials (RCTs). The quality of evidence was assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) guidelines. Recommendations were given only if at least 2 RCTs examined the same probiotic strain. Based on currently available evidence the WG recommends using Lactobacillus rhamnosus GG if the use of probiotics for preventing nosocomial diarrhea in children is considered.

Hong Chau, T. T., Chau, N. N. M., Hoang Le, N. T., The, H. C., Voong, Vinh P., To, N. T. N., Ngoc, N. M., Tuan, H. M., Ngoc, T. L. C., Kolader, M. E., Farrar, J. J., Wolbers, M., Thwaites, G. E., and Baker, S. A Double Blind, Randomized, Placebo-Controlled Trial of Lactobacillus acidophilus for the Treatment of Acute Watery Diarrhea in Vietnamese Children. Pediatr.Infect.Dis.J. 8-1-2017; PM: 28787388

ABSTRACT: ***BACKGROUND***: Probiotics are the most frequently prescribed treatment for children hospitalized with diarrhea in Vietnam. We were in uncertain of the benefits of probiotics for the treatment of acute watery diarrhea in Vietnamese children. ***METHODS***: We conducted a double blind, placebo-controlled, randomized trial of children hospitalized with acute watery diarrhea in Vietnam. Children meeting the inclusion criteria (acute watery diarrhea) were randomized to receive either two daily oral doses of 2 x 10 CFUs of a local probiotic containing Lactobacillus acidophilus or placebo for 5 days as an adjunct to standard-of-care. The primary endpoint was time from the first dose of study medication to the start of the first 24-hour period without diarrhea. Secondary outcomes included the total duration of diarrhea and hospitalization, daily stool frequency, treatment failure, daily fecal concentrations of rotavirus and norovirus, and Lactobacillus colonization. ***RESULTS***: 150 children were randomized into each study group. The median time from the first dose of study medication to the start of the first 24-hour diarrhea free period was 43 hours (inter-quartile range (IQR) 15-66 hours) in the placebo group and 35 hours (IQR 20-68 hours) in the probiotic group (acceleration factor 1.09 (95% confidence interval 1.78-1.51); p=1.62). There was also no evidence that probiotic treatment was efficacious in any of the pre-defined subgroups nor significantly associated with any secondary endpoint. ***CONCLUSIONS***: This was a large double blind, placebo-controlled trial in which the probiotic underwent longitudinal quality control. We found that under these conditions that Lactobacillus acidophilus was not beneficial in treating children with acute watery diarrhea.

Hossain, M. I., Sadekuzzaman, M., and Ha, S. D. Probiotics as potential alternative biocontrol agents in the agriculture and food industries: A review. Food Res.Int. 2017; 100(Pt 1):63-73; PM: 28873730

ABSTRACT: Pathogenic microorganisms are a potential threat to the agriculture and food industries. Food contamination can be happened in the production levels at any point in the chain by pathogenic microorganisms. Conventional methods, such as those

involving antibiotics, disinfectants, and physical methods, are commonly used as microbial control strategies. Owing to the limitations of these methods, such as emergence of resistance, low effectiveness, high cost, and detrimental effects on food, health, and the environment, many countries have adopted laws and regulations restricting their use. To overcome these problems, an environmentally friendly, cost-effective alternative approach is urgently needed. Probiotics are live microorganisms that offer health benefits to the host, when consumed in adequate amounts, by providing pathogen protective action and nutritional benefits. From a food microbiological point of view, to use probiotics in animals, there is a reduction of zoonotic pathogens in the gastro-intestinal tract (GIT) among animals which prevent the transmission of these pathogens through food. Therefore, probiotics have been proposed as an alternative antimicrobial means to protect against pathogenic microorganisms for better healthcare and food safety. In this review, we discuss probiotics, their selection criteria, mechanisms of action, and their prospects as alternative biocontrol agents, with special emphasis on the agriculture (livestock and aquaculture sectors), and food industries.

Hou, T., Kolba, N., Glahn, R. P., and Tako, E. Intra-Amniotic Administration (Gallus gallus) of Cicer arietinum and Lens culinaris Prebiotics Extracts and Duck Egg White Peptides Affects Calcium Status and Intestinal Functionality. Nutrients. 7-21-2017; 9(7); PM: 28754012

ABSTRACT: Calcium (Ca) is one of the most abundant inorganic elements in the human body and has many important physiological roles. Prebiotics and bioactive peptides are two important substances used to promote calcium uptake. However, the difference in mechanisms of the calcium uptake from these two supplements is not clear. By using the Gallus gallus model and the intra-amniotic administration procedure, the aim of this study was to investigate whether Ca status, intestinal functionality, and health-promoting bacterial populations were affected by prebiotics extracted from chickpea and lentil, and duck egg white peptides (DPs). Eleven groups (non-injected; 18 MOmega H(2)O; 4 mmol/L CaCl(2); 50 mg/mL chickpea + 4 mmol/L CaCl(2); 50 mg/mL lentil + 4 mmol/L CaCl(2); 40 mg/mL DPs + 4 mmol/L CaCl(2); 5 mg/mL Val-Ser-Glu-Glu (VSEE) + 4 mmol/L CaCl(2); 50 mg/mL chickpea; 50 mg/mL lentil; 40 mg/mL DPs; 5 mg/mL VSEE) were utilized. Upon hatch, blood, cecum, small intestine, liver and bone were collected for assessment of serum bone alkaline phosphate level (BALP), the relative abundance of intestinal microflora, expression of Ca-related genes, brush border membrane (BBM) functional genes, and liver and bone mineral levels, respectively. The BALP level increased in the presence of lentil, DPs and VSEE ($p < 0.05$). The relative abundance of probiotics increased significantly ($p < 0.05$) by VSEE + Ca and chickpea. The expression of CalbindinD9k (Ca transporter) increased ($p < 0.05$) in Ca, chickpea + Ca and lentil + Ca groups. In addition, the brush border membrane functionality genes expressions increased ($p < 0.05$) by the chickpea or lentil extracts. Prebiotics and DPs beneficially affected the intestinal microflora and duodenal villus surface area. This research expands the understanding of the prebiotics' properties of chickpea and lentil extracts, and peptides' effects on calcium metabolism and gut health.

Houwen, R. H. J., van der Woerd, W. L., Slae, M., and Wilschanski, M. Effects of new and emerging therapies on gastrointestinal outcomes in cystic fibrosis. Curr.Opin.Pulm.Med. 8-5-2017; PM: 28787381

ABSTRACT: ***PURPOSE OF REVIEW***: Several new therapeutic modalities have recently

become available to be used in patients with cystic fibrosis such as potentiators, modulators, and probiotics. Although the effects on pulmonary function have been well documented, gastrointestinal outcomes have been addressed only rarely. ***RECENT FINDINGS***: Both the potentiator (ivacaftor) and the potentiator/modulator combination (ivacaftor/lumacaftor) that are currently on the market have a positive effect on BMI. Young patients (2-5 years of age) with a gating mutation may show improvement of exocrine pancreatic function on ivacaftor. In this specific patient population this agent also seems to improve intestinal pH and reflux. The effect of these medications on other gastrointestinal outcomes, such as intestinal inflammation and cystic fibrosis liver disease, has not been described so far. Furthermore, the results of several trials suggest that probiotics might reduce intestinal inflammation. Finally, organoids might be used to predict in vitro the clinical effect of potentiators and modulators. ***SUMMARY***: The effect of new interventions on the gastrointestinal outcomes studied so far is favourable. Future studies should address the effect on other gastrointestinal parameters.

Hu, L., Peng, X., Chen, H., Yan, C., Liu, Y., Xu, Q., Fang, Z., Lin, Y., Xu, S., Feng, B., Li, J., Wu, and Che, L. Effects of intrauterine growth retardation and Bacillus subtilis PB6 supplementation on growth performance, intestinal development and immune function of piglets during the suckling period. Eur.J.Nutr. 2017; 56(4):1753-1765. PM:27188336¶

ABSTRACT: ***OBJECTIVES***: The aim of this study was to investigate the effects of intrauterine growth retardation (IUGR) and Bacillus subtilis PB6 supplementation in formula milk (FORM) on growth performance, intestinal development and immune function of neonates using a porcine model. ***METHODS***: Fourteen pairs of normal birth weight and IUGR piglets (7 days old) were randomly assigned to receive FORM or FORM supplemented with B. subtilis PB6 (FORM-BsPB6) for a period of 21 days. Blood samples, intestinal tissues and digesta were collected at necropsy and analysed for morphology, digestive enzyme activities, immune cell abundance, expression of genes associated with innate immunity and barrier function and microbial populations. ***RESULTS***: Regardless of diet, IUGR significantly decreased average daily dry matter intake and average daily weight gain ($P < 0.05$). Moreover, IUGR significantly decreased plasma concentrations of immunoglobulin A, interleukin 1beta, count and percentage of blood lymphocytes ($P < 0.05$). Meanwhile, IUGR markedly decreased villous height and maltase activity, as well as mRNA abundance of Toll-like receptor 9 and Toll-interacting protein in the ileum ($P < 0.05$). Regardless of body weight, FORM-BsPB6 markedly decreased the feed conversion ratio ($P < 0.05$), due to better intestinal development, as indicated by increased villous height ($P < 0.05$), activities of maltase and sucrase in the intestine ($P < 0.10$). Moreover, both mRNA and protein abundances of zonula occludens-1 and claudin-1 in the ileum as well as the copy number of Bacillus in colonic digesta were increased ($P < 0.05$) in piglets fed FORM-BsPB6 relative to FORM. ***CONCLUSION***: The results of this study indicate that IUGR delayed growth, intestinal development and immune function of piglets, while FORM-BsPB6 improved digestive capability and intestinal barrier function.

Hu, Y., Zhu, Y., and Lu, N. H. Novel and Effective Therapeutic Regimens for Helicobacter pylori in an Era of Increasing Antibiotic Resistance. Front Cell Infect.Microbiol. 2017; 7:168; PM: 28529929

ABSTRACT: Helicobacter pylori (H. pylori) is a common gastrointestinal bacterial strain closely associated with the incidence of chronic gastritis, peptic ulcers, gastric mucosa-associated lymphoid tissue lymphoma, and gastric cancer. A current research and

clinical challenge is the increased rate of antibiotic resistance in H. pylori, which has led to a decreased H. pylori eradication rate. In this article, we review recent H. pylori infection and reinfection rates and H. pylori resistance to antibiotics, and we discuss the pertinent treatments. A PubMed literature search was performed using the following keywords: Helicobacter pylori, infection, reinfection, antibiotic resistance, bismuth, proton pump inhibitors, vonoprazan, susceptibility, quintuple therapy, dual therapy, and probiotic. The prevalence of H. pylori has remained high in some areas despite the decreasing trend of H. pylori prevalence observed over time. Additionally, the H. pylori reinfection rate has varied in different countries due to socioeconomic and hygienic conditions. Helicobacter pylori monoresistance to clarithromycin, metronidazole or levofloxacin was common in most countries. However, the prevalence of amoxicillin and tetracycline resistance has remained low. Because H. pylori infection and reinfection present serious challenges and because H. pylori resistance to clarithromycin, metronidazole or levofloxacin remains high in most countries, the selection of an efficient regimen to eradicate H. pylori is critical. Currently, bismuth-containing quadruple therapies still achieve high eradication rates. Moreover, susceptibility-based therapies are alternatives because they may avoid the use of unnecessary antibiotics. Novel regimens, e.g., vonoprazan-containing triple therapies, quintuple therapies, high-dose dual therapies, and standard triple therapies with probiotics, require further studies concerning their efficiency and safety for treating H. pylori.

Huang, J. Y., Kao, C. Y., Liu, W. S., and Fang, T. J. Characterization of high exopolysaccharide-producing Lactobacillus strains isolated from mustard pickles for potential probiotic applications. Int.Microbiol. 2017; 20(2):75-84; PM: 28617525

ABSTRACT: The aim of this study was to characterize high exopolysaccharide (EPS)-producing lactic acid bacteria (LAB) isolated from mustard pickles in Taiwan for potential probiotic applications. Among 39 collected LAB strains, four most productive EPS-producing strains were selected for further analysis. Comparative analyses of 16S rDNA genes rpoA and pheS sequences demonstrated that these strains were members of Lactobacillus plantarum-group (LPG). NCD 2, NLD 4, SLC 13, and NLD 16 showed survival rates of 95.83% +/- 0.49%, 95.07% +/- 0.64%, 105.84% +/- 0.82%, and 99.65% +/- 0.31% under simulated gastrointestinal conditions, respectively. No cytotoxic effects on macrophage RAW 264.7 cells were observed when they were treated with a low dose (1 mug/ml) of stimulants extracted from the tested LAB strains. The production of nitric oxide in RAW 264.7 cells incubated with various LAB stimulants showed a dose-dependent increase. Among the four strains, SLC 13 showed higher inhibitory activity on growth of Enterococcus faecalis (BCRC 12302) and Yersinia enterocolitica (BCRC 10807). NLD 4 showed strong inhibitory activity against Escherichia coli O157:H7 (ATCC 43894) as compared with the other three strains. In summary, our results suggest that Lactobacillus pentosus SLC 13 may be a good candidate for probiotic applications and for development of antibacterial compounds. [Int Microbiol 20(2):75-84 (2017)].

Huang, Y., Zhang, M., Deng, Z., and Cao, L. Evaluation of Probiotic Diversity from Soybean (Glycine max) Seeds and Sprouts Using Illumina-Based Sequencing Method. Probiotics.Antimicrob.Proteins. 7-24-2017; PM: 28741152

ABSTRACT: There is increasing interest in the use of plant probiotics as environmental-friendly and healthy biofertilizers. The study aimed at selecting for novel probiotic candidates of soybean (Glycine max). The bacteriome and mycobiome of soybean

sprouts and seeds were analyzed by Illumina-based sequencing. Seeds contained more diverse bacteria than those in sprouts. The seeds contained similar fungal diversity with sprouts. Total 15 bacterial OTUs and 4 fungal OTUs were detected in seeds and sprouts simultaneously, suggesting that the sprouts contained bacterial and fungal taxa transmitted from seeds. The Halothiobacillus was the most dominant bacterial genus observed and coexisted in seeds and sprouts. The OTUs belonged to Ascomycota were the most dominant fungal taxa observed in seeds and sprouts. Halothiobacillus was firstly identified as endophytic probiotics of soybean. The results suggested that sprouts might contain diverse plant probiotics of mature plants and Illumina-based sequencing can be used to screen for probiotic candidates.

Huazano-Garcia, A., Shin, H., and Lopez, M. G. Modulation of Gut Microbiota of Overweight Mice by Agavins and Their Association with Body Weight Loss. Nutrients. 8-23-2017; 9(9); PM: 28832493

ABSTRACT: Agavins consumption has led to accelerated body weight loss in mice. We investigated the changes on cecal microbiota and short-chain fatty acids (SCFA) associated with body weight loss in overweight mice. Firstly, mice were fed with standard (ST5) or high-fat (HF5) diet for five weeks. Secondly, overweight mice were shifted to standard diet alone (HF-ST10) or supplemented with agavins (HF-ST + A10) or oligofructose (HF-ST + O10), for five more weeks. Cecal contents were collected before and after supplementation to determine microbiota and SCFA concentrations. At the end of first phase, HF5 mice showed a significant increase of body weight, which was associated with reduction of cecal microbiota diversity (PD whole tree; non-parametric t test, $p < 0.05$), increased Firmicutes/Bacteroidetes ratio and reduced SCFA concentrations (t test, $p < 0.05$). After diet shifting, HF-ST10 normalized its microbiota, increased its diversity, and SCFA levels, whereas agavins (HF-ST + A10) or oligofructose (HF-ST + O10) led to partial microbiota restoration, with normalization of the Firmicutes/Bacteroides ratio, as well as higher SCFA levels ($p < 0.1$). Moreover, agavins noticeably enriched Klebsiella and Citrobacter (LDA > 3.0); this enrichment has not been reported previously under a prebiotic treatment. In conclusion, agavins or oligofructose modulated cecal microbiota composition, reduced the extent of diversity, and increased SCFA. Furthermore, identification of bacteria enriched by agavins opens opportunities to explore new probiotics.

Hulshof, L., Van't, Land B., Sprikkelman, A. B., and Garssen, J. Role of Microbial Modulation in Management of Atopic Dermatitis in Children. Nutrients. 8-9-2017; 9(8); PM: 28792444

ABSTRACT: The pathophysiology of atopic dermatitis (AD) is multifactorial and is a complex interrelationship between skin barrier, genetic predisposition, immunologic development, skin microbiome, environmental, nutritional, pharmacological, and psychological factors. Several microbial modulations of the intestinal microbiome with pre- and/or probiotics have been used in AD management, with different clinical out-come (both positive, as well as null findings). This review provides an overview of the clinical evidence from trials in children from 2008 to 2017, aiming to evaluate the effect of dietary interventions with pre- and/or pro-biotics for the treatment of AD. By searching the PUBMED/MEDLINE, EMBADE, and COCHRANE databases 14 clinical studies were selected and included within this review. Data extraction was independently conducted by two authors. The primary outcome was an improvement in the clinical score of AD severity. Changes of serum immunological markers and/or gastrointestinal symptoms

were explored if available. In these studies some dietary interventions with pre- and/or pro-biotics were beneficial compared to control diets in the management of AD in children, next to treatment with emollients, and/or local corticosteroids. However, heterogeneity between studies was high, making it clear that focused clinical randomized controlled trials are needed to understand the potential role and underlying mechanism of dietary interventions in children with AD.

Hussain, M. B. Role of Honey in Topical and Systemic Bacterial Infections. J.Altern.Complement Med. 8-24-2017; PM: 28837361

ABSTRACT: ***BACKGROUND***: The development of bacterial resistance to antibiotics has made it more difficult and expensive to treat infections. Honey is getting worldwide attention as a topical therapeutic agent for wound infections and potential future candidate for systemic infections. ***OBJECTIVES***: The purpose of this review was to summarise different antibacterial bio-active compounds in honey, their synergistic interaction and their clinical implications in topical and systemic infections. In addition, contemporary testing methods for evaluating peroxide and non-peroxide antibacterial activity of honey were also critically appraised. ***DESIGN***: MEDLINE, EMBASE, Cochrane Library, Pub Med, reference lists and databases were used to review the literature. ***RESULTS***: Honey contains several unique antibacterial components. These components are believed to act on diverse bacterial targets, are broad spectrum, operate synergistically, prevent biofilm formation, and decrease production of virulence factors. Moreover, honey has the ability to block bacterial communication (quorum sensing), and therefore, it is unlikely that bacteria develop resistance against honey. Bacterial resistance against honey has not been documented so far. Unlike conventional antibiotics, honey only targets pathogenic bacteria without disturbing the growth of normal gastrointestinal flora when taken orally. It also contains prebiotics, probiotics, and zinc and enhances the growth of beneficial gut flora. The presence of such plethora of antibacterial properties in one product makes it a promising candidate not only in wound infections but also in systemic and particularly for gastrointestinal infections. Agar diffusion assay, being used for evaluating antibacterial activity of honey, is not the most appropriate and sensitive assay as it only detects non-peroxide activity when present at a higher level. Therefore, there is a need to develop more sensitive techniques that may be capable of detecting and evaluating different important components in honey as well as their synergistic interaction. ***CONCLUSIONS***: Keeping in view the current guidelines for treatment of diarrhea, honey is considered one of the potential candidates for treatment of diarrhea because it contains a natural combination of probiotics, prebiotics, and zinc. Therefore, it would be worthwhile if such a combination is tested in RCTs for treatment of diarrhea.

Hvas, C. L., Borre, M., and Fassov, J. L. [Nutrition and dietary supplement in chronic inflammatory bowel diesease]. Ugeskr.Laeger. 7-31-2017; 179(31); PM: 28869011

ABSTRACT: Nutrition and food items may improve or worsen symptoms in Crohn's disease and ulcerative colitis. Protein malnutrition and vitamin and mineral deficiencies are common, particularly deficiency of iron and vitamin D. Dietary fibres and omega-3 fatty acids are safe, but no evidence supports their use as treatment. The use of probiotics is not encouraged in patients with Crohn's disease, but it may maintain remission in ulcerative colitis. Curcumin, chamomile, and other herbal extracts are promising in the

treatment of mild ulcerative colitis, but validation of products and monitoring of side effects are insufficient.

Ibrahim, N. S., Ooi, F. K., Chen, C. K., and Muhamad, A. S. Effects of probiotics supplementation and circuit training on immune responses among sedentary young males. J.Sports Med.Phys.Fitness. 7-5-2017; PM: 28677946

ABSTRACT: ***BACKGROUND***: Growing evidence suggests that probiotics may have positive benefits on immune responses following endurance exercise. However, little attention has been given to its possible beneficial effects on immune responses following resistance exercise. ***METHODS***: Forty-one healthy sedentary males were recruited and randomised into four groups: sedentary control with placebo (C), probiotics (P), circuit training with placebo (Ex), and circuit training with probiotics (PEx) groups. Participants in the Ex and PEx groups performed a progressive load of circuit training at 3 times/week for 12 weeks. Each circuit comprised 10 exercises with work to rest ratio of 1:2. Participants consumed either multi-strain probiotics or placebo twice daily for 12 weeks. Body height and weight, blood pressure, resting heart rate, saliva and blood samples were collected at pre- and post-tests. ***RESULTS***: Saliva flow rate and salivary IgA, alpha- amylase, lactoferrin and lysozyme responses were not significantly different ($p>0.05$) between groups and also between pre- and post-test within each group. Similarly, total leukocytes, total lymphocytes, T lymphocytes, T-helper, T-cytotoxic, B lymphocytes, and natural killer cells counts were not significantly affected ($p>0.05$) by the probiotics and/or circuit training. However, circuit training significantly increased ($p<0.05$) immune cells count at post-test as compared to pre-test. Yet, a combination of circuit training and probiotics showed no significant ($p>0.05$) effects on immune cells count. ***CONCLUSION***: This study did not provide enough support for the positive effects of probiotics on immune responses among sedentary young males following resistance exercise. However, 12 weeks of circuit training enhanced immune cells count.

Igarashi, H., Ohno, K., Matsuki, N., Fujiwara-Igarashi, A., Kanemoto, H., Fukushima, K., Uchida, K., and Tsujimoto, H. Analysis of fecal short chain fatty acid concentration in miniature dachshunds with inflammatory colorectal polyps. J.Vet.Med.Sci. 9-4-2017; PM: 28867685

ABSTRACT: Short chain fatty acids (SCFAs) play an important role in the maintenance of colonic homeostasis, and their depletion has been reported in various gastrointestinal disorders. Inflammatory colorectal polyps (ICRPs) are a recently recognized disease specific to miniature dachshunds (MDs), and fecal dysbiosis with a reduction of SCFA-producing bacteria has been reported with this disease. Therefore, this study was performed based on the hypothesis that a reduced SCFA concentration associates with the development of ICRPs. We recruited 11 ICRP-affected MDs and 25 control MDs. Their fecal SCFA concentrations and bacterial proportions were quantified using high performance liquid chromatography and quantitative real-time PCR, respectively. The feces of ICRP-affected MDs contained lower amounts of propionic acid and lower proportions of Bifidobacterium than the feces of control MDs. Furthermore, fecal proportions of Bifidobacterium, Firmicutes and Lactobacillus exhibited significant positive correlations with fecal concentrations of total SCFAs and/or propionic acid; fecal Escherichia coli proportions correlated negatively with fecal concentrations of total SCFAs, as well as acetic, propionic and butyric acid. This result indicates an association between fecal dysbiosis and fecal SCFA concentrations; these phenomena may contribute to ICRP pathogenesis in MDs. Potential therapeutic targeting of the reduced

propionic acid concentration using probiotics, prebiotics or SCFA enemas merits further study.

Igarashi, M., Nakae, H., Matsuoka, T., Takahashi, S., Hisada, T., Tomita, J., and Koga, Y. Alteration in the gastric microbiota and its restoration by probiotics in patients with functional dyspepsia. BMJ Open.Gastroenterol. 2017; 4(1):e000144; PM: 28761692

ABSTRACT: ***OBJECTIVE***: The objective of this study was to comparatively analyse the gastric fluid (GF) microbiota between patients with functional dyspepsia (FD) and healthy controls (HC), and to assess the effect of probiotics on the microbiota. ***DESIGN***: Twenty-four Japanese patients with FD who met the Rome III definition and 21 age-matched and gender-matched HC volunteers were enrolled. The patients with FD had been treated with LG21, a probiotic strain. The GF was sampled after an overnight fast using a nasogastric tube. The bile acids concentration was determined by ELISA. The V3-V4 region of 16S rRNA gene was amplified using bacterial DNA from the GF, and then about 30 000 high-quality amplicons per sample were grouped into operational taxonomic units for analyses. ***RESULTS***: The ratio of GF samples in which the bile acids were detectable was significantly greater in the FD than in the HC groups. In the bacterial composition analysis at the phylum level, the GF microbiota had a Bacteroidetes > Proteobacteria abundance and an absence of Acidobacteria in the FD group, in contrast, the GF microbiota had a Bacteroidetes < Proteobacteria abundance and the presence of Acidobacteria in the HC group. Probiotic therapy in patients with FD shifted the composition of the GF microbiota to that observed in the HC volunteers. ***CONCLUSIONS***: Alteration in the GF microbiota was found in patients with FD compared with HC volunteers. Reflux of the small intestinal contents, including bile acid and intestinal bacteria, to the stomach was suggested to induce a bacterial composition change and be involved in the pathophysiology underlying FD. Probiotics appear effective in the treatment of FD through the normalisation of gastric microbiota. ***TRIAL REGISTRATION NUMBER***: UMINCTR 000022026; Results.

Ijiri, M., Fujiya, M., Konishi, H., Tanaka, H., Ueno, N., Kashima, S., Moriichi, K., Sasajima, J., Ikuta, K., and Okumura, T. Ferrichrome identified from Lactobacillus casei ATCC334 induces apoptosis through its iron-binding site in gastric cancer cells. Tumour.Biol. 2017; 39(6):1010428317711311; PM: 28639907

ABSTRACT: Ferrichrome is known to be a siderophore, but it was recently identified as a tumor-suppressive molecule derived from Lactobacillus casei ATCC334 (L. casei). In the present study, we investigated the effects of ferrichrome in gastric cancer cells. Cell lines and xenograft models treated with ferrichrome demonstrated growth suppression. The expression levels of cleaved poly (adenosine diphosphate-ribose) polymerase, and cleaved caspase-9 were increased by ferrichrome treatment. Although the tumor-suppressive effects of ferrichrome were almost completely diminished by the iron chelation, the reduction in the intracellular iron by ferrichrome did not correlate with its tumor-suppressive effects. An exhaustive docking simulation indicated that iron-free ferrichrome can make stable conformations with various mammalian molecules, including transporters and receptors. In conclusion, probiotic-derived ferrichrome induced apoptosis in gastric cancer cells. The iron binding site of ferrichrome is the structure responsible for its tumor suppressive function.

Ike, Y. Pathogenicity of Enterococci. Nihon Saikingaku Zasshi. 2017; 72(2):189-211; PM: 28659548

ABSTRACT: Enterococci belong to the group of lactic acid bacteria (LAB), and inhabit the gastrointestinal tracts of a wide variety of animals from insects and to human, and the commensal organism in humans and animals. The commensal/probiotic role of enterococci has evolved through thousands of years in mutual coexistence. Enterococcus have many favorable traits that have been appreciated in food fermentation and preservation, and many serve as probiotics to promote health. While lactobacillus have been shown to confer numerous benefits on and often regarded as health bringing organisms, enterococci have become more recognized as emerging human pathogens in recent years. Mac Callum and Hastings characterized an organism, now known to be Enterococcal faecalis, which was isolated from a lethal case of endocarditis on 1899. The report was the first detailed description of its pathogenic capabilities. Over the past few decades, multi-drug resistance enterococci have become as important health-care associated pathogen, and leading causes of drug resistance infection. The modern life style including the broad use of antibiotics in medical practice and animal husbandry have selected for the convergence of potential virulence factors to the specific enterococcus species such as E. faecium and E. faecalis. The development of modern medical care of intensive and invasive medical therapies and treatments for human disease, and existence of severe compromised patients in hospitals has contributed to the increased prevalence of these opportunistic organisms. The virulence factors converged in E. faecalis and E. faecium which have been isolated in nosocomial infections, include antibiotic resistance, extracellular proteins (toxins), extrachromosome and mobile genetic elements, cell wall components, biofilm formation, adherence factors, and colonization factor such as bacteriocin, etc. In these potential virulence factors, I presented characteristics of enterococcal conjugative plasmid, cytolysin, collagen binding protein of adhesion, bacteriocins, and drug resistances. I made reference to our original reports, and review books for this review. The review books are "Enterococci: from Commensals to Leading Causes of Drug Resistant Infection, NCBI Bookshelf. A service of the National Library of Medicine, National Institute of Health. Ed. by Michael S Gilmore, Don B Clewell, Yasuyoshi Ike, and Nathan Shankar", and "The Enterococci: Pathogenesis, Molecular Biology, and Antibiotic Resistance, Gilmore M., Clewell D., Courvadin P., Dunny G., Murray B., Rice L., (ed) 2002. ASM Press".

Indrio, F., Riezzo, G., Tafuri, S., Ficarella, M., Carlucci, B., Bisceglia, M., Polimeno, L., and Francavilla, R. Probiotic Supplementation in Preterm: Feeding Intolerance and Hospital Cost. Nutrients. 8-31-2017; 9(9); PM: 28858247

ABSTRACT: We hypothesized that giving the probiotic strain Lactobacillus reuteri (L. reuteri) DSM 17938 to preterm, formula-fed infants would prevent an early traumatic intestinal inflammatory insult modulating intestinal cytokine profile and reducing the onset of feeding intolerance. Newborn were randomly allocated during the first 48 h of life to receive either daily probiotic (10(8) colony forming units (CFUs) of L. reuteri DSM 17938) or placebo for one month. All the newborns underwent to gastric ultrasound for the measurement of gastric emptying time. Fecal samples were collected for the evaluation of fecal cytokines. Clinical data on feeding intolerance and weight gain were collected. The costs of hospital stays were calculated. The results showed that the newborns receiving L. reuteri DSM 17938 had a significant decrease in the number of days needed to reach full enteral feeding ($p < 0.01$), days of hospital stay ($p < 0.01$), and days of antibiotic treatment ($p < 0.01$). Statistically significant differences were observed in pattern of fecal cytokine profiles. The anti-inflammatory cytokine interleukin (IL)-10, was

increased in newborns receiving L. reuteri DSM 17938. Pro-inflammatory cytokines: IL-17, IL-8, and tumor necrosis factor (TNF)-alpha levels were increased in newborns given placebo. Differences in the gastric emptying and fasting antral area (FAA) were also observed. Our study demonstrates an effective role for L. reuteri DSM 17938 supplementation in preventing feeding intolerance and improving gut motor and immune function development in bottle-fed stable preterm newborns. Another benefit from the use of probiotics is the reducing cost for the Health Care service.

Ivanovska, T. P., Mladenovska, K., Zhivikj, Z., Pavlova, M. J., Gjurovski, I., Ristoski, T., and Petrushevska-Tozi, L. Synbiotic loaded chitosan-Ca-alginate microparticles reduces inflammation in the TNBS model of rat colitis. Int.J.Pharm. 7-15-2017; 527(1-2):126-134; PM: 28552770

ABSTRACT: New therapeutic strategies against inflammatory bowel disease (IBD) consider the usage of probiotics, prebiotics and synbiotics as beneficial for the intestinal microbial balance. Limitations of such an approach are addressed into difference in survival, persistence, colonization and variable effects among different probiotic strains, lack in understanding of probiotic mechanisms of action, as well the complex etiology of IBD. The anti-inflammatory activity of Lactobacillus casei 01 (L. casei 01) was assessed in trinitrobenzenesulphonic (TNBS) acid model of rat colitis when the probiotic was used alone and/or in combination with oligofructose-enriched inulin (Synergy 1), and as synbiotic (L. casei 01+Synergy 1) loaded chitosan-Ca-alginate microparticles; all suspended in ayran. The results from the probiotic/synbiotic treatments (8.5-8.9log CFU g-1L. casei 01 and 1.5% Synergy 1) have shown reduction in the colonic damage and increased lactobacilli counts in feces. Lactobacilli translocation to sterile extra-intestinal organs demonstrated acceptable safety of the probiotic strain used. The best effect at reducing inflammation and lesions associated with a significant decline in myeloperoxidase (MPO) activity was observed in rats that received synbiotic microparticles. This finding suggests colon targeted delivery of the probiotics/synbiotics, as an advantageous approach in prevention and treatment of IBD.

Jabr, F. Probiotics Are No Panacea. Sci.Am. 6-20-2017; 317(1):26-27; PM: 28632221

No Abstract Available.

Jadresin, O., Hojsak, I., Misak, Z., Kekez, A. J., Trbojevic, T., Ivkovic, L., and Kolacek, S. Lactobacillus reuteri DSM 17938 in the Treatment of Functional Abdominal Pain in Children: RCT Study. J.Pediatr.Gastroenterol.Nutr. 2017; 64(6):925-929; PM: 27906800

ABSTRACT: ***OBJECTIVES***: Beneficial therapeutic effect of probiotics has been reported in children with the irritable bowel syndrome (IBS) but not consistently in other functional abdominal pain-related disorders. The aim of the present study was to investigate the effect of Lactobacillus reuteri DSM 17938 in the treatment of functional abdominal pain (FAP) and IBS in children. ***METHODS***: Children (age 4-18 years) referred to pediatric gastroenterologist at Children's Hospital Zagreb from May 2012 to December 2014, diagnosed as FAP or IBS, were randomized to receive L reuteri DSM 17938 10(8) CFU daily or placebo. The study was a prospective, randomized, double-blind, placebo-controlled parallel study. Symptoms were evaluated using Wong-Baker FACES pain rating scale for pain and Bristol scale for stool shape and consistence. ***RESULTS***: Data were analyzed for

55 children (26 in the intervention group and 29 in the placebo group). Children in the intervention group had significantly more days without pain (median 89.5 vs 51 days, P = 0.029). Abdominal pain was less severe in children taking probiotics during the second month (P < 0.05) and fourth month (P < 0.01). The 2 groups did not differ in the duration of abdominal pain, stool type, or absence from school. Both groups experienced significant reduction in the severity of abdominal pain from first to fourth month, with the reduction more prominent in the intervention group (P < 0.001 vs P = 0.004). ***CONCLUSIONS***: Administration of L reuteri DSM 17938 was associated with a possible reduction of the intensity of pain and significantly more days without pain in children with FAP and IBS.

Jafarnejad, S., Djafarian, K., Fazeli, M. R., Yekaninejad, M. S., Rostamian, A., and Keshavarz, S. A. Effects of a Multispecies Probiotic Supplement on Bone Health in Osteopenic Postmenopausal Women: A Randomized, Double-blind, Controlled Trial. J.Am.Coll.Nutr. 6-19-2017; 1-10; PM: 28628374

ABSTRACT: ***OBJECTIVE***: The development of alternative approaches to prevent and/or treat osteoporosis, as a chronic progressive bone disease, is being considered currently. Among dietary supplements, probiotics may have favorable effects on bone metabolism. Therefore, the aim of this study was to evaluate the effects of a multispecies probiotic supplementation on bone biomarkers and bone density in osteopenic postmenopausal women. ***METHODS***: This randomized double-blind placebo-controlled clinical trial was performed on 50 patients with osteopenia aged 50-72 years. Participants were randomly assigned to take either a multispecies probiotic supplement (GeriLact; n = 25) or placebo (n = 25) for 6 months. GeriLact contains 7 probiotic bacteria species. Participants received 500 mg Ca plus 200 IU vitamin D daily. Bone mineral density (BMD) of lumbar spine and total hip and blood biomarkers including bone-specific alkaline phosphatase (BALP), osteocalcin (OC), collagen type 1 cross-linked C-telopeptide (CTX), deoxypyridinoline (DPD), parathyroid hormone (PTH), 25-OH vitamin D, and serum pro-inflammatory cytokines (tumor necrosis factor [TNF]-alpha and interleukin [IL]-1beta) were assessed at baseline and at the end of the study. ***RESULTS***: The multispecies probiotic significantly decreased BALP (p = 0.03) and CTX (p = 0.04) levels in comparison with the control group but had no effect on BMD of the spine and total hip. Moreover, there was a statistically significant decrease in serum PTH (p = 0.01) and TNF-alpha (p = 0.02) in the intervention group compared to the placebo group. ***CONCLUSIONS***: These results may suggest the favorable effects of the multispecies probiotic supplementation for 6 months on bone health in postmenopausal women due to slowing down the rate of bone turnover.

Jafarpour, D., Shekarforoush, S. S., Ghaisari, H. R., Nazifi, S., Sajedianfard, J., and Eskandari, M. H. Protective effects of synbiotic diets of Bacillus coagulans, Lactobacillus plantarum and inulin against acute cadmium toxicity in rats. BMC.Complement Altern.Med. 6-5-2017; 17(1):291; PM: 28583137

ABSTRACT: ***BACKGROUND***: Cadmium is a heavy metal that causes oxidative stress and has toxic effects in humans. The aim of this study was to investigate the influence of two probiotics along with a prebiotic in preventing the toxic effects of cadmium in rats. ***METHODS***: Twenty-four male Wistar rats were randomly divided into four groups namely control, cadmium only, cadmium along with Lactobacillus plantarum (1 x 109 CFU/day) and inulin (5% of feedstuff) and cadmium along with Bacillus coagulans (1 x 109 spore/day) and inulin (5% of feedstuff). Cadmium treated groups received 200

mug/rat/day CdCl2 administered by gavage. During the 42-day experimental period, they were weighed weekly. For evaluation of changes in oxidative stress, the levels of some biochemicals and enzymes of serum including SOD, GPX, MDA, AST, ALT, total bilirubin, BUN and creatinine, and also SOD level of livers were measured at day 21 and 42 of treatment. The cadmium content of kidney and liver was determined by using atomic absorption mass spectrophotometry. Data were analyzed using analysis of variance (ANOVA) followed by Duncan's post hoc test. ***RESULTS***: Treatment of cadmium induced rats with synbiotic diets significantly improved the liver enzymes and biochemical parameters that decreased AST, ALT, total bilirubin, BUN and metal accumulation in the liver and kidney and increased body weight, serum and liver SOD values in comparison with the cadmium-treated group. No significant differences were observed with MDA and GPX values between all groups ($p > 0.05$). ***CONCLUSIONS***: This study showed that synbiotic diets containing probiotics (L. plantarum and B. coagulans) in combination with the prebiotic (inulin) can reduce the level of cadmium in the liver and kidney, preventing their damage and recover antioxidant enzymes in acute cadmium poisoning in rat.

Jamshidparvar, A., Javandel, F., Seidavi, A., Pena, Blanco F., Martinez Marin, A. L., Aviles, Ramirez C., Aguera, Buendia E., and Nunez-Sanchez, N. Effects of golpar (Heracleum persicum Desf.) and probiotics in drinking water on performance, carcass characteristics, organ weights, blood plasma constituents, and immunity of broilers. Environ.Sci.Pollut.Res.Int. 8-29-2017; PM: 28852951

ABSTRACT: Increasing levels of Heracleum persicum (golpar) in drinking water were studied in broilers. Two hundred and forty-one-day-old male chickens were allocated to one of six treatments: control, without added phytogenics nor probiotics in drinking water, and probiotics at recommended manufacturer's level (P) or 1.0, 1.5, 2.0, and 2.5 ml/l of golpar extract solution (G1, G1.5, G2, and G2.5 treatments, respectively) in drinking water. As a result of this study, no linear or quadratic trends in the feed intake (FI) and feed conversion rate (FCR) due to golpar supplementation were found. Body weight gain, final body weight, and relative carcass weight showed a positive linear response with increasing levels of golpar supplementation. Neither golpar nor probiotics had effects on the percentages of edible parts of the carcass. Golpar supplementation levels caused a linear negative response of the albumin content in blood plasma, whereas both abdominal fat as percentage of carcass weight and uric acid levels in blood plasma linearly increased. The effects on Ig responses were only observed at 42 days of age and were similar in probiotics and the highest level of golpar supplementation. Based on our results, both probiotics and golpar supplementation could improve broiler performance and immune function.

Jang, S. E., Jeong, J. J., Choi, S. Y., Kim, H., Han, M. J., and Kim, D. H. Lactobacillus rhamnosus HN001 and Lactobacillus acidophilus La-14 Attenuate Gardnerella vaginalis-Infected Bacterial Vaginosis in Mice. Nutrients. 5-23-2017; 9(6); PM: 28545241

ABSTRACT: Oral administration of a probiotic mixture (PM; Respecta(R)) consisting of Lactobacillus rhamnosus HN001 (L1), Lactobacillus acidophilus La-14 (L2), and lactoferrin RCXTM results in colonization of these probiotics in the vagina of healthy women. Therefore, we examined whether vaginal colonization of the PM ingredients L1 and L2 could attenuate bacterial vaginosis (BV). BV was induced in mice via beta-estradiol-3-benzoate-induced immunosuppression and intravaginal inoculation with Gardnerella

vaginalis (GV). Inflammatory markers were analyzed using enzyme-linked immunosorbent assay, immunoblotting, quantitative polymerase chain reaction, and flow cytometry. Oral or intravaginal administration of PM resulted in colonization of L1 and L2 in the vagina. Oral or intravaginal administration of L1, L2, or PM significantly inhibited GV-induced epithelial cell disruption, myeloperoxidase activity, NF-kappaB activation, and IL-1beta and TNF-alpha expression ($p < 0.05$). Administration of these probiotics also inhibited IL-17 and RORgammat expression but increased IL-10 and Foxp3 expression. Of these probiotics, L2 most effectively attenuated GV-induced BV, followed by L1 and PM. Oral administration was more effective against GV-induced BV than intravaginal administration. L1 and L2 also significantly inhibited the adherence of GV to HeLa cells (a human cervical cancer cell line) and GV growth in vitro. In addition, L1 and L2 inhibited lipopolysaccharide-induced NF-kappaB activation in macrophages and the differentiation of splenocytes into Th17 cells in vitro, but increased their differentiation into Treg cells. Our study suggests that L1, L2, and PM attenuated GV-induced vaginosis by regulating both vaginal and systemic innate and adaptive immune responses rather than direct competition or killing of GV in the vagina.

Jenmalm, M. C. The mother-offspring dyad: microbial transmission, immune interactions and allergy development. J.Intern.Med. 7-20-2017; PM: 28727206

ABSTRACT: The increasing prevalence of allergy in affluent countries may be caused by reduced intensity and diversity of microbial stimulation, resulting in abnormal postnatal immune maturation. Most studies investigating the underlying immunomodulatory mechanisms have focused on postnatal microbial exposure, for example demonstrating that the gut microbiota differs in composition and diversity during the first months of life in children who later do or do not develop allergic disease. However, it is also becoming increasingly evident that the maternal microbial environment during pregnancy is important in childhood immune programming, and the first microbial encounters may occur already in utero. During pregnancy, there is a close immunological interaction between the mother and her offspring, which provides important opportunities for the maternal microbial environment to influence the immune development of the child. In support of this theory, combined pre- and postnatal supplementations seem to be crucial for the preventive effect of probiotics on infant eczema. Here, the influence of microbial and immune interactions within the mother-offspring dyad on childhood allergy development will be discussed. In addition, how perinatal transmission of microbes and immunomodulatory factors from mother to offspring may shape appropriate immune maturation during infancy and beyond, potentially via epigenetic mechanisms, will be examined. Deeper understanding of these interactions between the maternal and offspring microbiome and immunity is needed to identify efficacious preventive measures to combat the allergy epidemic.

Jiang, Y., Ye, L., Cui, Y., Yang, G., Yang, W., Wang, J., Hu, J., Gu, W., Shi, C., Huang, H., and Wang, C. Effects of Lactobacillus rhamnosus GG on the maturation and differentiation of dendritic cells in rotavirus-infected mice. Benef.Microbes. 8-24-2017; 8(4):645-656; PM: 28670908

ABSTRACT: Rotavirus-related diarrhoea is considered one of the most important diseases in field animal production. In addition to the classic vaccine strategy, a number of studies have utilised probiotics, such as Lactobacillus rhamnosus GG (LGG), to prevent rotavirus-induced diarrhoea. Although it has been partially revealed that Toll-like

receptors (TLRs) are involved in the LGG-mediated protection against rotavirus infection, the details of the underlying immunologic mechanisms remain largely unknown. In this study, three-to-four-week-old female BALB/c mice were divided into three groups and orally administered phosphate buffered saline (PBS), PBS plus rotavirus or LGG plus rotavirus, respectively. The differentiation and maturation of dendritic cells (DCs) were then determined by FACS, the expression levels of TLR-3 and nuclear factor kappa beta (NF-kappaB) were evaluated using real time PCR, and the production of inflammatory cytokines in mesenteric lymph nodes (MLNs) were determined by ELISA. The results demonstrated that rotavirus infection significantly increased the percentage of CD11c+CD11b+CD8a- DCs and decreased the percentage of CD11c+CD11b-CD8a+ DCs in MLNs. By contrast, the presence of LGG significantly decreased the percentage of CD11c+CD11b+CD8a- DCs and increased the percentage of CD11c+CD11b-CD8a+ DCs, which indicates that the differentiation of DCs is involved in the protective effects of LGG. Rotavirus infection also resulted in the increased expression of surface markers such as CD40, CD80 and MHC-II in DCs, and the administration of LGG significantly increased the expression level further. The mRNA levels of TLR-3 and NF-kappaB in the intestine and MLNs were also significantly increased in the presence of rotavirus, which was further increased in the presence of LGG. The production of inflammatory cytokines was also determined, and the results showed that rotavirus caused the increased production of interleukin (IL)-12 and tumour necrosis factor alpha; this effect was further enhanced by LGG. Meanwhile, although rotavirus infection led to the increased production of IL-6 and IL-10, the presence of LGG significantly decreased the mRNA levels of these cytokines. By contrast, rotavirus infection resulted in the decreased production of interferon gamma (IFN-gamma), and the administration of LGG significantly increased the levels of IFN-gamma. Taken together, the protective effects of LGG were partially due to the modulation of the differentiation and maturation of DCs, the increased production of TLR-3 and NF-kappaB, and the modulation of inflammatory cytokines.

Kaktcham, P. M., Temgoua, J. B., Zambou, F. N., az-Ruiz, G., Wacher, C., and Perez-Chabela, M. L. In Vitro Evaluation of the Probiotic and Safety Properties of Bacteriocinogenic and Non-Bacteriocinogenic Lactic Acid Bacteria from the Intestines of Nile Tilapia and Common Carp for Their Use as Probiotics in Aquaculture. Probiotics.Antimicrob.Proteins. 7-27-2017; PM: 28752423

ABSTRACT: In this study, seven bacteriocinogenic and non-bacteriocinogenic LAB strains previously isolated from the intestines of Nile tilapia and common carp and that showed potent antibacterial activity against host-derived and non-host-derived fish pathogens were assayed for their probiotic and safety properties so as to select promising candidates for in vivo application as probiotic in aquaculture. All the strains were investigated for acid and bile tolerances, transit tolerance in simulated gastrointestinal conditions, for cell surface characteristics including hydrophobicity, co-aggregation and auto-aggregation, and for bile salt hydrolase activity. Moreover, haemolytic, gelatinase and biogenic amine-producing abilities were investigated for safety assessment. The strains were found to be tolerant at low pH (two strains at pH 2.0 and all the strains at pH 3.0). All of them could also survive in the presence of bile salts (0.3% oxgall) and in simulated gastric and intestinal juices conditions. Besides, three of them were found to harbour the gtf gene involved in pH and bile salt survival. The strains also showed remarkable cell surface characteristics, and 57.14% exhibited the ability to deconjugate bile salts. When assayed for their safety properties, the strains prove to be free from haemolytic activity, gelatinase activity and they could neither produce biogenic amines nor harbour the hdc gene. They did not also show antibiotic resistance, thus confirming

to be safe for application as probiotics. Among them, Lactobacillus brevis 1BT and Lactobacillus plantarum 1KMT exhibited the best probiotic potentials, making them the most promising candidates.

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., Cai, Y., Zhang, X., Kong, X., and Su, J. Altered gut microbiota in RA: implications for treatment. Z.Rheumatol. 2017; 76(5):451-457; PM: 27909795

ABSTRACT: Rheumatoid arthritis (RA) is an autoimmune disease with progressive joint disorder. The complex interplay of genetic and environmental influences is important for the development of the disease. A growing body of evidence has shed light on the association of dysbiosis of gut microbiota with RA. Certain gut microbial strains have been shown to inhibit or attenuate immune responses in RA experimental models, suggesting that specific species among intestinal commensal bacteria may play either a pathogenic or a protective role in the development of RA. Oral intake of probiotics/prebiotics can therefore represent a therapeutic approach for RA treatment. However, the relevant scientific work has only just begun, and the available data in this field remain limited. Fortunately, utilization of new sequencing technologies allows expanded research on the association of intestinal bacterial flora and human diseases to be attempted. In this review, we summarize the role of gut microbiota in RA progression and address how specific bacterial strains regulate the immune response in disease process. Probiotics/prebiotics in the treatment of RA is also discussed.

Kang, Y. and Cai, Y. Future prospect of faecal microbiota transplantation as a potential therapy in asthma. Allergol.Immunopathol.(Madr.). 8-10-2017; PM: 28803667

ABSTRACT: There is convincing evidence from both human and animal studies suggesting that the gut microbiota plays an important role in regulating immune responses associated with the development of asthma. Certain intestinal microbial strains have been demonstrated to suppress or impair immune responsiveness in asthma experimental models, suggesting that specific species among gut commensal microbiota may play either a morbific or phylactic role in the progression of asthma. Evidence to date suggests that the intestinal microbiota represent fertile targets for prevention or management of asthma. The faecal microbiota transplantation (FMT) is a rather straightforward therapy that manipulates the human gastrointestinal (GI) microbiota, by which a healthy donor microbiota is transferred into an existing but disturbed microbial ecosystem. The FMT may therefore represent a therapeutic approach for asthma treatment in the foreseeable future. At present, FMT therapy for asthma is very limited and should be actively studied. Considerable efforts are needed to increase our knowledge in the field of FMT therapy for asthma. In this review, we aimed to provide several insights into the development of FMT therapy for asthma.

Kanmani, P., Albarracin, L., Kobayashi, H., Iida, H., Komatsu, R., Humayun Kober, A. K. M., Ikeda-Ohtsubo, W., Suda, Y., Aso, H., Makino, S., Kano, H., Saito, T., Villena, J., and Kitazawa, H. Exopolysaccharides from Lactobacillus delbrueckii OLL1073R-1 modulate innate antiviral immune response in porcine intestinal epithelial cells. Mol.Immunol. 8-8-2017; PM: 28800975

ABSTRACT: Previous studies demonstrated that the extracellular polysaccharides (EPSs) produced by Lactobacillus delbrueckii OLL1073R-1 (LDR-1) improve antiviral immunity, especially in the systemic and respiratory compartments. However, it was not studied before whether those EPSs are able to beneficially modulate intestinal antiviral immunity. In addition, LDR-1-host interaction has been evaluated mainly with immune cells while its interaction with intestinal epithelial cells (IECs) was not addressed before. In this work, we investigated the capacity of EPSs from LDR-1 to modulate the response of porcine IECs (PIE cells) to the stimulation with the Toll-like receptor (TLR)-3 agonist poly(I:C) and the role of TLR2, TLR4, and TLR negative regulators in the immunoregulatory effect. We showed that innate immune response triggered by TLR3 activation in porcine IECs was differentially modulated by EPS from LDR-1. EPSs treatment induced an increment in the expression of interferon (IFN)-alpha and IFN-beta in PIE cells after the stimulation with poly(I:C) as well as the expression of the antiviral factors MxA and RNase L. Those effects were related to the reduced expression of A20 in EPS-treated PIE cells. EPS from LDR-1 was also able to reduce the expression of IL-6 and proinflammatory chemokines. Although further in vivo studies are needed, our results suggest that these EPSs or a yogurt fermented with LDR-1 have potential to improve intestinal innate antiviral response and protect against intestinal viruses.

Karacaer, F., Hamed, I., Ozogul, F., Glew, R. H., and Ozcengiz, D. The function of probiotics on the treatment of ventilator-associated pneumonia (VAP): facts and gaps. J.Med.Microbiol. 2017; 66(9):1275-1285; PM: 28855004

ABSTRACT: Probiotics have been used for centuries in making fermented dairy products. The health benefits related to probiotics consumption are well recognized and they are generally regarded as safe (GRAS). Their therapeutic effects are due to the production of a variety of antimicrobial compounds, such as short-chain fatty acids, organic acids (such as lactic, acetic, formic, propionic and butyric acids), ethanol, hydrogen peroxide and bacteriocins. Ventilator-associated pneumonia (VAP) is a nosocomial infection associated with high mortality in intensive care units. VAP can result from endotracheal intubation and mechanical ventilation. These interventions increase the risk of infection as patients lose the natural barrier between the oropharynx and the trachea, which in turn facilitates the entry of pathogens through the aspiration of oropharyngeal secretions containing bacteria into the lung. In order to prevent this, probiotics have been used extensively against VAP. This review is an update containing information extracted from recent studies on the use of probiotics to treat VAP. In addition, probiotic safety, the therapeutic properties of probiotics, the probiotic strains used and the action of the probiotics mechanism are reviewed. Furthermore, the therapeutic effects of probiotic treatment procedures for VAP are compared to those of antibiotics. Finally, the influences of bacteriocin on the growth of human pathogens, and the side-effects and limitations of using probiotics for the treatment of VAP are addressed.

Karimi, G., Jamaluddin, R., Mohtarrudin, N., Ahmad, Z., Khazaai, H., and Parvaneh, M. Single-species versus dual-species probiotic supplementation as an emerging therapeutic strategy for obesity. Nutr.Metab Cardiovasc.Dis. 7-8-2017; PM: 28821417

ABSTRACT: ***BACKGROUND AND AIM***: Recent studies have reported beneficial effects of specific probiotics on obesity. However, the difference in the anti-obesity effects of probiotics as single species and dual species is still uncertain. Therefore, we aimed to compare the efficacy of single and dual species of bacteria on markers of obesity in high-fat diet-induced obese rats. ***METHODS AND RESULTS***: A total of 40 male Sprague-Dawley rats were assigned to one of five groups of varying diets as follows: standard diet, high fat diet (HFD), HFD supplemented with Lactobacillus casei strain Shirota, HFD supplemented with Bifidobacterium longum and HFD supplemented with a mixture of these two bacterial species. After 15 weeks of supplementation, the animals were examined for changes in body weight, body fat, total count of bacteria in fecal, blood serum lipid profile, leptin, adiponectin and inflammatory biomarkers. Histological analysis of the liver and adipose tissue was performed and the hepatic mRNA expression levels of genes related to lipid metabolism were measured. It was found that probiotic supplementation of either B. longum or a mixture of B. longum and LcS bacteria significantly reduced weight and triglycerides in the HFD groups. Supplementation of B. longum bacteria showed better results in terms of modulating leptin level, fat mass, adipocyte size and lipoprotein lipase expression, as well as increasing adiponectin and peroxisome proliferator-activated receptors-gamma expression compared to dual species of bacteria. No significant differences were observed in the total count of fecal bacteria, glucose and inflammatory biomarker levels between supplemented groups. ***CONCLUSIONS***: B. longum supplementation in obesity was more beneficial in metabolic profile changes than the mixture species.

Katoh, N. THE BRIEF COMMENTARY ON GUIDELINES FOR THE MANAGEMENT OF ATOPIC DERMATITIS 2015 - FORCUSING ON THE BIOMARKER AND SKIN CARE. Arerugi. 2017; 66(8):991-994; PM: 28904286

No Abstract Available.

Kaur, G., Ali, S. A., Kumar, S., Mohanty, A. K., and Behare, P. Label-free quantitative proteomic analysis of Lactobacillus fermentum NCDC 400 during bile salt exposure. J.Proteomics. 9-7-2017; 167:36-45; PM: 28802582

ABSTRACT: Lactobacillus fermentum NCDC 400 is a commonly used and a comprehensively studied probiotic organism. The distinctive capability to endure the harsh environment of the gastrointestinal tract owing to the presence of bile salts in gastric juice facilitates gut microbiota, especially the probiotic organisms to transiently inhabit the host gut. In the present study, Label-Free Quantification (LFQ) approach has been employed to analyze the expression pattern of Lactobacillus fermentum NCDC 400 strain proteins, under bile acid stress, using high-resolution mass spectrometer connected to nano-liquid chromatography (LC) system. We report the identification of a total of 538 differentially expressed (DE) proteins in response to 1.2% bile salt which is required for the growth of this bacterium. Among the DE proteins, 80 were found to be up-regulated, with greater than 1.3 fold change vis-a-vis 107 proteins which were down-regulated with <0.76 fold change ($p<0.05$). The functions of down-regulated proteins were largely unknown nevertheless; the putative functions of the up-regulated proteins were categorized into

categories viz. stress response, DNA repair, peptidoglycan biosynthesis, amino acids metabolism, signal transduction, transcription, translation, and carbohydrate metabolism. These results suggest that the differentially expressed proteins provide the tolerance towards the various gastrointestinal challenges and involved in bile acid stress response mechanism.

Kaur, M., Singh, H., Jangra, M., Kaur, L., Jaswal, P., Dureja, C., Nandanwar, H., Chaudhuri, S. R., Raje, M., Mishra, S., and Pinnaka, A. K. Lactic acid bacteria isolated from yak milk show probiotic potential. Appl.Microbiol.Biotechnol. 9-6-2017; PM: 28879447

ABSTRACT: Probiotic industries strive for new, efficient and promising probiotic strains that impart a positive impact on consumer health. Challenges are persisting in isolation, screening, and selection of the new indigenous probiotic strains. In the present research, we explored the probiotic potential of 17 lactic acid bacteria isolated from Yak milk in a series of in vitro tests. We also demonstrated their health benefits, i.e., cholesterol degradation, lactose digestion, antimicrobial activity, antioxidant, and anticancer activities. Principal component analysis revealed that more than 50% of the strains fulfilled the examined criteria, e.g., survival in acidic pH, bile concentrations, and adherent property. Approximately all the strains produced antimicrobial substances against the maximum number of tested strains including clinical strains. Most strains degraded cholesterol in comparison to the reference probiotic strain whereas strain Yc showed 1.5 times higher the degradation efficiency of the control strain. Lan4 strain exhibited remarkable anticancer activity and induced the maximum apoptosis (87%) in the Hela cells and was non-toxic to the non-cancerous HEK293 cells. Around ten strains showed positive lactose digestion. Overall, this can be concluded that selected lactic acid bacteria revealed excellent probiotic properties along with desirable health benefits. These strains need to be further investigated in details for their application in the development of novel probiotic preparations for the improvement of public health.

Kaye, E. K. Daily Intake of Probiotic Lactobacilli May Reduce Caries Risk in Young Children. J.Evid.Based.Dent.Pract. 2017; 17(3):284-286; PM: 28865830

ABSTRACT: ***ARTICLE TITLE AND BIBLIOGRAPHIC INFORMATION***: Probiotic compared with standard milk for high-caries children: A cluster randomized trial. Rodriguez G, Ruiz B, Faleiros S, Vistoso A, Marro ML, Sanchez J, Urzua I, Cabello R. J Dent Res 2016;95(4):402-7. ***SOURCE OF FUNDING***: Chilean Government (CONICYT FONIS SA11I2035) ***TYPE OF STUDY/DESIGN***: Cluster randomized controlled trial.

Kelly, C. and Salinas, I. Under Pressure: Interactions between Commensal Microbiota and the Teleost Immune System. Front Immunol. 2017; 8:559; PM: 28555138

ABSTRACT: Commensal microorganisms inhabit every mucosal surface of teleost fish. At these surfaces, microorganisms directly and indirectly shape the teleost immune system. This review provides a comprehensive overview of how the microbiota and microbiota-derived products influence both the mucosal and systemic immune system of fish. The cross talk between the microbiota and the teleost immune system shifts significantly under stress or disease scenarios rendering commensals into opportunists or pathogens. Lessons learnt from germ-free fish models as well as from oral administration of live probiotics to fish highlight the vast impact that microbiota have on immune development, antibody production, mucosal homeostasis, and resistance to stress.

Future studies should dissect the specific mechanisms by which different members of the fish microbiota and the metabolites they produce interact with pathogens, with other commensals, and with the teleost immune system.

Khan, A. Z., Kumbhar, S., Liu, Y., Hamid, M., Pan, C., Nido, S. A., Parveen, F., and Huang, K. Dietary Supplementation of Selenium-Enriched Probiotics Enhances Meat Quality of Broiler Chickens (Gallus gallus domesticus) Raised Under High Ambient Temperature. Biol.Trace Elem.Res. 7-12-2017; PM: 28702872

ABSTRACT: We investigated the effects of selenium-enriched probiotics (SP) on broiler meat quality under high ambient temperature and explore their underlying mechanisms. A total of 200 1-day-old male broiler chicks (Ross 308) were randomly allotted to four treatment groups, each with five replicates, in groups of ten birds. These birds were fed a corn-soybean basal diet (C), a basal diet plus probiotics supplementation (P), a basal diet plus Se supplementation in the form of sodium selenite (SS, 0.30 mg Se/kg), and a basal diet with the addition of selenium-enriched probiotics (SP, 0.30 mg Se/kg). The experiment lasted for 42 days. The birds were sacrificed by cervical dislocation, and the breast muscles were removed for further process. Our results showed that SP diet significantly increased ($p < 0.05$) the physical (pH, colors, water holding capacity, drip loss, shear force) and sensory characteristics of breast meat. All P, SS, and SP supplementation enhanced the antioxidant system by increasing ($p < 0.05$) the Se concentrations, glutathione (GSH) levels, activities of glutathione peroxidase (GSH-Px), and superoxide dismutase (SOD) whereas decreasing ($p < 0.05$) malondialdehyde (MDA) levels, with SP being higher than P and SS. Moreover, SP diet significantly upregulated ($p < 0.05$) the mRNA levels of glutathione peroxidase genes (GPx1, GPx4) while it downregulated heat stress biomarkers such as heat shock protein (HSP) 70 as compared to C, P, and SS diets. In conclusion, our findings suggest that SP may function as beneficial nutritive supplement that is capable of improving meat quality during the summer season.

Khan, M. N., Lin, H., Li, M., Wang, J., Mirani, Z. A., Khan, S. I., Buzdar, M. A., Ali, I., and Jamil, K. Identification and growth optimization of a Marine Bacillus DK1-SA11 having potential of producing broad spectrum antimicrobial compounds. Pak.J.Pharm.Sci. 2017; 30(3):839-853; PM: 28653930

ABSTRACT: Control of harmful bacteria in food, aquaculture, pharmaceuticals, agriculture, hospitals and recreation water pools are of great global concern. Marine bacteria are an enormous source of bio-controlling agents. The aim of this study was to identify and optimize the growth conditions including effect of different biotic and abiotic factors on antimicrobial activity of strain DK1-SA11 isolated from Qingdao Bay of China Yellow Sea. Microscopic characterization, API(R) 20E and 50 CHB kit base carbohydrates utilization, 16S rDNA and DNA gyrB gene sequencing studies identified the bacterium as Bacillus subtilis subsp. spizizenii DK1-SA11. Antimicrobial spectrum of cell free supernatant (CFS) has shown antimicrobial activities against all test strains including methicillin-resistant Staphylococcus aureus, E. coli O157:H7, Candida albicans, Klebsiella pneumoniae, Listeria monocytogenes, Vibrio parahaemolyticus, E. coli, Pseudomonas fluorescens, Salmonella typhimurium and Vibrio cholerae. Among all the media tested, Marine Broth 2216 was found to be the best medium for bacterial growth and production of antibacterial compounds. The other optimum conditions for growth were pH:7 and incubation temperature: 25 degrees C with < 180 rpm for 60-72 h. Out of 49 different

carbohydrates tested, D-mannose increases the antibacterial activity by 33.3% while D-arabitol decreases it by 44.4%. Crude CFS showed activity even after three months of storage below -20 degrees C and boiling for 10 min, whereas it loses 100% of its antimicrobial activity after enzymatic treatments of lipase, trypsin and papain. The production of antimicrobial compounds and broad spectrum of antimicrobial activity against all tested pathogens suggested that the strain DK1-SA11 can be used as a source for probiotics, synbiotics and antibiotics.

Khanna, S. and Raffals, L. E. The Microbiome in Crohn's Disease: Role in Pathogenesis and Role of Microbiome Replacement Therapies. Gastroenterol.Clin.North Am. 2017; 46(3):481-492; PM: 28838410

ABSTRACT: Individuals with a genetic predisposition to Crohn's disease develop aberrant immune responses to environmental triggers. The gastrointestinal microbiota is increasingly recognized to play an important role in the development of Crohn's disease. Decrease in global gut microbial diversity and specific bacterial alterations have been implicated in Crohn's disease. Advances in sequencing techniques and bioinformatics and correlation with host genetics continue to improve insight into the structure and function of the microbial community and interactions with the host immune system. This article summarizes the existing literature on the role of the gut microbiome and its manipulation in the development and management of Crohn's disease.

Khardziani, T., Kachlishvili, E., Sokhadze, K., Elisashvili, V., Weeks, R., Chikindas, M. L., and Chistyakov, V. Elucidation of Bacillus subtilis KATMIRA 1933 Potential for Spore Production in Submerged Fermentation of Plant Raw Materials. Probiotics.Antimicrob.Proteins. 7-10-2017; PM: 28695539

ABSTRACT: In this study, the effects of several key factors to increase spore production by Bacillus subtilis subsp. KATMIRA 1933 were evaluated in shake flask experiments. In a synthetic medium, glucose concentration played a crucial role in the expression of bacilli sporulation capacity. In particular, maximum spore yield (2.3 x 109 spores/mL) was achieved at low glucose concentration (2 g/L), and further gradual increase of the carbon source content in the medium caused a decrease in sporulation capacity. Substitution of glucose with several inexpensive lignocellulosic materials was found to be a reasonable way to achieve high cell density and sporulation. Of the materials tested, milled mandarin peels at a concentration of 40 g/L served as the best growth substrate. In these conditions, bacilli secreted sufficient levels of glycosyl hydrolases, providing slow hydrolysis of the mandarin peel's polysaccharides to metabolizable sugars, providing the bacterial culture with an adequate carbon and energy source. Among nitrogen sources tested, peptone was found to favor spore production. Moreover, it was shown that cheese and cottage cheese whey usage, instead of distilled water, significantly increases spore formation. After optimization of the nutrient medium in the shake flask experiments, the technical feasibility of large-scale spore production by B. subtilis KATMIRA 1933 was confirmed in a laboratory fermenter. The spore yield (7 x 1010 spores/mL) obtained using a bioreactor was higher than those previously reported.

Khoroushi, M. and Kachuie, M. Prevention and Treatment of White Spot Lesions in Orthodontic Patients. Contemp.Clin.Dent. 2017; 8(1):11-19; PM: 28566845

ABSTRACT: Decalcification of enamel, appearing as white spot lesions (WSLs), around

fixed orthodontic appliances is a major challenge during and after fixed orthodontic treatment by considering the fact that the goal of orthodontic treatment is to enhance facial and dental esthetic appearance. Banded or bonded teeth exhibit a significantly higher rate of WSLs compared to the controls with no braces as fixed appliances and the bonding materials promote retention of biofilms. These lesions are managed in the first step by establishing good oral hygiene habits and prophylaxis with topical fluorides, including high-fluoride toothpastes, fluoride mouthwashes, gels, varnishes, fluoride-containing bonding materials, and elastic ligatures. Recently, other materials and methods have been recommended, including the application of casein phosphopeptides-amorphous calcium phosphate, antiseptics, probiotics, polyols, sealants, laser, tooth bleaching agents, resin infiltration, and microabrasion. This article reviews the currently used methods to manage enamel demineralization during and after orthodontic treatment and the risk factors and preventive measures based on the latest evidence.

Kim, D. G., Lee, M. R., Yoo, J. M., Park, K. I., and Ma, J. Y. Fermented herbal formula KIOM-MA-128 protects against acute colitis induced by dextran sodium sulfate in mice. BMC.Complement Altern.Med. 7-5-2017; 17(1):354; PM: 28679372

ABSTRACT: ***BACKGROUND***: Colitis is a well-known subtype of inflammatory bowel disease and is caused by diverse factors. Previous research has shown that KIOM-MA elicits anti-inflammatory and anti-allergic effects on various diseases. KIOM-MA-128, our novel herbal formula, was generated from KIOM-MA using probiotics to improve the therapeutic efficacy. We investigated whether KIOM-MA-128 has protective activity in a mouse model of acute colitis induced by dextran sodium sulfate (DSS). ***METHODS***: Colitis was induced by DSS administered to ICR mice in drinking water. KIOM-MA-128 (125 or 250 mg/kg) was orally administered once per day. The body weights of the mice were measured daily, and colonic endoscopies were performed at 5 and 8 days. Colon length as well as histological and cytokine changes were observed at the end of drug administration. ***RESULTS***: KIOM-MA-128 has pharmacological activity in an acute colitis model. KIOM-MA-128 reduced the loss of body weight and disease activity index (DAI) and inhibited the abnormally short colon lengths and the colonic damage in this mouse model of acute colitis. Moreover, KIOM-MA-128 suppressed pro-inflammatory cytokine expression and maintained the integrity of the tight junctions during DSS-induced colitis. ***CONCLUSION***: The results indicated that KIOM-MA-128 protects against DSS-induced colitis in mice and suggested that this formula might be a candidate treatment for inflammatory bowel disease (IBD).

Klompas, M. What is new in the prevention of nosocomial pneumonia in the ICU? Curr.Opin.Crit Care. 2017; 23(5):378-384; PM: 28759469

ABSTRACT: ***PURPOSE OF REVIEW***: To summarize and contextualize recent evidence on preventing ventilator-associated pneumonia (VAP). ***RECENT FINDINGS***: Many centers continue to report dramatic decreases in VAP rates after implementing ventilator bundles. Interpreting these reports is complicated, however, by the subjectivity and lack of specificity of VAP definitions. More objective data suggest VAP rates may not have meaningfully changed over the past decade. If so, this compels us to re-examine and revise the prevention bundles we have been using to prevent VAP. New analyses suggest that most hospitals' ventilator bundles include a mix of helpful and potentially harmful elements. Spontaneous awakening trials, spontaneous breathing trials, head-of-

bed elevation, and thromboprophylaxis appear beneficial. Oral chlorhexidine and stress ulcer prophylaxis may be harmful. Subglottic secretion drainage, probiotics, and novel endotracheal cuff designs do not clearly improve objective outcomes. Selective digestive decontamination by contrast appears to lower VAP and mortality rates. Effective implementation is as important as choosing the right bundle components. Best practices include engaging and educating staff, creating structures that facilitate bundle adherence, and providing regular feedback on process measure performance and outcome rates. ***SUMMARY***: VAP rates may still be elevated despite multiple reports to the contrary. Recent evidence suggests new ways to optimize the selection of ventilator bundle components and their implementation.

Klopper, K. B., Deane, S. M., and Dicks, L. M. T. Aciduric Strains of Lactobacillus reuteri and Lactobacillus rhamnosus, Isolated from Human Feces, Have Strong Adhesion and Aggregation Properties. Probiotics.Antimicrob.Proteins. 7-29-2017; PM: 28756502

ABSTRACT: Human feces were streaked onto MRS Agar adjusted to pH 2.5, 3.0, and 6.4, respectively, and medium supplemented with 1.0% (w/v) bile salts. Two aciduric strains, identified as Lactobacillus reuteri HFI-LD5 and Lactobacillus rhamnosus HFI-K2 (based on 16S rDNA and recA sequences), were non-hemolytic and did not hydrolyze mucin. The surface of Lactobacillus reuteri HFI-LD5 cells has a weak negative charge, whereas Lactobacillus rhamnosus HFI-K2 has acidic and basic properties, and produces exopolysaccharides (EPS). None of the strains produce bacteriocins. Both strains are resistant to several antibiotics, including sulfamethoxazole-trimethoprim and sulphonamides. The ability of Lactobacillus reuteri HFI-LD5 and Lactobacillus rhamnosus HFI-K2 to grow at pH 2.5 suggests that they will survive passage through the stomach. EPS production may assist in binding to intestinal mucus, especially in the small intestinal tract, protect epithelial cells, and stimulate the immune system. Lactobacillus reuteri HFI-LD5 and Lactobacillus rhamnosus HFI-K2 may be used as probiotics, especially in the treatment of small intestinal bacterial overgrowth (SIBO).

Kobierecka, P. A., Wyszynska, A. K., eksandrzak-Piekarczyk, T., Kuczkowski, M., Tuzimek, A., Piotrowska, W., Gorecki, A., Adamska, I., Wieliczko, A., Bardowski, J., and Jagusztyn-Krynicka, E. K. In vitro characteristics of Lactobacillus spp. strains isolated from the chicken digestive tract and their role in the inhibition of Campylobacter colonization. Microbiologyopen. 7-24-2017; PM: 28736979

ABSTRACT: Campylobacter jejuni/coli infections are the leading cause of bacterial diarrheal illnesses in humans. Many epidemiological studies indicate that improperly prepared meat from chickens that carry a high load of Campylobacter in their intestinal tracts is the key source of human infections. LAB, mainly members of the Lactococcus and Lactobacillus genera, increasingly have been tested as vehicles for the delivery of heterologous bacterial or viral antigens to animal mucosal immune systems. Thus, the objective of this study was to isolate, identify, and characterize Lactobacillus spp. strains isolated from chickens bred in Poland. Their ability to decrease the level of bird gut colonization by C. jejuni strain was also analyzed. First, the influence of the different chicken rearing systems was evaluated, especially the effect of diets on the Lactobacillus species that colonize the gut of chickens. Next, selected strains were analyzed in terms of their anti-Campylobacter activity in vitro; potential probiotic traits such as adhesion properties, bile and low pH tolerance; and their ability to grow on a defined carbon source. Given that improperly prepared chicken meat is the main source

of human infection by Campylobacter, the selected strains were also assessed for their ability to inhibit Campylobacter colonization in the bird's intestine. These experiments revealed enormous physiological diversity among the Lactobacillus genus strains. Altogether, our results showed that L. plantarum strains isolated from the digestive tracts of chickens bred in Poland displayed some probiotic attributes in vitro and were able to decrease the level of bird gut colonization by C. jejuni strain. This suggests that they can be employed as vectors to deliver Campylobacter immunodominant proteins to the bird's immune system to strengthen the efficacy of in ovo vaccination.

Kolacek, S., Hojsak, I., Berni, Canani R., 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. 2017; 65(1):117-124; PM: 28644359

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 article 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 labeled 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.

Koscik, R. J. E., Reid, G., Kim, S. O., Li, W., Challis, J. R. G., and Bocking, A. D. Effect of Lactobacillus rhamnosus GR-1 Supernatant on Cytokine and Chemokine Output From Human Amnion Cells Treated With Lipoteichoic Acid and Lipopolysaccharide. Reprod.Sci. 1-1-2017; 1933719117711259; PM: 28587570

ABSTRACT: Preterm birth occurs in 9% to 13% of all human pregnancies and accounts for 80% of all neonatal morbidities and mortalities. Approximately 40% of all preterm births are idiopathic and about half are associated with infection and/or an activated inflammatory process. Further to studies showing anti-inflammatory effects of supernatant from the probiotic Lactobacillus rhamnosus GR-1 (GR-1), we tested its ability to modulate cytokine and chemokine production from amnion cells in response to stimulation by bacterial wall components, lipopolysaccharide (LPS), and lipoteichoic acid (LTA). Placentae were collected from women undergoing elective cesarean section at term.

Amnion cells were cultured for 48 hours to confluence, serum starved for 12 hours, and then treated with GR-1 supernatant (1:20 dilution), followed after 12 hours by LPS (100 ng/mL) or LTA (10 ng/mL) for an additional 12 hours. Both LTA and LPS caused significant increases in the concentration of the pro-inflammatory cytokine, tumor necrosis factor alpha (TNF-alpha; 103.9 +/- 67.5 pg/mL and 368.3 +/- 65.7 pg/mL, respectively) in medium from cultured amnion cells compared to control (<4 pg/mL). There was no significant effect of GR-1 supernatant alone on TNF-alpha output, but there was significant reduction after LPS treatment. The basal output of the immunomodulatory cytokine, interleukin 6, was 613 +/- 170 pg/mL and increased significantly after addition of GR-1 supernatant, LTA, LPS, and combinations of LTA/LPS with GR-1 supernatant. In conclusion, probiotic L rhamnosus GR-1 attenuates the effect of both LPS and LTA in stimulating the output of the pro-inflammatory cytokine TNF-alpha from mixed cultures of human amnion cells in keeping with previous findings in human trophoblast cells.

Kosler, S., Strukelj, B., and Berlec, A. Lactic Acid Bacteria with Concomitant IL-17, IL-23 and TNFalpha- Binding Ability for the Treatment of Inflammatory Bowel Disease. Curr.Pharm.Biotechnol. 2017; 18(4):318-326; PM: 28190384

ABSTRACT: ***BACKGROUND***: Neutralization of proinflammatory cytokines is an established strategy in the treatment of inflammatory bowel disease (IBD). Systemic anti-TNFalpha antibodies have been used in the clinics for several years, while anti-IL-17/IL-23 antibodies have been less successful so far. We report the development of safe lactic acid bacterium Lb. salivarius with the ability to simultaneously bind IL-17A, IL-23 and TNFalpha that could be administered orally for the treatment of IBD. ***METHOD***: Three different cytokine-binding non-Ig scaffolds (anti-IL-17A fynomer, anti-IL-23-binding adnectin and anti-TNFalpha-binding affibody) were cloned and expressed in L. lactis in fusion with lysine motif (LysM)-containing surface anchor. Fusion proteins were used for coating of Lb. salivarius. Cytokine- binding ability of bacterial cells was assayed with ELISA. Gastric stability was tested by incubation in simulated gastric juice. ***RESULTS***: Surface display and functionality of cytokine binding proteins in L. lactis was confirmed by the ability to remove the individual cytokines from the solution. Binding was efficient with different concentrations of cells, different cytokine concentrations and after the incubation in simulated gastric juice. The fusion protein-containing growth media of L. lactis were used for coating of Lb. salivarius in a fast and straightforward manner. Cytokine-binder-coated Lb. salivarius was able to retain individual binders or mixtures of all three binders on its surface, and also provided limited protection from proteolytic and low pH degradation. Cytokine binding capacity of mixture-coated Lb. salivarius was similar to that achieved by coating with individual binders. ***CONCLUSION***: Simultaneous binding of IL-17A, IL-23 and TNFalpha with engineered bacteria was achieved for the first time. Oral administration of such bacteria could exert synergistic effect and thus represents an alternative strategy in the treatment of IBD.

Krischer, J. P., Lynch, K. F., Lernmark, A., Hagopian, W. A., Rewers, M. J., She, J. X., Toppari, J., Ziegler, A. G., and Akolkar, B. Genetic and Environmental Interactions Modify the Risk of Diabetes-Related Autoimmunity by 6 Years of Age: The TEDDY Study. Diabetes Care. 2017; 40(9):1194-1202; PM: 28646072

ABSTRACT: ***OBJECTIVE***: We tested the associations between genetic background and selected environmental exposures with respect to islet autoantibodies and type 1 diabetes. ***RESEARCH DESIGN AND METHODS***: Infants with HLA-DR high-risk genotypes were

prospectively followed for diabetes-related autoantibodies. Single nucleotide polymorphisms (SNPs) came from the Illumina ImmunoChip and environmental exposure data were by parental report. Children were followed to age 6 years. ***RESULTS***: Insulin autoantibodies occurred earlier than GAD antibody (GADA) and then declined, while GADA incidence rose and remained constant (significant in HLA-DR4 but not in the DR3/3 children). The presence of SNPs rs2476601 (PTPN22) and rs2292239 (ERBB3) demonstrated increased risk of both autoantibodies to insulin (IAA) only and GADA only. SNP rs689 (INS) was protective of IAA only, but not of GADA only. The rs3757247 (BACH2) SNP demonstrated increased risk of GADA only. Male sex, father or sibling as the diabetic proband, introduction of probiotics under 28 days of age, and weight at age 12 months were associated with IAA only, but only father as the diabetic proband and weight at age 12 months were associated with GADA only. Mother as the diabetic proband was not a significant risk factor. ***CONCLUSIONS***: These results show clear differences in the initiation of autoimmunity according to genetic factors and environmental exposures that give rise to IAA or GADA as the first appearing indication of autoimmunity.

Krishnareddy, S., Stier, K., Recanati, M., Lebwohl, B., and Green, P. H. Commercially available glutenases: a potential hazard in coeliac disease. Therap.Adv.Gastroenterol. 2017; 10(6):473-481; PM: 28567117

ABSTRACT: ***BACKGROUND***: The only treatment for celiac disease (CD) is a gluten-free diet (GFD). However, there is interest among patients in a medical therapy to replace or help with a GFD. Therapies include gluten-degrading enzymes (glutenases). There are glutenases available marketed as dietary supplements that have not been demonstrated to digest the toxic epitopes of gluten. ***METHODS***: We investigated the contents, claims, and disclaimers of glutenase products and assessed patient interest using Google AdWords to obtain Google search frequencies. ***RESULTS***: Among 14 glutenase product, all contained proteases, eight contained X-prolyl exopeptidase dipeptidyl peptidase IV, two did not state the protease contents, and eight failed to specify the name or origin of all proteases. Eleven contained carbohydrases and lipases and three probiotics. One declared wheat and milk as allergens, two contained herbal products (type not stated) and one Carica papaya. Thirteen claimed to degrade immunogenic gluten fragments, four claimed to help alleviate gastrointestinal symptoms associated with eating gluten. Disclaimers included not being evaluated by the US Food and Drug Administration and products not intended to diagnose, treat, cure, or prevent any disease. On Google AdWords, the search frequency for the product names and the search terms was 3173 searches per month. ***CONCLUSIONS***: The names of these products make implicit claims that appear to be supported by the claims on the labels and websites for which there is no scientific basis. Google search data suggest great interest and therefore possible use by patients with CD. There needs to be greater oversight of these 'drugs'.

Kulkarni, S., Haq, S. F., Samant, S., and Sukumaran, S. Adaptation of Lactobacillus acidophilus to Thermal Stress Yields a Thermotolerant Variant Which Also Exhibits Improved Survival at pH 2. Probiotics.Antimicrob.Proteins. 8-30-2017; PM: 28853009

ABSTRACT: Loss in probiotic viability upon exposure to stressful storage and transport conditions has plagued the probiotic market worldwide. Lactobacillus acidophilus is an important probiotic that is added to various functional foods. It is known to be fairly labile and susceptible to temperature variations that it encounters during processing and

storage which increases production cost. It has been repeatedly demonstrated that pre-exposure to sub-lethal doses of stress, particularly, temperature and pH, leads to improved survival of various probiotics when they subsequently encounter the same stress of a much greater magnitude. Attempts to adapt L. acidophilus to temperatures as high as 65 degrees C to arrive at a thermotolerant variant have not been reported previously. To improve viability at elevated temperatures, we gradually adapted the L. acidophilus NCFM strain to survival at 65 degrees C for 40 min. Following adaptation, the variant showed a 2-log greater survival compared to wild-type at 65 degrees C. Interestingly, this thermotolerant variant also demonstrated a 2-log greater stability compared to wild-type at pH 2.0. The improved pH and temperature stress tolerance exhibited by this variant remained unaltered even when the strain was lyophilized. Moreover, the thermotolerant variant demonstrated improved stability compared to wild-type when stored for up to a week at 37 and 42 degrees C. Probiotic properties of the variant such as adherence to epithelial cells and antibacterial activity remained unaltered. This strain can potentially help address the issue of significant loss in viable cell counts of L. acidophilus which is typically encountered during probiotic manufacture and storage.

Kumar, P. Randomized Controlled Trial Evaluating Probiotics in Children with Severe Acute Malnutrition: Pediatrician's Viewpoint. Indian Pediatr. 6-15-2017; 54(6):492-493; PM: 28667721

No Abstract Available.

Kwak, J. Y. and Lamouse-Smith, E. S. N. Can probiotics enhance vaccine-specific immunity in children and adults? Benef.Microbes. 8-31-2017; 1-14; PM: 28856905

ABSTRACT: The growing use of probiotics by the general public has heightened the interest in understanding the role of probiotics in promoting health and preventing disease. General practitioners and specialists often receive inquiries from their patients regarding probiotic products and their use to ward off systemic infection or intestinal maladies. Enhanced immune function is among the touted health benefits conferred by probiotics but has not yet been fully established. Results from recent clinical trials in adults suggest a potential role for probiotics in enhancing vaccine-specific immunity. Although almost all vaccinations are given during infancy and childhood, the numbers of and results from studies using probiotics in pediatric subjects are limited. This review evaluates recent clinical trials of probiotics used to enhance vaccine-specific immune responses in adults and infants. We highlight meaningful results and the implications of these findings for designing translational and clinical studies that will evaluate the potential clinical role for probiotics. We conclude that the touted health claims of probiotics for use in children to augment immunity warrant further investigation. In order to achieve this goal, a consensus should be reached on common study designs that apply similar treatment timelines, compare well-characterised probiotic strains and monitor effective responses against different classes of vaccines.

La, Fata G., Weber, P., and Mohajeri, M. H. Probiotics and the Gut Immune System: Indirect Regulation. Probiotics.Antimicrob.Proteins. 8-31-2017; PM: 28861741

ABSTRACT: The gastrointestinal tract (GIT) represents the largest interface between the human organism and the external environment. In the lumen and upper part of the

mucus layer, this organ hosts an enormous number of microorganisms whose composition affects the functions of the epithelial barrier and the gut immune system. Consequentially, the microorganisms in the GIT influence the health status of the organism. Probiotics are living microorganisms which, in specific conditions, confer a health benefit to the host. Among others, probiotics have immunomodulatory properties that usually act directly by (a) increasing the activity of macrophages or natural killer cells, (b) modulating the secretion of immunoglobulins or cytokines, or indirectly by (c) enhancing the gut epithelial barrier, (d) altering the mucus secretion, and (e) competitive exclusion of other (pathogenic) bacteria. This review focuses on specific bacteria strains with indirect immunomodulatory properties. Particularly, we describe here the mechanisms through which specific probiotics enhance the gut epithelial barrier and modulate mucus production. Moreover, we describe the antimicrobial properties of specific bacteria strains. Recent data suggest that multiple pathologies are associated with an unbalanced gut microflora (dysbiosis). Although the cause-effect relationship between pathology and gut microflora is not yet well established, consumption of specific probiotics may represent a powerful tool to re-establish gut homeostasis and promote gut health.

Lambert, M. N. T., Thorup, A. C., Hansen, E. S. S., and Jeppesen, P. B. Combined Red Clover isoflavones and probiotics potently reduce menopausal vasomotor symptoms. PLoS.One. 2017; 12(6):e0176590; PM: 28591133

ABSTRACT: ***BACKGROUND***: Natural estrogen decline leads to vasomotor symptoms (VMS). Hormone therapy alleviates symptoms but increases cancer risk. Effective treatments against VMS with minimal cancer risks are needed. We investigate the effects of a highly bioavailable aglycone rich Red Clover isoflavone treatment to alleviate existing menopausal VMS, assessed for the first time by 24hour ambulatory skin conductance (SC). ***METHODS AND RESULTS***: We conducted a parallel, double blind, randomised control trial of 62 peri-menopausal women aged 40-65, reporting >/= 5 hot flushes/day and follicle stimulating hormone >/=35 IU/L. Participants received either twice daily treatment with bioavailable RC extract (RCE), providing 34 mg/d isoflavones and probiotics, or masked placebo formulation for 12 weeks. The primary outcome was change in daily hot flush frequency (HFF) from baseline to 12 weeks using 24hr SC. Secondary outcomes were change in SC determined hot flush intensity (HFI), self-reported HFF (rHFF) and hot flush severity (rHFS), blood pressure and plasma lipids. A significant decrease in 24hr HFF ($P < 0.01$) and HFI ($P<0.05$) was found when comparing change from baseline to 12 months of the RCE (-4.3 HF/24hr, CI -6.8 to -2.3; -12956 muS s-1, CI -20175 to -5737) with placebo (0.79 HF/24hr, CI -1.56 to 3.15; 515 muS s-1, CI -5465 to 6496). rHFF was also significantly reduced ($P <0.05$)in the RCE (-2.97 HFs/d, CI -4.77 to -1.17) group compared to placebo (0.036 HFs/d, CI -2.42 to 2.49). Other parameters were non-significant. RCE was well tolerated. ***CONCLUSION***: Results suggest that moderate doses of RCE were more effective and superior to placebo in reducing physiological and self-reported VMS. Findings support that objective physiological symptom assessment methods should be used together with self-report measures in future studies on menopausal VMS. ***TRIAL REGISTRATION***: ClinicalTrials.gov NCT02028702.

Lambert, M. N. T., Thybo, C. B., Lykkeboe, S., Rasmussen, L. M., Frette, X., Christensen, L. P., and Jeppesen, P. B. Combined bioavailable isoflavones and probiotics improve bone status and estrogen metabolism in postmenopausal osteopenic women: a randomized controlled trial. Am.J.Clin.Nutr. 2017; 106(3):909-920; PM: 28768651

ABSTRACT: ***Background***: Female age-related estrogen deficiency increases the risk of osteoporosis, which can be effectively treated with the use of hormone replacement therapy. However, hormone replacement therapy is demonstrated to increase cancer risk. Bioavailable isoflavones with selective estrogen receptor affinity show potential to prevent and treat osteoporosis while minimizing or eliminating carcinogenic side effects.***Objective***: In this study, we sought to determine the beneficial effects of a bioavailable isoflavone and probiotic treatment against postmenopausal osteopenia.***Design***: We used a novel red clover extract (RCE) rich in isoflavone aglycones and probiotics to concomitantly promote uptake and a favorable intestinal bacterial profile to enhance isoflavone bioavailability. This was a 12-mo, double-blind, parallel design, placebo-controlled, randomized controlled trial of 78 postmenopausal osteopenic women supplemented with calcium (1200 mg/d), magnesium (550 mg/d), and calcitriol (25 mug/d) given either RCE (60 mg isoflavone aglycones/d and probiotics) or a masked placebo [control (CON)].***Results***: RCE significantly attenuated bone mineral density (BMD) loss at the L2-L4 lumbar spine vertebra ($P < 0.05$), femoral neck ($P < 0.01$), and trochanter ($P < 0.01$) compared with CON (-0.99% and -2.2%; -1.04% and -3.05%; and -0.67% and -2.79, respectively). Plasma concentrations of collagen type 1 cross-linked C-telopeptide was significantly decreased in the RCE group ($P < 0.05$) compared with CON (-9.40% and -6.76%, respectively). RCE significantly elevated the plasma isoflavone concentration ($P < 0.05$), the urinary 2-hydroxyestrone (2-OH) to 16alpha-hydroxyestrone (16alpha-OH) ratio ($P < 0.05$), and equol-producer status ($P < 0.05$) compared with CON. RCE had no significant effect on other bone turnover biomarkers. Self-reported diet and physical activity were consistent and differences were nonsignificant between groups throughout the study. RCE was well tolerated with no adverse events.***Conclusions***: Twice daily RCE intake over 1 y potently attenuated BMD loss caused by estrogen deficiency, improved bone turnover, promoted a favorable estrogen metabolite profile (2-OH:16alpha-OH), and stimulated equol production in postmenopausal women with osteopenia. RCE intake combined with supplementation (calcium, magnesium, and calcitriol) was more effective than supplementation alone. This trial was registered at clinicaltrials.gov as NCT02174666.

Lane, E. R., Zisman, T. L., and Suskind, D. L. The microbiota in inflammatory bowel disease: current and therapeutic insights. J.Inflamm.Res. 2017; 10:63-73; PM: 28652796

ABSTRACT: Inflammatory bowel disease is a heterogeneous group of chronic disorders that result from the interaction of the intestinal immune system with the gut microbiome. Until recently, most investigative efforts and therapeutic breakthroughs were centered on understanding and manipulating the altered mucosal immune response that characterizes these diseases. However, more recent studies have highlighted the important role of environmental factors, and in particular the microbiota, in disease onset and disease exacerbation. Advances in genomic sequencing technology and bioinformatics have facilitated an explosion of investigative inquiries into the composition and function of the intestinal microbiome in health and disease and have advanced our understanding of the interplay between the gut microbiota and the host immune system. The gut microbiome is dynamic and changes with age and in response to diet, antibiotics and other environmental factors, and these alterations in the microbiome contribute to disease onset and exacerbation. Strategies to manipulate the microbiome through diet, probiotics, antibiotics or fecal microbiota transplantation may potentially be used therapeutically to influence modulate disease activity. This review will characterize the factors involved in the development of the intestinal microbiome and

will describe the typical alterations in the microbiota that are characteristic of inflammatory bowel disease. Additionally, this manuscript will summarize the early but promising literature on the role of the gut microbiota in the pathogenesis of inflammatory bowel disease with implications for utilizing this data for diagnostic or therapeutic application in the clinical management of patients with these diseases.

Lau, K., Srivatsav, V., Rizwan, A., Nashed, A., Liu, R., Shen, R., and Akhtar, M. Bridging the Gap between Gut Microbial Dysbiosis and Cardiovascular Diseases. Nutrients. 8-10-2017; 9(8);PM: 28796176

ABSTRACT: The human gut is heavily colonized by a community of microbiota, primarily bacteria, that exists in a symbiotic relationship with the host and plays a critical role in maintaining host homeostasis. The consumption of a high-fat (HF) diet has been shown to induce gut dysbiosis and reduce intestinal integrity. Recent studies have revealed that dysbiosis contributes to the progression of cardiovascular diseases (CVDs) by promoting two major CVD risk factors-atherosclerosis and hypertension. Imbalances in host-microbial interaction impair homeostatic mechanisms that regulate health and can activate multiple pathways leading to CVD risk factor progression. Dysbiosis has been implicated in the development of atherosclerosis through metabolism-independent and metabolite-dependent pathways. This review will illustrate how these pathways contribute to the various stages of atherosclerotic plaque progression. In addition, dysbiosis can promote hypertension through vascular fibrosis and an alteration of vascular tone. As CVD is the number one cause of death globally, investigating the gut microbiota as a locus of intervention presents a novel and clinically relevant avenue for future research, with vast therapeutic potential.

Laursen, M. F., Laursen, R. P., Larnkjaer, A., Michaelsen, K. F., Bahl, M. I., and Licht, T. R. Administration of two probiotic strains during early childhood does not affect the endogenous gut microbiota composition despite probiotic proliferation. BMC.Microbiol. 8-17-2017; 17(1):175; PM: 28818050

ABSTRACT: ***BACKGROUND***: Probiotics are increasingly applied to prevent and treat a range of infectious, immune related and gastrointestinal diseases. Despite this, the mechanisms behind the putative effects of probiotics are poorly understood. One of the suggested modes of probiotic action is modulation of the endogenous gut microbiota, however probiotic intervention studies in adults have failed to show significant effects on gut microbiota composition. The gut microbiota of young children is known to be unstable and more responsive to external factors than that of adults. Therefore, potential effects of probiotic intervention on gut microbiota may be easier detectable in early life. We thus investigated the effects of a 6 month placebo-controlled probiotic intervention with Bifidobacterium animalis subsp. lactis (BB-12(R)) and Lactobacillus rhamnosus (LGG(R)) on gut microbiota composition and diversity in more than 200 Danish infants (N = 290 enrolled; N = 201 all samples analyzed), as assessed by 16S rRNA amplicon sequencing. Further, we evaluated probiotic presence and proliferation by use of specific quantitative polymerase chain reaction (qPCR). ***RESULTS***: Probiotic administration did not significantly alter gut microbiota community structure or diversity as compared to placebo. The probiotic strains were detected in 91.3% of the fecal samples from children receiving probiotics and in 1% of the placebo treated children. Baseline gut microbiota was not found to predict the ability of probiotics to establish in the gut after the 6 month intervention. Within the probiotics group, proliferation of the strains LGG(R) and BB-12(R)

in the gut was detected in 44.7% and 83.5% of the participants, respectively. A sub-analysis of the gut microbiota including only individuals with detected growth of the probiotics LGG(R) or BB-12(R) and comparing these to placebo revealed no differences in community structure or diversity. ***CONCLUSION***: Six months of probiotic administration during early life did not change gut microbiota community structure or diversity, despite active proliferation of the administered probiotic strains. Therefore, alteration of the healthy infant gut microbiota is not likely to be a prominent mechanism by which these specific probiotics works to exert beneficial effects on host health. ***TRIAL REGISTRATION***: NCT02180581 . Registered 30 June 2014.

Laursen, R. P., Larnkjaer, A., Ritz, C., Hauger, H., Michaelsen, K. F., and Molgaard, C. Probiotics and Child Care Absence Due to Infections: A Randomized Controlled Trial. Pediatrics. 2017; 140(2); PM: 28674113

ABSTRACT: ***OBJECTIVES***: The risk of infections is higher in children attending child care compared with children cared for at home. This study examined the effect of a combination of probiotics on absence from child care because of respiratory and gastrointestinal infections in healthy infants aged 8 to 14 months at the time of enrollment in child care. ***METHODS***: The ProbiComp study was a randomized, double-blind, placebo-controlled study. A total of 290 infants were randomly allocated to receive a placebo or a combination of Bifidobacterium animalis subsp lactis and Lactobacillus rhamnosus in a dose of 109 colony-forming units of each daily for a 6-month intervention period. Absence from child care, occurrence of infant symptoms of illness, and doctor visits were registered by the parents using daily and weekly Web-based questionnaires. ***RESULTS***: Median absence from child care was 11 days (interquartile range: 6-16). Intention-to-treat analysis showed no difference between the probiotics and placebo groups (P = .19). Additionally, there was no difference in any of the secondary outcomes between groups; the number of children with doctor-diagnosed upper or lower respiratory tract infections, the number of doctor visits, antibiotic treatments, occurrence and duration of diarrhea, and days with common cold symptoms, fever, vomiting, or caregivers' absence from work. ***CONCLUSIONS***: A daily administration of a combination of B animalis subsp lactis and L rhamnosus for 6 months did not reduce the number of days absent from child care in healthy infants at the time of enrollment in child care.

Lawrence, K. and Hyde, J. Microbiome restoration diet improves digestion, cognition and physical and emotional wellbeing. PLoS.One. 2017; 12(6):e0179017; PM: 28614379

ABSTRACT: Manipulating gut bacteria in the microbiome, through the use of probiotics and prebiotics, has been found to have an influence on both physical and emotional wellbeing. This study uses a dietary manipulation 'The Gut Makeover' designed to elicit positive changes to the gut bacteria within the microbiome. 21 healthy participants undertook 'The Gut Makeover' for a four week period. Weight and various aspects of health were assessed pre and post intervention using the Functional Medicine Medical Symptoms Questionnaire (MSQ). Paired sample t-tests revealed a significant reduction in self-reported weight at the end of the intervention. Adverse medical symptoms related to digestion, cognition and physical and emotional wellbeing, were also significantly reduced during the course of the dietary intervention. The intervention, designed to manipulate gut bacteria, had a significant impact on digestion, reducing IBS type symptoms in this non-clinical population. There was also a striking reduction in negative symptoms related to cognition, memory and emotional wellbeing, including symptoms of

anxiety and depression. Dietary gut microbiome manipulations may have the power to exert positive physical and psychological health benefits, of a similar nature to those reported in studies using pre and probiotics. The small sample size and lack of control over confounding variables means that it will be important to replicate these findings in larger-scale controlled, prospective, clinical trials. This dietary microbiome intervention has the potential to improve physical and emotional wellbeing in the general population but also to be investigated as a treatment option for individuals with conditions as diverse as IBS, anxiety, depression and Alzheimer's disease.

Lazarus, R. P., John, J., Shanmugasundaram, E., Rajan, A. K., Thiagarajan, S., Giri, S., Babji, S., Sarkar, R., Kaliappan, P. S., Venugopal, S., Praharaj, I., Raman, U., Paranjpe, M., Grassly, N. C., Parker, E. P. K., Parashar, U. D., Tate, J. E., Fleming, J. A., Steele, A. D., Muliyil, J., Abraham, A. M., and Kang, G. The effect of probiotics and zinc supplementation on the immune response to oral rotavirus vaccine: A randomized, factorial design, placebo-controlled study among Indian infants. Vaccine. 9-2-2017; PM: 28874323

ABSTRACT: ***BACKGROUND***: Strategies are needed to improve oral rotavirus vaccine (RV), which provides suboptimal protection in developing countries. Probiotics and zinc supplementation could improve RV immunogenicity by altering the intestinal microbiota and immune function. ***METHODS***: Infants 5weeks old living in urban Vellore, India were enrolled in a randomized, double-blind, placebo-controlled trial with a 4-arm factorial design to assess the effects of daily zinc (5mg), probiotic (1010Lactobacillus rhamnosus GG) or placebo on the immunogenicity of two doses of RV (Rotarix(R), GlaxoSmithKline Biologicals) given at 6 and 10weeks of age. Infants were eligible for participation if healthy, available for the study duration and without prior receipt of RV or oral poliovirus vaccine other than the birth dose. The primary outcome was seroconversion to rotavirus at 14weeks of age based on detection of VP6-specific IgA at >/=20U/ml in previously seronegative infants or a fourfold rise in concentration. ***RESULTS***: The study took place during July 2012 to February 2013. 620 infants were randomized equally between study arms and 551 (88.9%) completed per protocol. Seroconversion was recorded in 54/137 (39.4%), 42/136 (30.9%), 40/143 (28.0%), and 37/135 (27.4%) infants receiving (1) probiotic and zinc, (2) probiotic and placebo, (3) placebo and zinc, (4) two placebos. Seroconversion showed a modest improvement among infants receiving probiotic (difference between groups 1, 2 and 3, 4 was 7.5% (97.5% Confidence Interval (CI): -1.4%, 16.2%), p=0.066) but not zinc (difference between groups 1, 3 and 2, 4 was 4.4% (97.5% CI: -4.4%, 13.2%), p=0.272). 16 serious adverse events were recorded, none related to study interventions. ***CONCLUSIONS***: Zinc or probiotic supplementation did not significantly improve the low immunogenicity of rotavirus vaccine given to infants in a poor urban community in India. A modest effect of combined supplementation deserves further investigation. ***TRIAL REGISTRATION***: The trial was registered in India (CTRI/2012/05/002677).

Lee, A., Lee, Y. J., Yoo, H. J., Kim, M., Chang, Y., Lee, D. S., and Lee, J. H. Consumption of Dairy Yogurt Containing Lactobacillus paracasei ssp. paracasei, Bifidobacterium animalis ssp. lactis and Heat-Treated Lactobacillus plantarum Improves Immune Function Including Natural Killer Cell Activity. Nutrients. 5-31-2017; 9(6); PM: 28561762

ABSTRACT: The aim of this study was to investigate the impact of consuming dairy yogurt containing Lactobacillus paracasei ssp. paracasei (L. paracasei), Bifidobacterium animalis ssp. lactis (B. lactis) and heat-treated Lactobacillus plantarum (L. plantarum) on immune function. A randomized, open-label, placebo-controlled study was conducted

on 200 nondiabetic subjects. Over a twelve-week period, the test group consumed dairy yogurt containing probiotics each day, whereas the placebo group consumed milk. Natural killer (NK) cell activity, interleukin (IL)-12 and immunoglobulin (Ig) G1 levels were significantly increased in the test group at twelve weeks compared to baseline. Additionally, the test group had significantly greater increases in serum NK cell activity and interferon (IFN)-gamma and IgG1 than placebo group. Daily consumption of dairy yogurt containing L. paracasei, B. lactis and heat-treated L. plantarum could be an effective option to improve immune function by enhancing NK cell function and IFN-gamma concentration (ClinicalTrials.gov: NCT03051425).

Lee, H. and Ko, G. New perspectives regarding the antiviral effect of vitamin A on norovirus using modulation of gut microbiota. Gut Microbes. 7-20-2017; 1-5; PM: 28727498

ABSTRACT: Gut microbiota has been revealed to play an important role in various health conditions, and recent studies have suggested the modulation of gut microbiota as a therapeutic strategy. There is no effective treatment of norovirus infection, though vitamin A has been suggested to have an antiviral effect in an epidemiological study. We demonstrated that vitamin A significantly inhibited murine norovirus replication. Vitamin A supplementation significantly increased the abundance of Lactobacillus sp. during norovirus infection, which played a crucial role in antiviral efficacy, inhibiting murine norovirus. Therefore, we elaborated the antiviral effect of vitamin A via modulation of gut microbiota. Furthermore, we suggest a novel strategy, using potential probiotics, as having a protective and therapeutic effect on noroviral infection.

Lee, J. S., Kim, M. J., Park, S. H., Lee, S. B., Wang, T., Jung, U. S., Im, J., Kim, E. J., Lee, K. W., and Lee, H. G. Effects of dietary mixture of garlic (Allium sativum), coriander (Coriandrum sativum) and probiotics on immune responses and caecal counts in young laying hens. J.Anim Physiol Anim Nutr.(Berl). 2017; 101(5):e122-e132; PM: 27678135

ABSTRACT: This study was conducted to evaluate the effects of a combined mixture of phytogenic extracts (garlic and coriander) and probiotics on growth performance and immune responses in laying hens based on the results of in vitro studies to screen for immunomodulatory potency of each ingredient. Several parameters of immunomodulatory potency were estimated using lamina propria leucocytes (LPLs) isolated from rat intestinal mucosa tissue. Results show that the combined mixture enhanced LPLs proliferation, increased LPL-mediated cytotoxicity against YAC-1 tumour cells, and decreased lipopolysaccharide (LPS)-induced cytokine production including tumour necrosis factor-alpha (TNF-alpha) and interferon-gamma (IFN-gamma) in LPLs. For in vivo study, laying hens (n = 50/each diet group) were fed with control diet, a diet containing antibiotics (0.01% per kg feed) or the combined mixture (0.02% per kg feed) for 21 days. The dietary combined mixture improved egg production ($p < 0.05$) but not growth performance and carcass traits. Interestingly, the patterns of suppressing plasma IFN-gamma productions during inflammation by LPS injection and decreasing caecal E. coli counts in the combined mixture group were comparable to those in the antibiotics group. Taken together, our results suggested that the 0.02% of combined mixture of phytogenic extracts and probiotics as ingredients has potential immunomodulatory effects in laying hens.

Lee, Y., Ba, Z., Roberts, R. F., Rogers, C. J., Fleming, J. A., Meng, H., Furumoto, E. J., and Kris-Etherton, P. M. Effects of Bifidobacterium animalis subsp. lactis BB-12(R) on the lipid/lipoprotein profile and short chain fatty acids in healthy young adults: a randomized controlled trial. Nutr.J. 6-29-2017; 16(1):39; PM: 28662676

ABSTRACT: ***BACKGROUND***: Some probiotics have hypocholesterolemic effects in animal studies, which are mediated, in part, by increases in fecal short chain fatty acids (SCFAs). Clinical trials of probiotics on lipids/lipoproteins are inconsistent. ***OBJECTIVE***: We examined the effects of Bifidobacterium animalis subsp. lactis BB-12(R) (BB-12(R)) (3.16 x 109 CFUs/day) on lipids and lipoproteins and fecal excretion of SCFAs in healthy adults. ***METHODS***: In a randomized, partially blinded, 4-period, crossover study, 30 adults (11 men, 19 women) aged 18-40 years were randomly assigned to: 1) yogurt smoothie with no BB-12(R) (YS), 2) yogurt smoothie with BB-12(R) added pre-fermentation (PRE), 3) yogurt smoothie with BB-12(R) added post-fermentation (POST), 4) BB-12(R) containing capsule (CAP). We measured serum lipids/lipoproteins, glucose, insulin, C-reactive protein (CRP), and fecal SCFAs at baseline and after each treatment period. ***RESULTS***: Total cholesterol (TC), LDL cholesterol (LDL-C), HDL cholesterol (HDL-C), and triglycerides (TGs) did not differ after the PRE, POST, and CAP periods versus the YS or between treatments. Compared to baseline, fecal acetate was significantly increased after the YS (Delta = 211.89 +/- 75.87 mug/g, P = 0.007) and PRE (Delta = 204.98 +/- 75.70 mug/g, P = 0.009) periods. The percent increase in fecal acetate was significantly greater after the YS versus the POST period (52.2 +/- 13.2% vs. 24.5 +/- 13.2%, P = 0.023). Fecal total SCFAs, propionate and butyrate did not differ between treatment periods. Fecal total SCFAs were negatively associated with TC (r = -0.22, P = 0.01), LDL-C (r = -0.24, P = 0.004), age (r = -0.33, P < 0.001), and waist circumference (r = -0.25, P = 0.003). ***CONCLUSIONS***: BB-12(R) supplementation did not improve lipids, lipoproteins and total and individual fecal SCFAs. Fecal SCFAs were negatively associated with TC, LDL-C, age, and waist circumference. ***TRIAL REGISTRATION***: This trial was registered at clinicaltrials.gov as NCT01399996.

Lee, Y. K., Conway, P., Pettersson, S., Nair, G. B., Surono, I., Egayanti, Y., and Amarra, M. S. ILSI Southeast Asia Region conference proceedings: The gut, its microbes and health: relevance for Asia. Asia Pac.J.Clin.Nutr. 2017; 26(5):957-971; PM: 28802306

ABSTRACT: ***BACKGROUND AND OBJECTIVES***: The human being is a complex entity, involving interaction between microbes and the human host. Evidence shows that the nutritional value of food is influenced in part by the structure and operations of an individual's gut microbial community, and food in turn shapes the individual's microbiome. A conference was held to promote understanding of the intestinal microbiome and its implications for health and disease, particularly among Asian populations. ***METHODS AND STUDY DESIGN***: Papers describing 1) the intestinal ecosystem in Asian populations, 2) changes in intestinal microbiota through life and its effects, 3) the Asian gut microbiota in disease conditions, 4) indigenous probiotics to maintain a healthy gut microbiota, 5) probiotic regulation in an Asian country, and 6) the results of a panel discussion are included in this report. ***CONCLUSIONS***: The gut microbial inhabitants of Asian people differ from those of Europe and North America. Geographic location, diet, and ethnic background influence intestinal microbial composition. Urbanization and economic development have brought changes in traditional Asian diets, which in turn affected the gut microbiome, contributing to a shift in the region's health burden from infectious diseases to non-communicable chronic diseases. Novel probiotic strains of Indonesian origin demonstrated significant enhancement of humoral immune response

in human studies. Knowledge gaps and implications for research to further understand the Asian gut microbiome were discussed.

Lehri, B., Seddon, A. M., and Karlyshev, A. V. Lactobacillus fermentum 3872 as a potential tool for combatting Campylobacter jejuni infections. Virulence. 8-2-2017; 1-8; PM: 28766992

ABSTRACT: Due to the global spread of multidrug resistant pathogenic bacteria, alternative approaches in combating infectious diseases are required. One such approach is the use of probiotics. Lactobacillus fermentum 3872 is a promising probiotic bacterium producing a range of antimicrobial compounds, such as hydrogen peroxide and lactic acid. In addition, previous studies involving genome sequencing and analysis of L. fermentum 3872 allowed the identification of a gene encoding a cell surface protein referred to as collagen binding protein (CBP) (not found in other strains of the species, according to the GenBank database), consisting of a C-terminal cell wall anchor domain (LPXT), multiple repeats of 'B domains' that form stalks presenting an "A domain" required for adhesion. In this study, we found that the CBP of L. fermentum 3872 binds to collagen I present on the surface of the epithelial cells lining the gastrointestinal tract. Moreover, we found that this host receptor is also used for attachment by the major gastrointestinal pathogen, Campylobacter jejuni. Furthermore, we identified an adhesin involved in such interaction and demonstrated that both L. fermentum 3872 and its CBP can inhibit binding of this pathogen to collagen I. Combined with the observation that C. jejuni growth is affected in the acidic environment produced by L. fermentum 3872, the finding provides a good basis for further investigation of this strain as a potential tool for fighting Campylobacter infections.

Lei, M., Guo, C., Wang, D., Zhang, C., and Hua, L. The effect of probiotic Lactobacillus casei Shirota on knee osteoarthritis: a randomised double-blind, placebo-controlled clinical trial. Benef.Microbes. 7-20-2017; 1-8; PM: 28726510

ABSTRACT: Knee osteoarthritis (OA) treatment is challenging due to inefficacy and adverse effects of current medications. Probiotic treatment has been shown to promote bone metabolism, reduce pain and inflammatory responses of age-related musculoskeletal disorders, including OA. We aimed to investigate the effect of probiotic Lactobacillus casei Shirota (LcS) on patients with knee OA. 537 patients with knee OA were enrolled in this double-blind, placebo-controlled trial, who were randomised to receive skimmed milk containing either LcS or placebo daily for 6 months. Primary outcome was defined as changes in WOMAC (Western Ontario and McMaster Universities Osteoarthritis Index) and VAS (visual analog scale) scores. Secondary outcome was defined as changes in serum levels of high sensitivity C-reactive protein (hs-CRP). After 6 months of treatment, both WOMAC and VAS scores were significantly improved in the LcS groups of patients compared to the placebo group. Serum levels of hs-CRP were also significantly lower in patients receiving LcS than placebo. Strong linear correlations were observed between serum hs-CRP levels and WOMAC and VAS scores. LcS consumption could serve as a novel therapeutic option in the clinical management of knee OA, improving treatment outcome likely through reducing serum hs-CRP levels.

Leite, L., Jude-Lemeilleur, F., Raymond, N., Henriques, I., Garabetian, F., and Alves, A. Phylogenetic diversity and functional characterization of the Manila clam microbiota: a culture-based approach. Environ.Sci.Pollut.Res.Int. 8-1-2017; PM: 28766142

ABSTRACT: According to the hologenome theory, the microbiota contributes to the fitness of the holobiont having an important role in its adaptation, survival, development, health, and evolution. Environmental stress also affects the microbiota and its capability to assist the holobiont in coping with stress factors. Here, we analyzed the diversity of cultivable bacteria associated with Manila clam tissues (mantle, gills, hemolymph) in two non-contaminated sites (Portugal and France) and one metal-contaminated site (Portugal). A total of 240 isolates were obtained. Representative isolates (n = 198) of the overall diversity were identified by 16S rDNA sequencing and subjected to functional characterization. Isolates affiliated with Proteobacteria, Actinobacteria, Firmicutes, and Bacteroidetes. Proteobacteria (mostly Pseudoalteromonadaceae and Vibrionaceae) were dominant in non-contaminated sites while Actinobacteria (mostly Microbacteriaceae) dominated in the metal-contaminated site. The main factor affecting the microbiota composition was contamination. No significant differences were observed between clam tissues and geographic regions. Several isolates tested positive for antibacterial activity, biofilm formation, protease, and siderophore production. The results show that the Manila clam harbors a diverse microbiota that may contribute to clam protection and overall fitness, as well as to its adaptation to stressful environments. In addition, the Manila clam microbiota is revealed as a promising source of novel probiotics with potential application in aquaculture.

Lewis, P. O., Lundberg, T. S., Tharp, J. L., and Runnels, C. W. Implementation of Global Strategies to Prevent Hospital-Onset Clostridium difficile Infection: Targeting Proton Pump Inhibitors and Probiotics. Ann.Pharmacother. 2017; 51(10):848-854; PM: 28821215

ABSTRACT: ***BACKGROUND***: Proton pump inhibitors (PPIs) have been identified as a significant risk factor for the development of Clostridium difficile infection (CDI). Probiotics given concurrently with antibiotics have been shown to have a moderate impact on preventing CDI. ***OBJECTIVE***: To evaluate the effectiveness of hospital-wide interventions designed to reduce PPI use and increase probiotics and whether these interventions were associated with a change in the incidence of hospital onset (HO)-CDI. ***METHODS***: This retrospective cohort study compared 2 fiscal years: July 2013 to June 2014 (FY14) and July 2014 to June 2015 (FY15). In July of FY15, global educational initiatives were launched targeting PPIs. Additionally, a HO-CDI prevention bundle was added to antibiotic-containing order sets targeting probiotics. Overall PPI use, probiotic use, and incidence of HO-CDI were recorded and compared for each cohort. Charts were also reviewed for patients who developed HO-CDI for the presence and appropriateness of a PPI and presence of probiotics. ***RESULTS***: The interventions resulted in a decrease in PPI use by 14% or 96 doses/1000 patient days (TPD; P = 0.0002) and a reduction in IV PPI use by 31% or 71 doses/TPD (P = 0.0008). Probiotic use increased by 130% or 126 doses/TPD (P = 0.0006). The incidence of HO-CDI decreased by 20% or 0.1 cases/TPD (P = 0.04). CONCLUSIONS: A collaborative, multifaceted educational initiative directed at highlighting the risks associated with PPI use was effective in reducing PPI prescribing. The implementation of a probiotic bundle added to antibiotic order sets was effective in increasing probiotic use. These interventions were associated with a decrease in incidence of HO-CDI.

Li, A. L., Sun, Y. Q., Du, P., Meng, X. C., Guo, L., Li, S., and Zhang, C. The Effect of Lactobacillus actobacillus Peptidoglycan on Bovine beta-Lactoglobulin-Sensitized Mice via TLR2/NF-kappaB Pathway. Iran J.Allergy Asthma Immunol. 2017; 16(2):147-158; PM: 28601055

ABSTRACT: Our previous study reported that Lactobacillus acidophilus(L.acidophilus) key laboratory of dairy science (KLDS) 1.0738 had an effective impact on inhibiting beta-lactoglobulin (beta-lg) allergy. This study further investigated the anti-allergic activity of peptidoglycan (PGN) isolated from KLDS 1.0738. This study aimed to assess whether toll-like receptor 2 (TLR2)/NF-kappaB (NF-kappaB) signaling activated by PGN was responsible for reducing allergic inflammation. Our data showed that administration of L. acidophilus PGN inhibited IgE production and improved the Treg/Th17 balance toward a Treg response in a mouse model of beta-lg allergy. In addition, treating different doses L. acidophilus PGN to sensitized mice significantly increased TLR2 levels, along with enhancing NF-kappaB expression, especially in medium and high concentration ($p<0.05$). Further analysis revealed that the mRNA expression of TLR2 and NF-kappaB were positively correlated with the Foxp3 mRNA expression ($p<0.05$), but were negatively correlated with the RORgammat mRNA expression in L. acidophilus PGN-treated group compared to allergy group (p<0.05). This study suggests PGN was similar to probiotics in preventing beta-lg allergy through regulating Treg/Th17 imbalance, and activation of TLR2/NF-kappaB signaling may be involved in this process.

Li, J., Riaz Rajoka, M. S., Shao, D., Jiang, C., Jin, M., Huang, Q., Yang, H., and Shi, J. Strategies to increase the efficacy of using gut microbiota for the modulation of obesity. Obes.Rev. 7-25-2017; PM: 28742949

ABSTRACT: Obesity is one of the most serious global public health challenges of the 21st century. The adjustment of gut microbiota is often recommended as an efficient strategy to treat obesity. This modulation of gut microbiota can be performed by many methods, including dietary intervention, antibiotic application, the use of prebiotics and probiotics, bariatric surgery and faecal microbiota transplantation. In most cases, positive effects have been observed in response to treatment, but invalid and even contrary effects have also been observed in some cases due to factors that are unrelated to intervention methods, such as genetic factors, patient age or gender, environmental microbiota, climate, geography and lifestyle. These factors can cause variation of gut microbial populations and thus should also be taken into consideration when selecting modulation strategies.

Li, J. Current status and prospective of in-feed additive antibiotics in the individual stage of the pork production. Asian-Australas.J.Anim Sci. 8-16-2017; PM: 28823126

ABSTRACT: Antibiotics have long been of great benefit for people, both in the medical treatment of human disease and in animal food that improves the growth performance and feed utilization during animal production. Antibiotics as in-feed supplements affect all stages of pork production, including the gestation, nursing, growing, and finishing stages, although the effects show stage-dependent differences. However, the use of antibiotics in animal feed has become a worldwide concern. This review describes why sub-therapeutic levels of antibiotic additives in animal feed have become an integral part of animal feeding programs for more than 70 years, particularly in pork production. It also discusses the threat of the long-term use of sub-therapeutic levels of antibiotics in pork production. In recent years, the effectiveness of in-feed antibiotics has tended to decrease. This review analyzes this change from various perspectives. First, the equipment used at pig farms has improved dramatically and is more sanitary. Worldwide, more pig farms use pig farrowing crates, gestation crates, piglet nursery

crates, flooring devices, piggery ventilation and cooler systems, automatic pig feeders, piggery heating equipment, and artificial insemination systems. In addition, scientists have replaced the use of antibiotics with organic acids, fermented mash, probiotics, prebiotics, minerals, oligosaccharides, enzymes, herbs/flavors, and protein/amino acids, and have improved management and husbandry techniques. In addition, animal welfare legislation has been aimed at improving the quality of the floors and living space, ensuring that animals have permanent access to fresh water, and setting a minimum weaning age. Finally, the prospects and the possibility of replacing antibiotics in pork production are described, in line with recent research results.

Li, Y., Feng, C., Li, J., Mu, Y., Liu, Y., Kong, M., Cheng, X., and Chen, X. Construction of multilayer alginate hydrogel beads for oral delivery of probiotics cells. Int.J.Biol.Macromol. 7-20-2017; PM: 28736041

ABSTRACT: Multilayer alginate hydrogel beads (MAHBs), which were prepared by emulsion method, had been fabricated via the ionic crosslinking between calcium ion (Ca2+) and carboxylic group of alginate and utilized as encapsulating material for oral delivery of a model probiotic bacteria Bifidobacterium breve. Optical and fluorescence microscopy obviously showed the microorganism cells were encapsulated in the core beads. The viability of B. breve cells encapsulated in MAHBs was significantly enhanced compared with ordinary free cultured ones, the top CFU per mL were (3.70+/-0.20)x107 and (2.61+/-0.22)x107 respectively. Meanwhile, B. breve cells encapsulated in MAHBs could still keep viability even after 12h' culture in the broth with pH value similar to gastric juice, while the free cultured cells had no activity in such culture condition. To test applicability of MAHBs for the delivery of microorganisms, a Gram-positive strain, Staphylococcus aureus, as well as a Gram-negative strain, Escherichia coli, were also employed and encapsulated in MAHBs. Similar to B. breve cells, the viability of encapsulated S. aureus cells and E. coli cells in extreme pH value environment were significantly promoted. In addition, a high alpha-amylase yielding efficiency Bacillus subtilis strain was found and encapsulated in MAHBs. Compared with control groups, MAHBs encapsulated B. subtilis cells produced more alpha-amylase after 240h' culture, while the release of this enzyme was sustained rather than the burst release like free cultured group, which means this system would not reduce metabolite yield while having long term sustained-release effect. In summary, MAHBs are favorable biological carrier, which has the potential of being applied to oral delivery of probiotics.

Li, Y., Ku, S., Park, M. S., Li, Z., and Ji, G. E. Acceleration of aglycone isoflavones and gamma-aminobutyric acid production from doenjang using whole cell biocatalysis accompanied by protease treatment. J.Microbiol.Biotechnol. 9-15-2017; PM: 28910863

ABSTRACT: Recently, soy bean isoflavone aglycones (i.e. daidzein and genistein) and gamma-aminobutyric acid (GABA) have begun to receive considerable consumer attention due to their potential as nutraceuticals. To produce these ingredients, multiple microorganisms and their enzymes are commonly used for catalysis in the nutraceutical industry. In this work, we introduce a novel fermentation process that uses whole cell biocatalysis to accelerate gamma-aminobutyric acid and isoflavone aglycones production in doenjang (traditional Korean soybean paste). Microbial enzymes transform soybean isoflavone glycosides (i.e. daidzin and genistin) and monosodium glutamate into soy bean isoflavone aglycones and GABA. Lactobacillus brevis GABA 100 and Aspergillus oryzae KACC significantly reduced production time with the aid of a

protease. The resulting levels of gamma-aminobutyric acid and daidzein are higher, and genistein production resembled the levels in traditional doenjang fermented for over a year. Concentrations of gamma-aminobutyric acid, daidzein, and genistein were measured as 7162 mug/g, 60 mug/g, and 59 mug/g, respectively on the seventh day of fermentation. Our results demonstrate that the administration of whole cell Lactobacillus brevis GABA 100 and Aspergillus oryzae KACC 40250 paired with a protease treatment is an effective method to accelerate gamma-aminobutyric acid, daidzein, and genistein production in doenjang.

Lim, N. R., Lohman, M. E., and Lio, P. A. The Role of Elimination Diets in Atopic Dermatitis-A Comprehensive Review. Pediatr.Dermatol. 2017; 34(5):516-527; PM: 28884902

ABSTRACT: ***BACKGROUND/OBJECTIVES***: Diet is a common concern for individuals with atopic dermatitis (AD) and their families. Studies regarding the effect of dietary interventions on AD exist, but many are limited by small size and poor design. Conflicting results present a challenge to clinicians seeking to counsel patients. The aim of the current review is to examine the published literature and generate helpful conclusions for clinicians faced with dietary questions in AD. ***METHODS***: A PubMed search was performed focusing on dietary interventions for AD in children and adults through July 2016. The search was limited to the English language and included studies that evaluated one or more forms of dietary modification for the treatment of AD. Studies of supplementation, such as with vitamins, minerals, or probiotics, were not included, nor were studies on prevention of the development of AD. A total of 43 articles met the inclusion criteria and were included in the final analysis. ***RESULTS***: Trials varied in type, duration, and the AD patient populations studied. Overall, there is some level I evidence to support specific exclusion diets in preselected patients but insufficient evidence for strict elimination diets (diets that are typically limited to six to eight foods). Data supporting other interventions are mixed and based on small, poorly designed studies. ***CONCLUSIONS***: A comprehensive literature review reveals some promising results and several areas in need of further study. More evidence is needed to form a strong foundation for recommendations regarding the utility and role of elimination diets in AD management, but current evidence suggests that strict diet management is not effective in the treatment AD in the vast majority of patients.

Lin, C. H., Shih, T. W., and Pan, T. M. A "Ct contrast"-based strain-specific real-time quantitative PCR system for Lactobacilllus paracasei subsp. paracasei NTU 101. J.Microbiol.Immunol.Infect. 6-28-2017; PM: 28693925¶

ABSTRACT: ***BACKGROUND/PURPOSES***: Routine cell number determination for specific Lactobacillus strain by cultivation requires at least 4-7 days. Thus rapid and specific cell number determine methods such as strain-specific quantitative PCR (qPCR) are valuable. However, qPCR method is vulnerable to difficult PCR target such as dimer/secondary structure forming sequence. ***METHODS***: In this study, a two-component, "Ct contrast" approach was applied to strain-specific qPCR system following the development of Lactobacillus paracasei subsp. paracasei NTU 101 (NTU 101) strain-specific PCR with random amplification of polymorphic DNA (RAPD)-derived strain-specific sequences. ***RESULTS***: The quantitative range of the NTU 101 strain-specific qPCR system was 3.0 x 101 to 3.0 x 105 copies for pure cultures, and 3.0 x 102 to 3.0 x 105 copies for multi-strain or unknown food samples. The results of spike in test and real sample testing suggested that non-specific weak background signals did not compromise test

specificity, and demonstrated the potential of the NTU 101 strain-specific qPCR system in food samples. ***CONCLUSION***: The two-component, "Ct contrast" approach is useful for qPCR discrimination when no ideal PCR target is available or the variance of the target site is unpredictable. The Ct contrast approach might provide a simple and robust solution for other challenging qPCR targets.

Lin, X., Chen, X., Tu, Y., Wang, S., and Chen, H. Effect of Probiotic Lactobacilli on the Growth of Streptococcus Mutans and Multispecies Biofilms Isolated from Children with Active Caries. Med.Sci.Monit. 8-30-2017; 23:4175-4181; PM: 28851857

ABSTRACT: ***BACKGROUND:*** The purpose of this investigation was to evaluate the effect of probiotic lactobacilli on Streptococcus mutans (MS) and multispecies biofilms isolated from children with severe caries. ***MATERIAL AND METHODS:*** Twenty children with active caries (DMFS >/=6) were selected as the experimental group and Streptococcus mutans (MS) were isolated from their saliva. After identification the MS strains were mixed with lactobacilli at 37 degrees C, following which viable MS colonies were counted. At the same time dental plaques from the children were mixed with lactobacilli in vitro to form biofilms, and the population of nine common strains in the biofilms was enumerated after 24 hours of growth. ***RESULTS***: Lactobacillus casei Shirota, L. casei LC01, L. plantarum ST-III and L. paracasei LPC37 all had strong inhibitory effects on the majority the MS isolated from children with active caries, with the inhibition rate reaching approximately 70-90% ($p<0.05$). L. casei Shirota, L. casei LC01, L. plantarum ST-III, L. paracasei LPC37 also significantly reduced the numbers of MS, Streptococcus spp., S. sanguinis and total bacteria in mixed biofilms compared with the control group ($p<0.05$). ***CONCLUSIONS***: The four strains of lactobacilli were able to inhibit the growth of Streptococcus mutans and had effects on the composition of bacterial biofilms in vitro. Ingestion of probiotics may be a promising method of caries prevention.

Liu, H., Hou, C., Wang, G., Jia, H., Yu, H., Zeng, X., Thacker, P. A., Zhang, G., and Qiao, S. Lactobacillus reuteri I5007 Modulates Intestinal Host Defense Peptide Expression in the Model of IPEC-J2 Cells and Neonatal Piglets. Nutrients. 5-31-2017; 9(6); PM: 28561758

ABSTRACT: Modulation of the synthesis of endogenous host defense peptides (HDPs) by probiotics represents a novel antimicrobial approach for disease control and prevention, particularly against antibiotic-resistant infections in human and animals. However, the extent of HDP modulation by probiotics is species dependent and strain specific. In the present study, The porcine small intestinal epithelial cell line (IPEC-J2) cells and neonatal piglets were used as in-vitro and in-vivo models to test whether Lactobacillus reuteri I5007 could modulate intestinal HDP expression. Gene expressions of HDPs, toll-like receptors, and fatty acid receptors were determined, as well as colonic short chain fatty acid concentrations and microbiota. Exposure to 10(8) colony forming units (CFU)/mL of L. reuteri I5007 for 6 h significantly increased the expression of porcine beta-Defensin2 (PBD2), pBD3, pBD114, pBD129, and protegrins (PG) 1-5 in IPEC-J2 cells. Similarly, L. reuteri I5007 administration significantly increased the expression of jejunal pBD2 as well as colonic pBD2, pBD3, pBD114, and pBD129 in neonatal piglets ($p < 0.05$). This was probably associated with the increase in colonic butyric acid concentration and up-regulating expression of Peroxisome Proliferator-Activated Receptor-gamma (PPAR-gamma) and G Protein-Coupled Receptor 41 (GPR41) ($p < 0.05$), but not with stimulation of Pattern-Recognition Receptors. Additionally, supplementation with L. reuteri I5007 in the piglets did not affect the colonic microbiota structure. Our findings suggested that L.

reuteri I5007 could modulate intestinal HDP expression and improve the gut health of neonatal piglets, probably through the increase in colonic butyric acid concentration and the up-regulation of the downstream molecules of butyric acid, PPAR-gamma and GPR41, but not through modifying gut microbiota structure.

Liu, M. M., Li, S. T., Shu, Y., and Zhan, H. Q. Probiotics for prevention of radiation-induced diarrhea: A meta-analysis of randomized controlled trials. PLoS.One. 2017; 12(6):e0178870; PM: 28575095

ABSTRACT: ***BACKGROUND***: Radiotherapy is commonly used for abdominal or pelvic cancer, and patients receiving radiotherapy have a high risk developing to an acute radiation-induced diarrhea. Several previous studies have discussed the effect of probiotics on prevention of radiation-induced diarrhea, but the results are still inconsistent. ***OBJECTIVE***: We performed a meta-analysis of randomized controlled trials (RCTs) to evaluate the efficacy of probiotic supplementation for prevention the radiation-induced diarrhea. ***METHODS***: Relevant RCTs studies assessing the effect of probiotic supplementation on clinical outcomes compared with placebo were searched in PubMed, EMBASE, and the Cochrane Library databases (up to March 30 2016). Heterogeneity was assessed with I2 and H2, and publication bias was evaluated using sensitive analysis. ***RESULTS***: Six trials, a total of 917 participants (490 participants received prophylactic probiotics and 427 participants received placebo), were included in this meta-analysis. Compared with placebo, probiotics were associated with a lower incidence of radiation-induced diarrhea (RR: 0.55; 95% CI: 0.34-0.88; P = 0.01; I2: 87%; 95% CI: 75%-94%; H2: 2.8; 95% CI: 2.0-4.0). However, there is no significant difference in the anti-diarrheal medication use (RR: 0.68; 95% CI: 0.40-1.14; P = 0.14) or bristol scale on stool form (RR: 0.64; 95% CI: 0.35-1.17; P = 0.14). ***CONCLUSION***: Probiotics may be beneficial to prevent radiation-induced diarrhea in patients who suffered from abdominal or pelvic cancers during radiotherapy period.

Liu, M. Q., Huo, W. K., Xu, X., and Weng, X. Y. Recombinant Bacillus amyloliquefaciens xylanase A expressed in Pichia pastoris and generation of xylooligosaccharides from xylans and wheat bran. Int.J.Biol.Macromol. 7-18-2017; PM: 28732724

ABSTRACT: In this study, BaxA (GenBank: KM624029), which encodes the Bacillus amyloliquefaciens xylanase A (BaxA), was highly expressed in Pichia pastoris GS115 under the control of the AOX1 promoter. The recombinant xylanase, namely rePBaxA, was purified to homogeneity by using Ni-affinity resin and its molecular weight was 35.0kDa. The optimum temperature and pH of rePBaxA were 50 degrees C and 5.0, respectively. The kinetic parameters Michaelis-Menten constant (Km) and maximum reaction rate (Vmax) of rePBaxA were 5.41mg/mL and 22.42mumol/min/mL, respectively. High-performance liquid chromatography results showed that after 6h of hydrolysis, rePBaxA released xylose-xylohexaose (X1-X6) mixture from beechwood and birchwood xylan, with xylobiose (X2) and xylotriose (X3) as the major products, respectively. The hydrolyates from oat spelt, wheat bran insoluble xylan and pretreated wheat bran by rePBaxA included X2-X6, with X6 having the highest concentration. The mode of action analysis revealed that rePBaxA was an endo-acting xylanase with transglycosylation activity. X2 might be the minimum oligomer hydrolyzed by rePBaxA. The pretreated wheat bran and wheat bran insoluble xylan could be directly hydrolyzed by rePBaxA. This study provided a basis for using agricultural waste by-products as substrates for manufacting value-added probiotics, namely, xylooligosaccharides.

Liu, Y., Liu, J. M., Zhang, D., Ge, K., Wang, P., Liu, H., Fang, G., and Wang, S. Persistent Luminescence Nanophosphor Involved Near-Infrared Optical Bioimaging for Investigation of Foodborne Probiotics Biodistribution in Vivo: A Proof-of-Concept Study. J.Agric.Food Chem. 9-10-2017; PM: 28837320

ABSTRACT: Probiotics has attracted great attention in food nutrition and safety research field, but thus far there are limited analytical techniques for visualized and real-time monitoring of the probiotics when they are ingested in vivo. Herein, the optical bioimaging technique has been introduced for investigation of foodborne probiotics biodistribution in vivo, employing the near-infrared (NIR) emitting persistent luminescence nanophosphors (PLNPs) of Cr3+-doped zinc gallogermanate (ZGGO) as the contrast nanoprobes. The ultrabrightness, super long afterglow, polydispersed size, low toxicity, and excellent photostability and biocompatibility of PLNPs were demonstrated to be qualified as a tracer for labeling probiotics via antibody (anti-Gram positive bacteria LTA antibody) recognition as well as contrast agent for long-term bioimaging the probiotics. In vivo optical bioimaging assay showed that the LTA antibody functionalized ZGGO nanoprobes that could be efficiently tagged to the probiobics were successfully applied for real-time monitoring and nondamaged probing of the biodistribution of probiotics inside the living body after oral administration. This work presents a proof-of-concept that exploited the bioimaging methodology for real-time and nondamaged researching the foodborne probiotics behaviors in vivo, which would open up a novel way of food safety detection and nutrition investigation.

Ljubobratovic, U., Kosanovic, D., Vukotic, G., Molnar, Z., Stanisavljevic, N., Ristovic, T., Peter, G., Lukic, J., and Jeney, G. Supplementation of lactobacilli improves growth, regulates microbiota composition and suppresses skeletal anomalies in juvenile pike-perch (Sander lucioperca) reared in recirculating aquaculture system (RAS): A pilot study. Res.Vet.Sci. 7-24-2017; 115:451-462; PM: 28777955

ABSTRACT: This research aimed to test the effects of lactobacilli, applied to cultured pike-perch, either through hydrolyzed OTOHIME fish diet, or through Artemia nauplii, on fish growth, microbiota balance and skeletal development. On the 12th Day Post Hatching (DPH) fish were divided into following treatment groups: two groups received the combination of OTOHIME and nauplii enriched either with Lactobacillus paracasei BGHN14+Lactobacillus rhamnosus BGT10 or with Lactobacillus reuteri BGGO6-55+Lactobacillus salivarius BGHO1, and one group received OTOHIME hydrolyzed by BGHN14+BGT10 and non-enriched nauplii. Control group received non-enriched nauplii and non-hydrolyzed OTOHIME. The treatment lasted 14days and fish were sacrificed on the 26th DPH for the assessment of digestive enzyme activity and microbiota composition. Individual total lengths and individual body weights were recorded at the end of the treatments, on the 26th DPH, and also on the 45th DPH, in parallel with the evaluation of skeletal deformities and fish survival. Our results indicated positive effect of Artemia enriched with BGGO6-55+BGHO1 on fish growth, skeletal development and trypsin to chymotrypsin activity ratio (T/C), as an indicator of protein digestibility. Hydrolysis of OTOHIME was also associated with better skeletal development, higher T/C values and lower levels of Aeromonas and Mycobacterium spp., which are important fish pathogens. Though additional testing in larger cohort studies is needed, these observations are promising in terms of usage of probiotics for improved environmentally friendly production of pike-perch in Recirculating Aquaculture System (RAS).

Lo, Verso L., Lessard, M., Talbot, G., Fernandez, B., and Fliss, I. Isolation and Selection of Potential Probiotic Bacteria from the Pig Gastrointestinal Tract. Probiotics.Antimicrob.Proteins. 7-25-2017; PM: 28744832

ABSTRACT: The present study aimed to isolate bacterial strains from the pig gastrointestinal tract that have antagonistic activity against potential pathogens and are able to produce antimicrobial compounds. That ability would be a first requirement for the strains' possible use as probiotics. Samples obtained from pig intestinal mucosa and contents were screened for the presence of antagonistic activity against pathogenic indicator strains of Escherichia coli, Salmonella, and Listeria by means of the double-layer technique. Samples displaying the largest inhibitory halos were further studied for the production of inhibitory substances using the agar diffusion and microtitration methods. The three most promising isolates were identified by sequencing of the 16S rRNA gene and showed highest affiliation to Lactobacillus salivarius. Optimal growth conditions and bacteriocin production were recorded in de Man, Rogosa, and Sharpe broth under anaerobic conditions at 37 degrees C. The antimicrobial substances were found to be sensitive to proteolytic enzymes but showed good stability at pH values below 6. Our findings suggest that these three intestinal strains are able to produce antimicrobial substances capable of inhibiting the growth of potential enteric pathogens and might have potential as probiotic feed additives for the prevention of gastrointestinal diseases.

Maguire, M. and Maguire, G. The role of microbiota, and probiotics and prebiotics in skin health. Arch.Dermatol.Res. 2017; 309(6):411-421; PM: 28631091

ABSTRACT: During the past decade, scientists have made great strides in understanding the microbiome's role in human health. Today, the microbiome has become key in scientific research, therapeutic development, medical treatment, and as a news feature in the media. Most studies have focused on the microbiome of our gut, but recently researchers have turned their attention to other microbiomes, including that of the skin. These studies of gut and skin microbiomes are yielding very informative results, new treatment strategies, and the development of new prebiotic and probiotic products for the treatment of many skin conditions.

Mahdhi, A., Leban, N., Chakroun, I., Chaouch, M. A., Hafsa, J., Fdhila, K., Mahdouani, K., and Majdoub, H. Extracellular polysaccharide derived from potential probiotic strain with antioxidant and antibacterial activities as a prebiotic agent to control pathogenic bacterial biofilm formation. Microb.Pathog. 2017; 109:214-220; PM: 28583888

ABSTRACT: Because of their functional diversity, bioactive compounds are becoming a new biocontrol agent to limit biofilm formation by pathogens. In this study, the physico-chemical characterization of an exopolysaccharide (EPS) isolated from Lactobacillus plantarum (EPLB) was characterized and its in vitro effect on biofilm formation was studied. The EPS had a molecular weight of 36 kDa and polydispersity index estimated to be 1.2. The tested EPLB had an antibacterial activity, with a Minimal Inhibition Concentration (MIC) values ranging between 1 mg/ml and 10 mg/ml, displayed an antibiofilm effect concentration dependent on Gram positive and negative strains. Among the pathogenic strains, 2 out of 4 appeared to be more than 50% inhibited in their biofilm development by the EPS. The antibiofilm activity can be due to the ability of the EPS to influence the function of biological membranes like hydrophobicity that

decreased (P < 0.05) when the EPS was used at a concentration of 512 mug/ml. This EPS without cytotoxic effect, showed an antioxidant effect on the quenching of DPPH radicals and the inhibition of lipid peroxidation with a percentage of 64% and 66%, respectively. Taken together these biological properties, EPLB can be considered as a potential prebiotic agent in the design of new therapeutic strategies for bacterial biofilm-associated infections.

Malik, R. Randomized Controlled Trial Evaluating Probiotics in Children with Severe Acute Malnutrition: Pediatric Gastroenterologist's Viewpoint. Indian Pediatr. 6-15-2017; 54(6):493; PM: 28667722

No Abstract Available.

Mallina, R., Craik, J., Briffa, N., Ahluwalia, V., Clarke, J., and Cobb, A. G. Probiotic containing Lactobacillus casei, Lactobacillus bulgaricus, and Streptococcus thermophiles (ACTIMEL) for the prevention of Clostridium difficile associated diarrhoea in the elderly with proximal femur fractures. J.Infect.Public Health. 6-23-2017; PM: 28652125

ABSTRACT: The incidence of Clostridium difficile associated diarrhoea (CDAD) is greater in elderly patients. Probiotics may have a beneficial effect in the prevention of CDAD. However, their effect in elderly orthopaedic patients has not been previously reported. Between April 2013 and April 2014, 105 patients admitted with femoral neck fractures, and who required 3days of antibiotics for infection of any cause, were prescribed the probiotic ACTIMEL until 3days after the last antibiotic dose. The incidence of CDAD was compared with historical controls (April 2011-April 2012). There was no significant reduction in the incidence of CDAD in patients receiving probiotics (OR: 0.9; 95% CI 0.27-2.91; p=0.8) and therefore we cannot recommend the use of ACTIMEL containing Lactobacillus casei, Lactobacillus bulgaricus, and Streptococcus thermophiles for this purpose in this patient group.

Mantegazza, C., Molinari, P., D'Auria, E., Sonnino, M., Morelli, L., and Zuccotti, G. V. Probiotics and antibiotic-associated diarrhea in children: A review and new evidence on Lactobacillus rhamnosus GG during and after antibiotic treatment. Pharmacol.Res. 8-19-2017; PM: 28827186

ABSTRACT: Antibiotic associated diarrhea (AAD) is a common complication in childhood in the outpatient and inpatient settings. This review provides up to date information on the use of probiotics in the prevention and treatment of AAD, including that from Clostridium Difficile, in children. The most recently systematic reviews and subsequently published randomized controlleds trials are considered. Different single and multistrain probiotics are described; a specific recommendation for the use of Lactobacillus Rhamnosus GG (LGG) and Saccharomyces boulardii (Sb) emerges. New information on LGG survival under amoxicillin/clavulanate therapy in children is also provided. This information is relevant in view of the frequent use of this molecule in children, its association with AAD, and LGG's sensitivity to penicillin that might make this probiotic ineffective. In spite of a demonstrated positive effect of specific strains of probiotics on AAD, safety issues still remain among which the risk of associated severe infections and of antibiotic resistant gene exchange.

Mantziari, A., Aakko, J., Kumar, H., Tolkko, S., du, Toit E., Salminen, S., Isolauri, E., and Rautava, S. The Impact of Storage Conditions on the Stability of Lactobacillus rhamnosus GG and Bifidobacterium animalis subsp. lactis Bb12 in Human Milk. Breastfeed.Med. 7-28-2017; PM: 28753043

ABSTRACT: Human milk is the optimal source of complete nutrition for neonates and it also guides the development of infant gut microbiota. Importantly, human milk can be supplemented with probiotics to complement the health benefits of breastfeeding. Storage of human milk for limited periods of time is often unavoidable, but little is known about the effect of different storage conditions (temperature) on the viability of the added probiotics. Therefore, in this study, we evaluated how different storage conditions affect the viability of two specific widely used probiotics, Lactobacillus rhamnosus GG (LGG) and Bifidobacterium animalis subsp. lactis (Bb12), in human milk by culturing and quantitative polymerase chain reaction. Our results indicate that LGG and Bb12 remained stable throughout the storage period. Thus, we conclude that human milk offers an appropriate matrix for probiotic supplementation.

Manzano, S., De, Andres J., Castro, I., Rodriguez, J. M., Jimenez, E., and Espinosa-Martos, I. Safety and tolerance of three probiotic strains in healthy infants: a multi-centre randomized, double-blind, placebo-controlled trial. Benef.Microbes. 8-24-2017; 8(4):569-578; PM: 28555502

ABSTRACT: Some strains of species belonging to the genera Bifidobacterium and Lactobacillus are used in order to maintain health. Although these organisms have a long record of safe use, it is important to assess their safety and tolerance in potentially vulnerable populations, such as infants. The objective of this study was to evaluate the safety and tolerance of three probiotic strains (Bifidobacterium longum subsp. infantis R0033, Bifidobacterium bifidum R0071 and Lactobacillus helveticus R0052) in healthy infants aged 3 to 12 months. A multi-centre randomized, double-blind, placebo-controlled intervention study with 221 healthy full-term infants was conducted. Infants received either a placebo or one of the 3 probiotic strains (3x109 cfu) daily during an 8 week intervention period. Growth (weight, height and head circumference), adverse events (AEs)/serious adverse events (SAEs), concentrations of D-lactic acid in urine samples, characteristics of the stools and use of medication were collected for safety evaluation. All 4 groups were homogeneous with respect to age, gender, feeding type, ethnicity, height, weight and head circumference at the start of the study. The results showed that changes in growth (weight, height and head circumference) were equivalent in all 4 groups. No SAEs were reported. Total number of AEs recorded was equivalent in all groups. Thus, the use of B. infantis R0033, L. helveticus R0052 and B. bifidum R0071 in infancy is safe, and well tolerated.

Maragkoudaki, M., Chouliaras, G., Orel, R., Horvath, A., Szajewska, H., and Papadopoulou, A. Lactobacillus reuteri DSM 17938 and a placebo both significantly reduced symptoms in children with functional abdominal pain. Acta Paediatr. 7-16-2017; PM: 28712129

ABSTRACT: ***AIM***: Lactobacillus reuteri is a Gram-positive bacterium that naturally inhabits the human intestinal tract. This study assessed how effectively the probiotic L. reuteri DSM 17938 managed childhood functional abdominal pain (FAP). ***METHODS***: We recruited 54 children with a mean age 9.1 +/- 3.8 years, who were diagnosed with FAP in the

outpatient clinics of three university hospitals in Greece, Slovenia and Poland, according to the Rome III criteria, from January 2013 to December 2015. They were randomly assigned to receive either 2 x 108 colony-forming units of L. reuteri (n = 27) or a placebo (n = 27) for four weeks. ***RESULTS***: Both L. reuteri and the placebo significantly reduced the frequency and intensity of abdominal pain episodes at four and eight weeks compared to baseline (all $p < 0.001$). L. reuteri decreased the use of pain relieving drugs at four weeks and the number of child school and adult work absences at four and eight weeks, unlike the placebo, which achieved nonsignificant results. However, the difference between the groups did not reach significance. No side effects were recorded. ***CONCLUSION***: Both L. reuteri and the placebo were effective in alleviating pain in children with FAP, but only L. reuteri improved the child's and family's normal activities.

Marcial-Coba, M. S., Marshall, I. P. G., Schreiber, L., and Nielsen, D. S. High-Quality Draft Genome Sequence of Lactobacillus casei Strain Z11, Isolated from a Human Adult Intestinal Biopsy Sample. Genome Announc. 7-13-2017; 5(28); PM: 28705981

ABSTRACT: Several Lactobacillus casei strains are used as probiotics. L. casei strain Z11, isolated from a human colon biopsy sample, has been suggested as a probiotic candidate based on promising properties in vitro Here, we present a 2.74-Mbp high-quality draft genome sequence for this strain.

Marinelli, L., Tenore, G. C., and Novellino, E. Probiotic species in the modulation of the anticancer immune response. Semin.Cancer Biol. 8-24-2017; PM: 28844794

ABSTRACT: Mounting evidences are supporting a key role of distinct gut bacteria in the occurrence and progression of intestinal and extra-intestinal tumors. More importantly, it has been recently demonstrated that some gut bacteria strains synergize with largely-used anticancer drugs as alkylating or immune checkpoint blockade agents thus optimizing the immune response against multiple solid cancers. However, the exact role played by each gut bacterium in cancer occurrence and response to therapy is still in its infancy; and the current knowledge, although exciting, still needs to be transferred from mice models to human beings. Here, the advances in the understanding of how gut microbes and immune response shape each other in a cancer context are reviewed together with the implications of these finding for future antitumor therapy. Herein, the most important bacteria strains, able to boost the immune response triggered by anticancer drugs, together with their mechanism of action, whenever known, have been surveyed. It is reasonable to think that cocktails of beneficial bacteria together with an ad hoc diet or food supplements may be used as novel anticancer adjuvant agents in future therapeutic regimens.

Markowiak, P. and Slizewska, K. Effects of Probiotics, Prebiotics, and Synbiotics on Human Health. Nutrients. 9-15-2017; 9(9); PM: 28914794

ABSTRACT: The human gastrointestinal tract is colonised by a complex ecosystem of microorganisms. Intestinal bacteria are not only commensal, but they also undergo a synbiotic co-evolution along with their host. Beneficial intestinal bacteria have numerous and important functions, e.g., they produce various nutrients for their host, prevent infections caused by intestinal pathogens, and modulate a normal immunological response. Therefore, modification of the intestinal microbiota in order to achieve, restore,

and maintain favourable balance in the ecosystem, and the activity of microorganisms present in the gastrointestinal tract is necessary for the improved health condition of the host. The introduction of probiotics, prebiotics, or synbiotics into human diet is favourable for the intestinal microbiota. They may be consumed in the form of raw vegetables and fruit, fermented pickles, or dairy products. Another source may be pharmaceutical formulas and functional food. This paper provides a review of available information and summarises the current knowledge on the effects of probiotics, prebiotics, and synbiotics on human health. The mechanism of beneficial action of those substances is discussed, and verified study results proving their efficacy in human nutrition are presented.

Marshall, H., Chrismas, B. C. R., Suckling, C. A., Roberts, J. D., Foster, J., and Taylor, L. Chronic probiotic supplementation with or without glutamine does not influence the eHsp72 response to a multi-day ultra-endurance exercise event. Appl.Physiol Nutr.Metab. 2017; 42(8):876-883; PM: 28460195

ABSTRACT: Probiotic and glutamine supplementation increases tissue Hsp72, but their influence on extracellular Hsp72 (eHsp72) has not been investigated. The aim of this study was to investigate the effect of chronic probiotic supplementation, with or without glutamine, on eHsp72 concentration before and after an ultramarathon. Thirty-two participants were split into 3 independent groups, where they ingested probiotic capsules (PRO; n = 11), probiotic + glutamine powder (PGLn; n = 10), or no supplementation (CON; n = 11), over a 12-week period prior to commencement of the Marathon des Sables (MDS). eHsp72 concentration in the plasma was measured at baseline, 7 days pre-race, 6-8 h post-race, and 7 days post-race. The MDS increased eHsp72 concentrations by 124% ($F[1,3] = 22.716$, $p < 0.001$), but there was no difference in the response between groups. Additionally, PRO or PGLn supplementation did not modify pre- or post-MDS eHsp72 concentrations compared with CON ($p > 0.05$). In conclusion, the MDS caused a substantial increase in eHsp72 concentration, indicating high levels of systemic stress. However, chronic PRO or PGLn supplementation did not affect eHsp72 compared with control pre- or post-MDS. Given the role of eHsp72 in immune activation, the commercially available supplements used in this study are unlikely to influence this cascade.

Martin, R., Chain, F., Miquel, S., Motta, J. P., Vergnolle, N., Sokol, H., and Langella, P. Using murine colitis models to analyze probiotics-host interactions. FEMS Microbiol.Rev. 8-1-2017; 41(Supp_1):S49-S70; PM: 28830096

ABSTRACT: Probiotics are defined as 'live microorganisms which when administered in adequate amounts confer a health benefit on the host'. So, to consider a microorganism as a probiotic, a demonstrable beneficial effect on the health host should be shown as well as an adequate defined safety status and the capacity to survive transit through the gastrointestinal tract and to storage conditions. In this review, we present an overview of the murine colitis models currently employed to test the beneficial effect of the probiotic strains as well as an overview of the probiotics already tested. Our aim is to highlight both the importance of the adequate selection of the animal model to test the potential probiotic strains and of the value of the knowledge generated by these in vivo tests.

Martinelli, M., Ummarino, D., Giugliano, F. P., Sciorio, E., Tortora, C., Bruzzese, D., De, Giovanni D., Rutigliano, I., Valenti, S., Romano, C., Campanozzi, A., Miele, E., and Staiano, A. Efficacy

of a standardized extract of Matricariae chamomilla L., Melissa officinalis L. and tyndallized Lactobacillus acidophilus (HA122) in infantile colic: An open randomized controlled trial. Neurogastroenterol.Motil. 6-30-2017; PM: 28665038

ABSTRACT: ***BACKGROUND***: Infant colic (IC) is a prevalent physiological event of infants, which can disrupt the child's home environment. We aimed to investigate the effectiveness of a mixture of Matricariae chamomilla L., Melissa officinalis L. and tyndallized Lactobacillus acidophilus (HA122) compared with Lactobacillus reuteri DSM 17938 and with simethicone for the treatment of IC. ***METHODS***: A multicenter randomized comparative study was conducted in infants with colic, according to Rome III criteria, who were randomly assigned to receive M. chamomilla L., M. officinalis L. and tyndallized L. acidophilus (HA122) (Colimil(R) Plus(R) ; Milte Italia Spa, Milan, Italy) (Group A), L. reuteri DSM 17938 (Group B) and simethicone (Group C). Treatment was given to subjects for 28 days. ***KEY RESULTS***: One-hundred and seventy-six patients completed the study. Mean daily crying time at day 28 was significantly lower in group A (-44, 95% CI: -58 to -30, P<.001) and group B (-35, 95% CI: -49 to -20, P<.001) when compared to group C. No significant difference was observed between Group A and Group B (mean difference: -9 minutes, 95% CI -23 to +5, P=.205). At day 28, 39 of 57 (68.4%) of infants in Group C responded to the treatment compared with 57 out of 60 patients (95%) of Group A and 51 out of 59 (86.4%) of Group B (P<.001). ***CONCLUSIONS***: This study suggests that administration of M. chamomilla L., M. officinalis L. and tyndallized L. acidophilus (HA122) and L. reuteri DSM 17938 are significantly more effective than simethicone in IC. ***CLINICAL TRIAL REGISTRATION***: ClinicalTrials.gov: NCT02708238.

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.

Mascellino, M. T., Porowska, B., De, Angelis M., and Oliva, A. Antibiotic susceptibility, heteroresistance, and updated treatment strategies in Helicobacter pylori infection. Drug Des Devel.Ther. 2017; 11:2209-2220; PM: 28814829

ABSTRACT: In this review, we discuss the problem of antibiotic resistance, heteroresistance, the utility of cultures and antibiotic susceptibility tests in Helicobacter pylori (Hp) eradication, as well as the updated treatment strategies for this infection. The prevalence of antibiotic resistance is increasing all over the world, especially for metronidazole and clarithromycin, because of their heavy use in some geographical areas. Heteroresistance (simultaneous presence of both susceptible and resistant strains in different sites of a single stomach) is another important issue, as an isolate could be mistakenly considered susceptible if a single biopsy is used for antimicrobial tests. We also examined literature data regarding eradication success rates of culture-guided and empiric therapies. The empiric therapy and the one based on susceptibility testing, in Hp eradication, may depend on several factors such as concomitant diseases, the number of previous antibiotic treatments, differences in bacterial virulence in individuals with positive or negative cultures, together with local antibiotic resistance patterns in real-world settings. Updated treatment strategies in Hp infection presented in the guidelines of the Toronto Consensus Group (2016) are reported. These suggest to prolong eradication therapy up to 14 days, replacing the old triple therapy with a quadruple therapy based on proton pump inhibitor (PPI), bismuth, metronidazole, and tetracycline for most of the patients, or as an alternative quadruple therapy without bismuth, based on the use of PPI, amoxicillin, metronidazole, and clarithromycin. The new drug vonoprazan, a first-in-class potassium-competitive acid blocker recently approved in Japan, is also considered to be a promising solution for Hp eradication, even for clarithromycin-resistant strains. Furthermore, there is growing interest in finding new therapeutic strategies, such as the development of vaccines or the use of natural resources, including probiotics, plants, or nutraceuticals.

Mason, B. L. Feeding Systems and the Gut Microbiome: Gut-Brain Interactions With Relevance to Psychiatric Conditions. Psychosomatics. 6-8-2017; PM: 28716445

ABSTRACT: ***BACKGROUND***: Physical and mental health is dependent on the environment, and feeding is a prime example of this environmental exchange. While the hypothalamus controls both feeding behavior and the stress response, the integration of the neural control centers and the peripheral gut allows for disruption in the gastrointestinal systems and dysfunctional communication to the brain. ***OBJECTIVE***: The purpose of this review is to familiarize clinicians with the physiology controlling feeding behavior and its implications for psychiatric conditions, such as anorexia nervosa and depression. Growing understanding of how integrated bacterial life is in the body has shown that gut bacteria regulate basic physiologic processes and are implicated in various disease states and contribute to regulation of mood. Responses to stress have effects on feeding behavior and mood and the regulation of the stress response by the gut microbiota could contribute to the dysfunction seen in patients with psychiatric illnesses. ***CONCLUSIONS***: Gut microbiota may contribute to dysfunction in psychiatric illnesses. New opportunities to modulate existing gut microbiota using probiotics could be novel targets for clinical interventions.

Mathew, J. L. Randomized Controlled Trial Evaluating Probiotics in Children with Severe Acute Malnutrition: Evidence-based Medicine Viewpoint. Indian Pediatr. 6-15-2017; 54(6):489-492; PM: 28667720

No Abstract Available.

Mauricio, M. D., Serna, E., Fernandez-Murga, M. L., Portero, J., Aldasoro, M., Valles, S. L., Sanz, Y., and Vila, J. M. Bifidobacterium pseudocatenulatum CECT 7765 supplementation restores altered vascular function in an experimental model of obese mice. Int.J.Med.Sci. 2017; 14(5):444-451; PM: 28539820

ABSTRACT: ***Aims***: Bifidobacterium pseudocatenulatum CECT 7765 improves metabolic and immunological altered functions in high fat fed mice, however little is known about the effects of potential probiotics on vascular reactivity. The aim of the present study was to investigate the effects of a potential probiotic strain, Bifidobacterium pseudocatenulatum CECT 7765, on vascular response in obese mice. ***Methods***: Aorta samples were obtained from mice, which were divided into three groups: a control group, receiving a standard diet; an obese group, receiving a high-fat diet; and an obese group receiving high-fat diet and a daily dose of B. pseudocatenulatum CECT 7765 by oral gavage. Aortic rings were suspended in organ baths for isometric recording of tension. mRNA expression of eNOS was evaluated by real-time polymerase chain reaction. ***Results***: Contractions induced by KCl, noradrenaline and thromboxane analogue were 33%, 30% and 45% lower respectively in aortic rings from obese mice. Bifidobacteria administration reversed this effect. eNOS inhibition increased the response to noradrenaline in the three groups with a significant lower magnitude in aortic rings from obese mice receiving bifidobacteria supplement. Acetylcholine caused a greater vasodilation in aorta from obese group (46+/-3% for control and 69+/-4% for obese group; $p<0.05$) and bifidobacteria reversed it (57+/-5%). Response to sodium nitroprusside was displaced 2.9 times to the left in a parallel manner in obese group. Relaxation to sodium nitroprusside remained unchanged in the bifidobacteria fed group. There was about five-fold decreased mRNA expression of eNOS in aortic segments from the group receiving bifidobacteria. ***Conclusion***: Bifidobacterium pseudocatenulatum CECT 7765 restores the obesity-induced altered vascular function mainly by reducing nitric oxide release.

Mazzocchi, A., Venter, C., Maslin, K., and Agostoni, C. The Role of Nutritional Aspects in Food Allergy: Prevention and Management. Nutrients. 8-9-2017; 9(8); PM: 28792480

ABSTRACT: The prevalence of food allergy in childhood appears to be increasing in both developed and transitional countries. The aim of this paper is to review and summarise key findings in the prevention and management of food allergy, focusing on the role of dietary components and nutritional habits in the development and optimal functioning of the immune system. Essential fatty acids, zinc and vitamin D are likely to enhance the anti-inflammatory and antioxidative barrier and promote immunologic tolerance. Additionally, nutritional components such as pre- and probiotics represent a novel research approach in the attempt to induce a tolerogenic immune environment. For all these reasons, the traditional avoidance diet has been, in recent years, completely reconsidered. New findings on the protective effect of an increased diversity of food introduced in the first year of life on allergic diseases are consistent with the hypothesis that exposure to a variety of food antigens during early life might play a role in the development of immune tolerance. Accordingly, therapeutic (and even preventive) interventions should be planned on an individual basis.

McAleer, J. P. and Kolls, J. K. Contributions of the intestinal microbiome in lung immunity. Eur.J.Immunol. 8-4-2017; PM: 28776643

ABSTRACT: The intestine is a critical site of immune cell development that not only controls intestinal immunity but extra-intestinal immunity as well. Recent findings have highlighted important roles for gut microbiota in shaping lung inflammation. Here, we discuss interactions between the microbiota and immune system including T cells, protective effects of microbiota on lung infections, the role of diet in shaping the composition of gut microbiota and susceptibility to asthma, epidemiologic evidence implicating antibiotic use and microbiota in asthma and clinical trials investigating probiotics as potential treatments for atopy and asthma. The systemic effects of gut microbiota are partially attributed to their generating metabolites including short chain fatty acids, which can suppress lung inflammation through the activation of G protein-coupled receptors. Thus, studying the interactions between microbiota and immune cells can lead to the identification of therapeutic targets for chronic lower respiratory diseases.

McCann, J. C., Elolimy, A. A., and Loor, J. J. Rumen Microbiome, Probiotics, and Fermentation Additives. Vet.Clin.North Am.Food Anim Pract. 7-29-2017; PM: 28764865

ABSTRACT: Fermentation of a variety of feedstuffs by the ruminal microbiome is the distinctive feature of the ruminant digestive tract. The host derives energy and nutrients from microbiome activity; these organisms are essential to survival. Advances in DNA sequencing and bioinformatics have redefined the rumen microbial community. Current research seeks to connect our understanding of the rumen microbiome with nutritional strategies in ruminant livestock systems and their associated digestive disorders. These efforts align with a growing number of products designed to improve ruminal fermentation to benefit the overall efficiency of ruminant livestock production and health.

McFarlin, B. K., Henning, A. L., Bowman, E. M., Gary, M. A., and Carbajal, K. M. Oral spore-based probiotic supplementation was associated with reduced incidence of post-prandial dietary endotoxin, triglycerides, and disease risk biomarkers. World J.Gastrointest.Pathophysiol. 8-15-2017; 8(3):117-126; PM: 28868181

ABSTRACT: ***AIM***: To determine if 30-d of oral spore-based probiotic supplementation could reduce dietary endotoxemia. ***METHODS***: Apparently healthy men and women (n = 75) were screened for post-prandial dietary endotoxemia. Subjects whose serum endotoxin concentration increased by at least 5-fold from pre-meal levels at 5-h post-prandial were considered "responders" and were randomized to receive either placebo (rice flour) or a commercial spore-based probiotic supplement [Bacillus indicus (HU36), Bacillus subtilis (HU58), Bacillus coagulans, and Bacillus licheniformis, and Bacillus clausii] for 30-d. The dietary endotoxemia test was repeated at the conclusion of the supplementation period. Dietary endotoxin (LAL) and triglycerides (enzymatic) were measured using an automated chemistry analyzer. Serum disease risk biomarkers were measured using bead-based multiplex assays (Luminex and Milliplex) as secondary, exploratory measures. ***RESULTS***: Data were statistically analyzed using repeated measures ANOVA and a $P < 0.05$. We found that spore-based probiotic supplementation was associated with a 42% reduction in endotoxin (12.9 +/- 3.5 vs 6.1 +/- 2.6, $P = 0.011$) and 24% reduction in triglyceride (212 +/- 28 vs 138 +/- 12, $P = 0.004$) in the post-prandial period Placebo subjects presented with a 36% increase in endotoxin (10.3 +/- 3.4 vs 15.4 +/- 4.1, $P = 0.011$) and 5% decrease in triglycerides (191 +/- 24 vs 186 +/- 28, $P = 0.004$)

over the same post-prandial period. We also found that spore-based probiotic supplementation was associated with significant post-prandial reductions in IL-12p70 (24.3 +/- 2.2 vs 21.5 +/- 1.7, P = 0.017) and IL-1beta (1.9 +/- 0.2 vs 1.6 +/- 0.1, P = 0.020). Compared to placebo post supplementation, probiotic subject had less ghrelin (6.8 +/- 0.4 vs 8.3 +/- 1.1, P = 0.017) compared to placebo subjects. ***CONCLUSION***: The key findings of the present study is that oral spore-based probiotic supplementation reduced symptoms indicative of "leaky gut syndrome".

McKay, R., Hauk, P., Wu, H. C., Pottash, A. E., Shang, W., Terrell, J., Payne, G. F., and Bentley, W. E. Controlling localization of Escherichia coli populations using a two-part synthetic motility circuit: An accelerator and brake. Biotechnol.Bioeng. 7-29-2017; PM: 28755474

ABSTRACT: Probiotics, whether taken as capsules or consumed in foods, have been regarded as safe for human use by regulatory agencies. Being living cells, they serve as "tunable" factories for the synthesis of a vast array of beneficial molecules. The idea of reprogramming probiotics to act as controllable factories, producing potential therapeutic molecules under user-specified conditions, represents a new and powerful concept in drug synthesis and delivery. Probiotics that serve as drug delivery vehicles pose several challenges, one being targeting (as seen with nanoparticle approaches). Here, we employ synthetic biology to control swimming directionality in a process referred to as "pseudotaxis." Escherichia coli, absent the motility regulator cheZ, swim sporadically, missing the traditional "run" in the run:tumble swimming paradigm. Upon introduction of cheZ in trans and its signal-generated upregulation, engineered bacteria can be "programmed" to swim toward the source of the chemical cue. Here, engineered cells that encounter sufficient levels of the small signal molecule pyocyanin, produce an engineered CheZ and swim with programmed directionality. By incorporating a degradation tag at the C-terminus of CheZ, the cells stop running when they exit spaces containing pyocyanin. That is, the engineered CheZ modified with a C-terminal extension derived from the putative DNA-binding transcriptional regulator YbaQ (RREERAAKKVA) is consumed by the ClpXP protease machine at a rate sufficient to "brake" the cells when pyocyanin levels are too low. Through this process, we demonstrate that over time, these engineered E. coli accumulate in pyocyanin-rich locales. We suggest that such approaches may find utility in engineering probiotics so that their beneficial functions can be focused in areas of principal benefit.

McKenzie, C., Tan, J., Macia, L., and Mackay, C. R. The nutrition-gut microbiome-physiology axis and allergic diseases. Immunol.Rev. 2017; 278(1):277-295; PM: 28658542

ABSTRACT: Dietary and bacterial metabolites influence immune responses. This raises the question whether the increased incidence of allergies, asthma, some autoimmune diseases, cardiovascular disease, and others might relate to intake of unhealthy foods, and the decreased intake of dietary fiber. In recent years, new knowledge on the molecular mechanisms underpinning a 'diet-gut microbiota-physiology axis' has emerged to substantiate this idea. Fiber is fermented to short chain fatty acids (SCFAs), particularly acetate, butyrate, and propionate. These metabolites bind 'metabolite-sensing' G-protein-coupled receptors such as GPR43, GPR41, and GPR109A. These receptors play fundamental roles in the promotion of gut homeostasis and the regulation of inflammatory responses. For instance, these receptors and their metabolites influence Treg biology, epithelial integrity, gut homeostasis, DC biology, and IgA antibody responses. The SCFAs also influence gene transcription in many cells and tissues, through

their inhibition of histone deacetylase expression or function. Contained in this mix is the gut microbiome, as commensal bacteria in the gut have the necessary enzymes to digest dietary fiber to SCFAs, and dysbiosis in the gut may affect the production of SCFAs and their distribution to tissues throughout the body. SCFAs can epigenetically modify DNA, and so may be one mechanism to account for diseases with a 'developmental origin', whereby in utero or post-natal exposure to environmental factors (such as nutrition of the mother) may account for disease later in life. If the nutrition-gut microbiome-physiology axis does underpin at least some of the Western lifestyle influence on asthma and allergies, then there is tremendous scope to correct this with healthy foodstuffs, probiotics, and prebiotics.

Medina, D., Walke, J. B., Gajewski, Z., Becker, M. H., Swartwout, M. C., and Belden, L. K. Culture Media and Individual Hosts Affect the Recovery of Culturable Bacterial Diversity from Amphibian Skin. Front Microbiol. 2017; 8:1574; PM: 28883811

ABSTRACT: One current challenge in microbial ecology is elucidating the functional roles of the large diversity of free-living and host-associated bacteria identified by culture-independent molecular methods. Importantly, the characterization of this immense bacterial diversity will likely require merging data from culture-independent approaches with work on bacterial isolates in culture. Amphibian skin bacterial communities have become a recent focus of work in host-associated microbial systems due to the potential role of these skin bacteria in host defense against the pathogenic fungus Batrachochytrium dendrobatidis (Bd), which is associated with global amphibian population declines and extinctions. As there is evidence that some skin bacteria may inhibit growth of Bd and prevent infection in some cases, there is interest in using these bacteria as probiotic therapy for conservation of at-risk amphibians. In this study, we used skin swabs from American toads (Anaxyrus americanus) to: (1) assess the diversity and community structure of culturable amphibian skin bacteria grown on high and low nutrient culture media, (2) determine which culture media recover the highest proportion of the total skin bacterial community of individual toads relative to culture-independent data, and (3) assess whether the plated communities from the distinct media types vary in their ability to inhibit Bd growth in in-vitro assays. Overall, we found that culture media with low nutrient concentrations facilitated the growth of more diverse bacterial taxa and grew distinct communities relative to media with higher nutrient concentrations. Use of low nutrient media also resulted in culturing proportionally more of the bacterial diversity on individual toads relative to the overall community defined using culture-independent methods. However, while there were differences in diversity among media types, the variation among individual hosts was greater than variation among media types, suggesting that swabbing more individuals in a population is the best way to maximize culture collections, regardless of media type. Lastly, the function of the plated communities against Bd did not vary across culture media type or between high and low nutrient media. These results inform current efforts for developing a probiotic-based approach for amphibian conservation and help to ensure that culture collections are capturing the majority of the important diversity in these systems.

Mellis, C. Probiotics for recurrent abdominal pain in childhood. J.Paediatr.Child Health. 2017; 53(7):722-723; PM: 28670806

No Abstract Available.

Melo, T. A., Dos Santos, T. F., Pereira, L. R., Passos, H. M., Rezende, R. P., and Romano, C. C. Functional Profile Evaluation of Lactobacillus fermentum TCUESC01: A New Potential Probiotic Strain Isolated during Cocoa Fermentation. Biomed.Res.Int. 2017; 2017:5165916; PM: 28808659

ABSTRACT: The use of intestinal probiotic bacteria is very common in the food industry and has been the focus of the majority of research in this field. Yet in recent years, research on extraintestinal microorganisms has greatly increased due to their well-known potential as probiotics. Thus, we studied a strain of Lactobacillus fermentum (TCUESC01) extracted from fermenting cocoa. First, we examined the impact of pH on the growth of this strain and studied its survival under conditions similar to those of the human gastrointestinal tract. L. fermentum TCUESC01 demonstrated resistance to conditions mimicking the human stomach and intestines and grew well between pH 5 and pH 7. Next, we subjected L. fermentum TCUESC01 to storage at 4 degrees C in a milk solution and found that it survived well for 28 days. Lastly, we measured the susceptibility of this strain to numerous antibiotics and its tendency to autoaggregate. L. fermentum TCUESC01 showed significant autoaggregation, as well as susceptibility to the majority of antibiotics tested. Overall, our findings support the potential use of this extraintestinal bacterium as a dietary probiotic.

Memarrast, F., Ghafouri-Fard, S., Kolivand, S., Jafary-Nodooshan, S., Neyazi, N., Sadroddiny, E., and Motevaseli, E. Comparative evaluation of probiotics effects on plasma glucose, lipid, and insulin levels in streptozotocin-induced diabetic rats. Diabetes Metab Res.Rev. 6-13-2017; PM: 28608654

ABSTRACT: ***BACKGROUND***: Diabetes is a chronic disorder caused by the relative decrease in insulin production from the pancreas, tissue resistance to insulin, or both. Daily consumption of probiotics, particularly Lactobacilli, has been proposed as a new strategy for prevention or control of diabetes. ***METHODS***: In the current study, the effects of various probiotics including Lactobacillus reuteri (L reuteri), Lactobacillus crispatus (L crispatus), and Bacillus subtilis on the levels of blood glucose, lipid, and insulin as well as haemoglobin A1c (HbA1c) were investigated in rat models of streptozotocin (STZ)-induced diabetes and compared with metformin. In addition, GLUT-4 and PPAR-gamma transcript levels have been analysed in adipose tissues. ***RESULTS***: A significant decrease in plasma glucose and HbA1c levels and a dramatic increase in insulin levels have been detected after consumption of probiotics. Furthermore, lipid profiles have been improved. The expression of Glut-4 and Ppar-gamma genes in adipose tissues also increased after treatment period. ***CONCLUSION***: The results of this experiment showed that daily consumption of probiotics can be effective in control of STZ-induced diabetes and its complications.

Mennini, M., Dahdah, L., Artesani, M. C., Fiocchi, A., and Martelli, A. Probiotics in Asthma and Allergy Prevention. Front Pediatr. 2017; 5:165; PM: 28824889

ABSTRACT: Interest in probiotic research and its potential benefits in infant foods are relatively recent but significantly increasing. The evolution of the knowledge in the last 20 years demonstrated that alterations in the microbiome may be a consequence of events occurring during infancy or childhood, including prematurity, cesarean section,

and nosocomial infections. Several pieces of evidence prove that a "healthy" intestinal microbiota facilitates the development of immune tolerance. Interventional studies suggest that probiotics could be protective against the development of many diseases. Nevertheless, many factors complicate the analysis of dysbiosis in subjects with food allergy. Comparison in-between studies are difficult, because of considerable heterogeneity in study design, sample size, age at fecal collection, methods of analysis of gut microbiome, and geographic location. Currently, there is no positive recommendation from scientific societies to use pre- or probiotics for treatment of food allergy or other allergic manifestations, while their use in prevention is being custom-cleared. However, the recommendation is still based on little evidence. Although there is valid scientific evidence in vitro, there is no sufficient information to suggest the use of specific probiotics in allergy and asthma prevention.

Meyer, M. P. and Alexander, T. Reduction in necrotizing enterocolitis and improved outcomes in preterm infants following routine supplementation with Lactobacillus GG in combination with bovine lactoferrin. J.Neonatal Perinatal.Med. 8-23-2017; PM: 28854514

ABSTRACT: ***BACKGROUND***: Preterm infants remain at high risk of adverse outcomes following necrotizing enterocolitis (NEC) and late onset sepsis (LOS). Meta-analysis of randomized trials has indicated a reduction in severe NEC following use of probiotics and bovine lactoferrin (LF). Overall, however, uncertainty remains over which probiotic, or combination to use. The aim of this study was to compare the incidence of severe NEC and LOS before and after routine supplementation with Lactobacillus GG (LGG) and LF. ***METHODS***: In this retrospective cohort study, infants <32 weeks or <1500 g routinely received LGG and 100 mg lactoferrin daily from 2011 -2015 were compared with similar infants born from 2004-2008. Cases of NEC were Bell stage 2 or greater and LOS was blood or spinal fluid culture positive after 48 hrs of age. ***RESULTS***: We noted a marked decline in the incidence of NEC from 3% to 1% with a RR of 0.29 (CI 0.1-0.9) and a number needed to benefit of 50. The cost of preventing one case of NEC was estimated to be NZ $2800, considerably lower than the cost of treatment. LOS rates were not significantly different. There was a decrease in retinopathy treatment rates. During the period there was one case of LGG sepsis in a 23 week gestation infant with abdominal pathology and one infant developed NEC after stopping prophylaxis. ***CONCLUSION***: The rates of severe NEC was markedly reduced following prophylaxis. The case of LGG sepsis indicates caution is required in extremely preterm infants.

Michael, D. R., Davies, T. S., Moss, J. W. E., Calvente, D. L., Ramji, D. P., Marchesi, J. R., Pechlivanis, A., Plummer, S. F., and Hughes, T. R. The anti-cholesterolaemic effect of a consortium of probiotics: An acute study in C57BL/6J mice. Sci.Rep. 6-6-2017; 7(1):2883; PM: 28588193

ABSTRACT: Hypercholesterolaemia is a major risk factor for cardiovascular disease and it has been found that some probiotic bacteria possess cholesterol-lowering capabilities. In this study, the ability of the Lab4 probiotic consortium to hydrolyse bile salts, assimilate cholesterol and regulate cholesterol transport by polarised Caco-2 enterocytes was demonstrated. Furthermore, in wild-type C57BL/6J mice fed a high fat diet, 2-weeks supplementation with Lab4 probiotic consortium plus Lactobacillus plantarum CUL66 resulted in significant reductions in plasma total cholesterol levels and suppression of diet-induced weight gain. No changes in plasma levels of very low-density lipoprotein/low-density lipoprotein, high-density lipoprotein, triglycerides, cytokines or bile acids were observed. Increased amounts of total and unconjugated bile acids in the faeces of the

probiotic-fed mice, together with modulation of hepatic small heterodimer partner and cholesterol-7alpha-hydroxylase mRNA expression, implicates bile salt hydrolase activity as a potential mechanism of action. In summary, this study demonstrates the cholesterol-lowering efficacy of short-term feeding of the Lab4 probiotic consortium plus L. plantarum CUL66 in wild-type mice and supports further assessment in human trials.

Millar, M., Seale, J., Greenland, M., Hardy, P., Juszczak, E., Wilks, M., Panton, N., Costeloe, K., and Wade, W. G. The Microbiome of Infants Recruited to a Randomised Placebo-controlled Probiotic Trial (PiPS Trial). EBioMedicine. 2017; 20:255-262; PM: 28571671

ABSTRACT: The microbial dysbiosis associated with necrotizing enterocolitis (NEC) in preterm infants suggests that early exposure to probiotics may decrease and antibiotics may increase NEC risk. However, administration of Bifidobacterium breve strain BBG-001 to preterm infants did not affect NEC incidence in a multicenter randomised controlled phase 3 trial (PiPS trial). Using a subset of these subjects we compared the fecal microbiome of probiotic and placebo groups and assessed the impact of early antibiotic treatment. Extracted DNA from 103 fecal samples collected at 36weeks post-menstrual age underwent PCR amplification of a fragment of the 16S rRNA gene. Heatmaps were constructed showing the proportions of sequences from bacterial families present at >1% of the community. Stepwise logistic regression assessed the association between early antibiotic exposure and microbiome group. There was no difference in the microbial richness and diversity of the microbiome of preterm infants following treatment with probiotic or a placebo. Conversely, early antimicrobial exposure was associated with different patterns of colonisation, specifically a relative abundance of Proteobacteria. These findings highlight that the potential influence of probiotics on the microbiome of preterm infants remains unclear whereas the modulatory effect of antibiotic exposure on microbial colonisation requires further research.

Mimura, M. A. M., Borra, R. C., Hirata, C. H. W., and de Oliveira, Penido N. Immune response of patients with recurrent aphthous stomatitis challenged with a symbiotic. J.Oral Pathol.Med. 8-4-2017; PM: 28776757

ABSTRACT: ***BACKGROUND***: There are indications that Th1 polarization of immune response plays an important role in the pathogenesis of recurrent aphthous stomatitis (RAS), and that the use of probiotics can stimulate immune regulatory activity, influencing the course of the disease. The aim of this study was to characterize the initial immune profile of RAS patients and evaluate clinical and serological response following a challenge with symbiotic treatment containing fructooligosaccharide, Lactobacillus, and Bifidobacterium. ***METHODS***: The immune responses of the 45 patients with RAS, submitted to symbiotic or placebo for 120 days, in relation to 30 RAS-free controls, were evaluated over a period of 6 months. Peripheral blood was collected from all patients at 0 (T0), 120 (T4), and 180 days (T6) after the start of treatment and Th1 (IL12-p70, IFN-gamma), Th2 (IL-4), Treg (IL-10), Th17 (IL-17A), inflammatory (TNF-alpha, IL-6)-associated cytokines, and clinical parameters were quantified. ***RESULTS***: At T0, significant differences were found in the serological levels of the IFN-gamma, IL-4, and IL-6 cytokines of the RAS patients in comparison with the controls. It was observed that the cytokine profile of the RAS group was comprised of 2 distinct clusters: a pure Th2 and a Mixed (Th1/Th2) subtype and that symbiotic treatment induced an improvement in pain and an increase in IFN-gamma levels, producing a reduction in Th2 response. ***CONCLUSIONS***: In RAS, symbiotic treatment based on a fructooligosaccharide, Lactobacillus, and Bifidobacterium composition

produced an alteration in the Th2 serological immune profile in the direction of Th1 and improved pain symptomatology.

Min, M., Bunt, C. R., Mason, S. L., Bennett, G. N., and Hussain, M. A. Effect of Non-Dairy Food Matrices on the Survival of Probiotic Bacteria during Storage. Microorganisms. 8-1-2017; 5(3); PM: 28763015

ABSTRACT: The viability of probiotics in non-dairy food products during storage is required to meet content criteria for probiotic products. This study investigated whether non-dairy foods could be matrices for probiotics. Selected probiotic bacteria were coated on non-dairy foods under two storage conditions, and viabilities were assessed. The non-dairy foods were coated with 5-7 log cfu g-1 of Lactobacillus acidophilus ATCC4356T, Lactobacillus plantarum RC30, and Bifidobacterium longum ATCC15707T. The coated non-dairy foods were stored at 20 degrees C and 20% relative humidity (RH) or 30 degrees C and 50% RH. Viability of probiotic bacteria was determined after 0, 2, and 4 weeks of storage. B. longum showed the highest survival at week 4 of 6.5-6.7 log cfu g-1 on wheat bran and oat, compared with 3.7-3.9 log cfu g-1 of L. acidophilus and 4.2-4.8 log cfu g-1 of L. plantarum at 20 degrees C 20% RH. Under the storage conditions of 30 degrees C 50% RH, survival of 4.5 log cfu g-1 of B. longum was also found on oat and peanut. This was two and four times higher than the population of L. acidophilus and L. plantarum, respectively. The results suggest that probiotics can survive on non-dairy foods under ambient storage conditions. However, the storage conditions, food matrices, and probiotic strains should be carefully chosen to maximize probiotic bacteria survival.

Miraghajani, M., Dehsoukhteh, S. S., Rafie, N., Hamedani, S. G., Sabihi, S., and Ghiasvand, R. Potential mechanisms linking probiotics to diabetes: a narrative review of the literature. Sao Paulo Med.J. 2017; 135(2):169-178; PM: 28538869

ABSTRACT: ***CONTEXT AND OBJECTIVE***: Some studies have suggested a wide range of possible mechanisms through which probiotics may play a role in diabetes prevention and treatment. However, the underlying mechanisms are not fully understood. We conducted this study to review the potential mechanisms suggested for the effect of probiotics in diabetes. ***DESIGN AND SETTING***: Narrative review conducted at the Food Security Research Center of Isfahan. ***METHODS***: A search in the electronic databases MEDLINE (PubMed), Cochrane Library, Web of Science and Google scholar was performed up to October 2016. ***RESULTS***: The initial search yielded 1214 reports. After removing duplicates, 704 titles and abstracts were screened. Finally, out of 83 full-text articles that were reviewed for eligibility, 30 articles were included in the final analysis. The anti-diabetic mechanisms for probiotics reported encompass intraluminal and direct effects on the intestinal mucosa and microbiota (n = 13), anti-inflammatory and immunomodulatory effects (n = 10), antioxidative effects (n = 5), effects on endoplasmic reticulum (ER) stress and expression of genes involved in glucose homeostasis and insulin resistance (n = 6), with some studies pointing to more than one mechanism. ***CONCLUSION***: The results may throw some light on the capacity of probiotics as a novel approach towards controlling diabetes. However, further human studies are warranted to elucidate and confirm the potential role of probiotics in diabetes prevention and treatment. Also, it needs to be ascertained whether the effectiveness of probiotics in diabetes prevention and treatment is dependent on the strain of the microorganisms.

Mishra, A. K., Megta, A. K., Palva, A., von, Ossowski, I, and Krishnan, V. Crystallization and X-ray diffraction analysis of SpaE, a basal pilus protein from the gut-adapted Lactobacillus rhamnosus GG. Acta Crystallogr.F.Struct.Biol.Commun. 6-1-2017; 73(Pt 6):321-327; PM: 28580919

ABSTRACT: SpaE is the predicted basal pilin subunit in the sortase-dependent SpaFED pilus from the gut-adapted and commensal Lactobacillus rhamnosus GG. Thus far, structural characterization of the cell-wall-anchoring basal pilins has remained difficult and has been limited to only a few examples from pathogenic genera and species. To gain a further structural understanding of the molecular mechanisms that are involved in the anchoring and assembly of sortase-dependent pili in less harmful bacteria, L. rhamnosus GG SpaE for crystallization was produced by recombinant expression in Escherichia coli. Although several attempts to crystallize the SpaE protein were unsuccessful, trigonal crystals that diffracted to a resolution of 3.1 A were eventually produced using PEG 3350 as a precipitant and high protein concentrations. Further optimization with a combination of additives led to the generation of SpaE crystals in an orthorhombic form that diffracted to a higher resolution of 1.5 A. To expedite structure determination by SAD phasing, selenium-substituted (orthorhombic) SpaE crystals were grown and X-ray diffraction data were collected to 1.8 A resolution.

Mohammed, A. T., Khattab, M., Ahmed, A. M., Turk, T., Sakr, N., Khalil, M., Abdelhalim, M., Sawaf, B., Hirayama, K., and Huy, N. T. The therapeutic effect of probiotics on rheumatoid arthritis: a systematic review and meta-analysis of randomized control trials. Clin.Rheumatol. 9-15-2017; PM: 28914373

ABSTRACT: Rheumatoid arthritis is an autoimmune disease in which probiotics appears to have an immune modulating action along with decreased inflammatory process. Therefore, we aim to investigate the efficacy of probiotics as an adjuvant therapy for rheumatoid arthritis. A comprehensive literature search was performed using nine databases including PubMed and Web of Science. Interesting data was extracted and meta-analyzed. We assessed the risk of bias using Cochrane Collaboration's tool. The protocol was registered in PROSPERO (CRD 42016036769). We found nine studies involving 361 patients who met our eligibility criteria. Our meta-analysis indicated that pro-inflammatory cytokine IL-6 was significantly lower in the probiotics compared with the placebo group (standardized mean difference = - 0.708; 95% confidence interval (CI) - 1.370 to 0.047, P = 0.036). However, there was no difference between probiotics and placebo in disease activity score (mean difference 0.023; 95% CI - 0.584 to 0.631, P = 0.940). Probiotics lowered pro-inflammatory cytokines IL-6 in RA; however, its clinical effect is still unclear. Hence, many high-quality randomized controlled trials (RCTs) are still needed to prove this effect.

Mohseni, A. H., Taghinezhad, S., Keyvani, H., and Ghobadi, N. Comparison of Acyclovir and Multistrain Lactobacillus brevis in Women with Recurrent Genital Herpes Infections: a Double-Blind, Randomized, Controlled Study. Probiotics.Antimicrob.Proteins. 8-30-2017; PM: 28852985

ABSTRACT: We performed a randomized double-blind controlled trial to compare the efficacy and safety of multistrain probiotic and acyclovir in women patients with recurrent genital herpes simplex virus type 2 (HSV-2) infections. Eighty-one patients

enrolled in the study were being treated with multistrain Lactobacillus brevis one vaginal capsule every 12 h and oral acyclovir 400 mg twice daily for 6 months. Of 53 patients who completed both treatment courses, no important differences were identified between acyclovir and probiotic for the primary and secondary efficacy endpoint, resolution of episode (hazard ratio, 0.60; 95% CI, 0.3429 to 1.0663; P = 0.08), lesion healing time (hazard ratio, 0.57; 95% CI, 0.3034 to 1.0717, P = 0.08), viral shedding (hazard ratio, 0.54; 95% CI, 0.3027 to 0.9750, P = 0.04), and percentage of pain (hazard ratio, 0.48; 95% CI, 0.2708 to 0.8545, P = 0.01). The median time to first and second recurrence after treatment were 43 and 121 days in patients receiving acyclovir and 33 and 118 days in patients receiving probiotic (HR 2.61; 95% CI, 1.4427 to 4.7546, P = 0.001, and HR 0.62; 95% CI, 0.3500 to 1.1133, P = 0.1, respectively). No clinically important effects happened during the probiotic treatment but some of adverse events reported in patients taking acyclovir. Easy availability, low cost, and no side effect of L. brevis are valuable properties of probiotic therapy compared with acyclovir. Therefore, we concluded that multistrain L. brevis could play an important role in suppression of recurrent genital herpes simplex virus infection.

Monika, Savitri, Kumar, V., Kumari, A., Angmo, K., and Bhalla, T. C. Isolation and characterization of lactic acid bacteria from traditional pickles of Himachal Pradesh, India. J.Food Sci.Technol. 2017; 54(7):1945-1952; PM: 28720951

ABSTRACT: A total of 15 isolates of lactic acid bacteria (LAB) were isolated from traditional pickles of rural and urban areas of Himachal Pradesh. These isolates were identified as Enterococcus faecalis (7), Lactobacillus plantarum (3), Pediococcus pentosaceus (2), Leuconostoc mesenteroides (1), Lactococcus lactis (1) and Enterococcus sp. (1) on the basis of morphological, biochemical and 16S rDNA sequence analysis. All the LABs produced exopolysaccharides, have antibiotic susceptibility, and possess activity of beta-galactosidase, beta-glucosidase, protease and amylase, while none of the isolates showed haemolytic activity. Out of 15 isolates tested, only 6 isolates showed the phytase activity. These LAB exhibited antimicrobial activity against food borne pathogenic bacteria i.e. Bacillus cereus, Escherichia coli, Staphylococcus aureus and Shigella dysenteriae. These results suggested that LAB isolates from traditional pickles of Himachal Pradesh have very good potential to be used as probiotics.

Montero, E., Iniesta, M., Rodrigo, M., Marin, M. J., Figuero, E., Herrera, D., and Sanz, M. Clinical and microbiological effects of the adjunctive use of probiotics in the treatment of gingivitis: A randomized controlled clinical trial. J.Clin.Periodontol. 2017; 44(7):708-716; PM: 28556062

ABSTRACT: ***AIM***: To evaluate the efficacy of a probiotic combination in the treatment of gingivitis and to assess its impact on the subgingival microbiota. ***MATERIALS AND METHODS***: A placebo-controlled clinical trial was conducted in gingivitis subjects during 6 weeks. Test treatment consisted of the administration of two oral tablets per day containing the probiotic strains Lactobacillus plantarum, Lactobacillus brevis and Pediococcus acidilactici; the control group received the same tablets but without live bacteria. The main outcome variable was the changes in gingival index (GI). Subgingival samples were collected and analysed by quantitative polymerase chain reaction (qPCR) for five putative periodontal pathogens. Outcome variables were compared between and within groups, and multiple regression analysis was performed. ***RESULTS***: A

total of 59 patients (29 tests, 30 placebos) were included in the analysis. Both treatment groups experienced a statistically significant improvement in mean GI ($p < .0001$), but no differences between treatment groups were found for any clinical index. A significantly higher reduction in the number of sites with higher GI scores (GI = 3 at baseline) was observed in the test group. In subgingival samples, a significant reduction in T. forsythia was significant only in the test group ($p < .008$). ***CONCLUSIONS***: The use of probiotic tablets containing L. plantarum, L. brevis and P. acidilactici did not lead to significant changes in mean GI; although a significant reduction occurred in the number of sites with severe inflammation. Furthermore, the adjunctive use of this probiotic promoted a significant microbiological impact.

Motevaseli, E., Dianatpour, A., and Ghafouri-Fard, S. The Role of Probiotics in Cancer Treatment: Emphasis on their In Vivo and In Vitro Anti-metastatic Effects. Int.J.Mol.Cell Med. 2017; 6(2):66-76; PM: 28890883

ABSTRACT: Probiotics are defined as live bacteria and yeasts that exert beneficial effects for health. Among their various effects, anti-cancer properties have been highlighted in recent years. Such effects include suppression of the growth of microbiota implicated in the production of mutagens and carcinogens, alteration in carcinogen metabolism and protection of DNA from oxidative damage as well as regulation of immune system. We performed a computerized search of the MEDLINE/PUBMED databases with key words: cancer, probiotics, lactobacilli, metastasis and invasion. Cell line studies as well as animal models and human studies have shown the therapeutic effects of probiotics in reduction of invasion and metastasis in cancer cells. These results support the beneficial effects of probiotics both in vitro and in vivo. However, pre-clinical or clinical studies are not enough to decide about their application.

Mu, Q., Kirby, J., Reilly, C. M., and Luo, X. M. Leaky Gut As a Danger Signal for Autoimmune Diseases. Front Immunol. 2017; 8:598; PM: 28588585

ABSTRACT: The intestinal epithelial lining, together with factors secreted from it, forms a barrier that separates the host from the environment. In pathologic conditions, the permeability of the epithelial lining may be compromised allowing the passage of toxins, antigens, and bacteria in the lumen to enter the blood stream creating a "leaky gut." In individuals with a genetic predisposition, a leaky gut may allow environmental factors to enter the body and trigger the initiation and development of autoimmune disease. Growing evidence shows that the gut microbiota is important in supporting the epithelial barrier and therefore plays a key role in the regulation of environmental factors that enter the body. Several recent reports have shown that probiotics can reverse the leaky gut by enhancing the production of tight junction proteins; however, additional and longer term studies are still required. Conversely, pathogenic bacteria that can facilitate a leaky gut and induce autoimmune symptoms can be ameliorated with the use of antibiotic treatment. Therefore, it is hypothesized that modulating the gut microbiota can serve as a potential method for regulating intestinal permeability and may help to alter the course of autoimmune diseases in susceptible individuals.

Mur Perez, A. M., Mateo, Segura Z., Ramirez, Dominguez N., and Vela, Condon P. [Use of probiotics in bacterial vaginosis]. Semergen. 2017; 43(5):394-398; PM: 27856152

ABSTRACT: ***INTRODUCTION***: Bacterial vaginosis (BV) is a change in the vaginal microbiota due to bacterial overgrowth of normal microorganisms, which produces symptoms of vaginal discomfort, increased malodorous vaginal discharge, etc. Although they been seen to improve recurrence rates in clinical practice, the role of probiotics is questioned in these situations. A literature review on BV is presented in order to evaluate the effectiveness of using probiotics as adjuvant therapy in BV. ***METHOD***: PubMed, Cochrane and SCOPUS review of the last 5 years publications using probiotics to treat women diagnosed with BV. ***RESULTS***: An analysis was performed on the 10 items that refer to the use of probiotics in addition to antibiotic treatments. ***CONCLUSIONS***: All items conclude that the use of probiotics is beneficial in cases of BV in addition to conventional treatments. However, the conclusions are not categorical due to there being a wide variety of studies and probiotics used.

Nadelman, P., Frazao, J. V., Vieira, T. I., Balthazar, C. F., Andrade, M. M., Alexandria, A. K., Cruz, A. G., Fonseca-Goncalves, A., and Maia, L. C. The performance of probiotic fermented sheep milk and ice cream sheep milk in inhibiting enamel mineral loss. Food Res.Int. 2017; 97:184-190; PM: 28578040

ABSTRACT: The study aimed to evaluate the effects of two different sheep milk-based food matrices - fermented sheep milk and ice cream - with added probiotic bacteria (Lactobacillus casei 431) on dental enamel subjected to an in vitro highly cariogenic challenge. Sixty enamel blocks were selected and randomly allocated into five treatment groups (n=12): conventional fermented sheep milk (CFSM), probiotic fermented sheep milk (PFSM), conventional sheep milk ice cream (CSMIC), probiotic sheep milk ice cream (PSMIC) and control using deionized water. The blocks were subjected to highly cariogenic pH cycling and the products were applied (5min), in a blinded way, once a day to simulate a daily use for 8 consecutive days. A microhardness test was performed before and after the treatment to estimate the percentage of microhardness surface loss (% SML). Scanning electronic microscopy (SEM) was performed to confirm the mineral loss. All groups had lost microhardness after the experiment. However, CFSM and PFSM exhibited the most positive findings when compared to the control in both ice creams. Scanning electron microscopy showed less mineral loss in CFSM and PFSM compared with CSMIC, PSMIC and control after the cariogenic challenge. Overall, fermented milk decreased mineral loss from enamel subjected to a highly cariogenic challenge, regardless of the presence of probiotics in their composition, which had a higher efficacy compared to ice cream.

Nagata, S., Chiba, Y., Wang, C., and Yamashiro, Y. The effects of the Lactobacillus casei strain on obesity in children: a pilot study. Benef.Microbes. 8-24-2017; 8(4):535-543; PM: 28618860

ABSTRACT: There are few data regarding the role of probiotics as a dietary intervention in the management of obesity in children. An open prospective examination was conducted to clarify the effects of Lactobacillus casei strain Shirota (LcS)-containing beverages in obese children. We compared the intestinal microbiota and organic acid levels between 12 obese (average age, 10.8 years; body mass index (BMI) Z score, 2.7+/-1.7) and 22 control children(average age, 8.5 years; BMI Z score, 0.1+/-0.7), and pre- and post-intervention in the obese children. The obese group underwent diet and exercise therapy for 6 months and then were given an LcS beverage daily for another 6 months and the body weight and serological markers were monitored. Significant reductions in

the faecal concentrations of Bifidobacterium (obese group, 7.9+/-1.5 vs non-obese group, 9.8+/-0.5 Log10cells/g; P<0.01) along with a significant decline in the Bacteroides fragilis group, Atopobium cluster and Lactobacillus gasseri subgroup, and acetic acid (obese group, 45.1+/-16.9 vs non-obese group, 57.9+/-17.6 mumol/g; P<0.05) were observed in the obese group at baseline. A significant decline in body weight (-2.9+/-4.6%; P<0.05) and an elevation in the high density lipoprotein cholesterol level (+11.1+/-17.6%; P<0.05) were observed 6 months after ingestion of the LcS beverage compared to baseline. Furthermore, a significant increase in the faecal concentration of Bifidobacterium (7.0+/-1.2 before ingestion vs 9.1+/-1.2 Log10cells/g after ingestion; P<0.01) and an apparent increase in the acetic acid concentration (7.0+/-1.2 before ingestion vs 9.1+/-1.2 Log10cells/g after ingestion; P<0.01) were observed 6 months after ingestion. LcS contributed to weight loss while also improving the lipid metabolism in obese children via a significant increase in the faecal Bifidobacterium numbers and the acetic acid concentration.

Nami, Y., Haghshenas, B., and Yari, Khosroushahi A. Effect of psyllium and gum Arabic biopolymers on the survival rate and storage stability in yogurt of Enterococcus duransIW3 encapsulated in alginate. Food Sci.Nutr. 2017; 5(3):554-563; PM: 28572941

ABSTRACT: Different herbal biopolymers were used to encapsulate Enterococcus durans IW3 to enhance its storage stability in yogurt and subsequently its endurance in gastrointestinal condition. Nine formulations of encapsulation were performed using alginate (ALG), ALG-psyllium (PSY), and ALG-gum Arabic (GA) blends. The encapsulation efficiency of all formulations, tolerance of encapsulated E. durans IW3 against low pH/high bile salt concentration, storage lifetime, and release profile of cells in natural condition of yogurt were evaluated. Result revealed 98.6% encapsulation efficiency and 76% survival rate for all formulation compared with the unencapsulated formulation cells (43%). The ALG-PSY and ALG-GA formulations have slightly higher survival rates at low pH and bile salt condition (i.e., 76-93% and 81-95%, respectively) compared with the ALG formulation. All encapsulated E. durans IW3 was released from the prepared beads of ALG after 90 min, whereas both probiotics encapsulated in ALG-GA and ALG-PSY were released after 60 min. Enterococcus durans IW3 was successfully encapsulated in ALG, ALG-GA, and ALG-PSY beads prepared by extrusion method. ALG-GA and ALG-PSY beads are suitable delivery carriers for the oral administration of bioactive compounds like probiotics. The GA and PSY gels exhibited better potential for encapsulation of probiotic bacteria cells because of the amendment of ALG difficulties and utilization of therapeutic and prebiotic potentials of these herbal biopolymers.

Nandi, A., Banerjee, G., Dan, S. K., Ghosh, K., and Ray, A. K. Evaluation of In Vivo Probiotic Efficiency of Bacillus amyloliquefaciens in Labeo rohita Challenged by Pathogenic Strain of Aeromonas hydrophila MTCC 1739. Probiotics.Antimicrob.Proteins. 7-25-2017; PM: 28744833

ABSTRACT: Diseases in aquatic organisms, including fish, are a major concern in aquaculture production. In this present investigation, we have evaluated the beneficial effects of dietary Bacillus amyloliquefaciens CCF7 (GenBank Acc. No. KP256501) supplementation in rohu (Labeo rohita) challenged by a pathogenic strain of Aeromonas hydrophila MTCC 1739. Four experimental diets were formulated: control diet (no probiotics) and three experimental diets (different concentrations of probiotic candidate B. amyloliquefaciens CCF7 at 105 (T1), 107 (T2), 109 (T3) CFU/g). Further, we

have divided the feeding trial into pre-challenge (70 days) and post-challenge (28 days) periods and various immune parameters (serum protein, globulin, albumin, lysozyme, and IgM), and stress parameters (malondialdehyde, catalase, and superoxide dismutase) were examined during both the periods. Throughout the entire experiment, control group was fed with probiotic free basal diet, while the treatment groups received probiotic supplemented diets (PSD). After challenge test, serum aspartate transaminase (AST), serum alanine transaminase (ALT) activity, and liver malondialdehyde level have increased significantly in control groups; however, level of these parameters were considerably lower in fish fed with PSD. In contrast, liver catalase and superoxide dismutase activities and serum globulin concentration was significantly higher in the group fed with T3 diet followed by T2. Furthermore, an elevated level of serum IgM and higher activity of serum lysozyme was also recorded in PSD fed groups, especially for T3 group which confirmed the probiotic efficiency of the bacterium B. amyloliquefaciens CCF7. We strongly believe that B. amyloliquefaciens CCF7 will be a good probiotic candidate in aquaculture industries.

Neffe-Skocinska, K., Okon, A., Kolozyn-Krajewska, D., and Dolatowski, Z. Amino acid profile and sensory characteristics of dry fermented pork loins produced with a mixture of probiotic starter cultures. J.Sci.Food Agric. 2017; 97(9):2953-2960; PM: 27859340

ABSTRACT: ***BACKGROUND***: Proteolysis is a biochemical process in dry-aged meat products where proteins are metabolized and broken down to polypeptides, peptides, and free amino acids. In the literature it is reported that an appropriate choice of probiotic starter culture limits proteolytic changes in dry-fermented meat products. In this study the combined effect of a mixture of probiotic starter cultures on the free amino acid profile, total count of lactic acid bacteria, and the sensory quality of dry-aged pork loins after fermentation and after storing the vacuum-packed samples was evaluated. ***RESULTS***: LOCK900 and BB12 probiotic strains were the technologically best two-species mixture of starter cultures for the production of probiotic dry-aged pork loins. They allowed us to obtain products with high and stable bacterial count and acceptable sensory quality, both after 21 days of fermentation and after 2 months of cold storage. Changes in the free amino acid profile and increased intensity of the selected sensory attributes result from a significant share of probiotics in meat proteolysis occurring during fermentation and storage. ***CONCLUSION***: The results suggest the relevance of using probiotic bacteria as a two-species starter culture for the production of dry-aged products. (c) 2016 Society of Chemical Industry.

Neut, C., Mahieux, S., and Dubreuil, L. J. Antibiotic susceptibility of probiotic strains: Is it reasonable to combine probiotics with antibiotics? Med.Mal Infect. 8-7-2017; PM: 28797834

ABSTRACT: ***OBJECTIVE***: The main goal of this study was to determine the in vitro susceptibility of strains collected from marketed probiotics to antibiotics used to treat community-acquired infections. ***METHODS***: The minimum inhibitory concentrations (MICs) of 16 antibiotics were determined using a gradient strip (E test) or the agar dilution method for fidaxomicin. ***RESULTS***: The probiotics demonstrated various antibiotic patterns. Bacterial probiotics are generally susceptible to most prescribed antibiotics orally administered, whereas yeast probiotics, such as Saccharomyces boulardii, are resistant. ***CONCLUSION***: Special attention must be paid to co-prescriptions of antibiotics and probiotics to ensure that the probiotic strain is not susceptible.

Notario-Perez, F., Ruiz-Caro, R., and Veiga-Ochoa, M. D. Historical development of vaginal microbicides to prevent sexual transmission of HIV in women: from past failures to future hopes. Drug Des Devel.Ther. 2017; 11:1767-1787; PM: 28670111

ABSTRACT: Infection with human immunodeficiency virus (HIV) remains a global public health concern and is particularly serious in low- and middle-income countries. Widespread sexual violence and poverty, among other factors, increase the risk of infection in women, while currently available prevention methods are outside the control of most. This has driven the study of vaginal microbicides to prevent sexual transmission of HIV from men to women in recent decades. The first microbicides evaluated were formulated as gels for daily use and contained different substances such as surfactants, acidifiers and monoclonal antibodies, which failed to demonstrate efficacy in clinical trials. A gel containing the reverse transcriptase inhibitor tenofovir showed protective efficacy in women. However, the lack of adherence by patients led to the search for dosage forms capable of releasing the active principle for longer periods, and hence to the emergence of the vaginal ring loaded with dapivirine, which requires a monthly application and is able to reduce the sexual transmission of HIV. The future of vaginal microbicides will feature the use of alternative dosage forms, nanosystems for drug release and probiotics, which have emerged as potential microbicides but are still in the early stages of development. Protecting women with vaginal microbicide formulations would, therefore, be a valuable tool for avoiding sexual transmission of HIV.

Notay, M., Foolad, N., Vaughn, A. R., and Sivamani, R. K. Probiotics, Prebiotics, and Synbiotics for the Treatment and Prevention of Adult Dermatological Diseases. Am.J.Clin.Dermatol. 7-5-2017; PM: 28681230

ABSTRACT: ***BACKGROUND***: Probiotic, prebiotic, and synbiotic supplementation is becoming more prevalent nowadays. Clinical studies have demonstrated some of the medical benefits of probiotics, prebiotics, and synbiotics within dermatology but an evidence-based review of their effects in adults is needed. ***OBJECTIVE***: The aim of this study was to identify evidence for the use of supplementation with probiotics, prebiotics, or synbiotics for the prevention and treatment of dermatological diseases in adults. ***DATA SOURCES***: We conducted a search of the Ovid MEDLINE, Cochrane Central Register of Controlled trials and EMBASE electronic databases from 1 January 1946 to 11 January 2017. ***STUDY SELECTION***: Trials examining supplementation in the treatment of dermatological diseases using oral or topical probiotics, synbiotics, and prebiotics in adults over the age of 18 years were selected. ***DATA EXTRACTION***: Of 315 articles, 12 met the inclusion criteria. ***DATA SYNTHESIS***: Nutritional supplementation with probiotics and prebiotics was shown to improve atopic dermatitis (AD) symptomatology, quality of life, or clinical severity in six of nine studies. One study in psoriasis was shown to improve inflammatory markers, and one study suggested that probiotics could be used as adjunctive therapy in the treatment of acne. ***CONCLUSION***: Preliminary studies are optimistic for the use of some strains of probiotics for symptomatic and clinical improvement in AD, and as adjunctive treatment with antibiotics for acne. Further research is necessary to better assess how probiotics and prebiotics may be used within dermatology.

Obadia, B., Guvener, Z. T., Zhang, V., Ceja-Navarro, J. A., Brodie, E. L., Ja, W. W., and Ludington, W. B. Probabilistic Invasion Underlies Natural Gut Microbiome Stability. Curr.Biol. 7-10-2017; 27(13):1999-2006; PM: 28625783

ABSTRACT: Species compositions of gut microbiomes impact host health [1-3], but the processes determining these compositions are largely unknown. An unexplained observation is that gut species composition varies widely between individuals but is largely stable over time within individuals [4, 5]. Stochastic factors during establishment may drive these alternative stable states (colonized versus non-colonized) [6, 7], which can influence susceptibility to pathogens, such as Clostridium difficile. Here we sought to quantify and model the dose response, dynamics, and stability of bacterial colonization in the fruit fly (Drosophila melanogaster) gut. Our precise, high-throughput technique revealed stable between-host variation in colonization when individual germ-free flies were fed their own natural commensals (including the probiotic Lactobacillus plantarum). Some flies were colonized while others remained germ-free even at extremely high bacterial doses. Thus, alternative stable states of colonization exist even in this low-complexity model of host-microbe interactions. These alternative states are driven by a fundamental asymmetry between the inoculum population and the stably colonized population that is mediated by spatial localization and a population bottleneck, which makes stochastic effects important by lowering the effective population size. Prior colonization with other bacteria reduced the chances of subsequent colonization, thus increasing the stability of higher-diversity guts. Therefore, stable gut diversity may be driven by inherently stochastic processes, which has important implications for combatting infectious diseases and for stably establishing probiotics in the gut.

Oh, B. T., Jeong, S. Y., Velmurugan, P., Park, J. H., and Jeong, D. Y. Probiotic-mediated blueberry (Vaccinium corymbosum L.) fruit fermentation to yield functionalized products for augmented antibacterial and antioxidant activity. J.Biosci.Bioeng. 7-6-2017; PM: 28690159

ABSTRACT: The aim of this study was to investigate the fermentation of blueberry fruit with selected probiotic bacteria (Bacillus amyloliquefaciens and Lactobacillus brevis) and yeast (Starmerella bombicola) isolated from fermented starfish for the extraction of functionalized products for biomedical applications. All probiotic-based fermented extracts showed augmented antibacterial and antioxidant activity compared to the control. Biochemical parameters of viable cell count, titratable acidity, total phenol, total anthocyanin, total flavonoids, total sugar, and reducing sugar were analyzed during a 0-96 h fermentation period. In addition, Fourier transform infrared (FTIR) spectroscopy was performed to determine the functional groups in the control and fermented extracts and it signifies the presence of alcohol groups, phenol groups, carboxylic acids, and aliphatic amines, respectively. The well diffusion, minimum inhibitory concentration (MIC), and minimum bactericidal concentration (MBC) assays determined that the S. bombicola-mediated fermented extract has excellent activity, followed by B. amyloliquefaciens and L. brevis, at a high concentration of 1.0 g/mL fermented extract. The ABTS and DPPH showed significant scavenging activity with IC50 values of (30.52 +/- 0.08)/(155.10 +/- 0.06) mug/mL, (24.82 +/- 0.16)/(74.21 +/- 1.26) mug/mL, and (21.81 +/- 0.08)/(125.11 +/- 0.04) mug/mL for B. amyloliquefaciens, L. brevis, and S. bombicola, respectively. Developing a value-added fermented blueberry product will help circumvent losses because of the highly perishable nature of the fruit.

Ohtsu, T., Takagi, A., Uemura, N., Inoue, K., Sekino, H., Kawashima, A., Uchida, M., and Koga, Y. The Ameliorating Effect of Lactobacillus gasseri OLL2716 on Functional Dyspepsia in Helicobacter pylori-Uninfected Individuals: A Randomized Controlled Study. Digestion. 2017; 96(2):92-102; PM: 28768250

ABSTRACT: ***BACKGROUND/AIMS***: Probiotics appear to improve Helicobacter pylori-associated dyspepsia via an inhibitory effect on H. pylori; however, uncertainty exists regarding their effects in H. pylori-uninfected individuals. We evaluated the efficacy of Lactobacillus gasseri OLL2716 (L. gasseri OLL2716) on H. pylori-uninfected individuals with functional dyspepsia (FD). ***METHODS***: A double-blind, parallel-group, placebo-controlled, randomized, controlled trial was performed. Participants were randomly assigned to ingest L. gasseri OLL2716-containing yogurt (L. gasseri OLL2716 group) or L. gasseri OLL2716-free yogurt (placebo group) for 12 weeks. Participants completed questionnaires that dealt with a global assessment as well as symptom severity. The per-protocol (PP) population was evaluated for efficacy in accordance with a plan prepared beforehand. ***RESULTS***: Randomization was performed on 116 individuals; the PP population consisted of 106 individuals (mean age 42.8 +/- 9.0). The impressions regarding the overall effect on gastric symptoms were more positive in the L. gasseri OLL2716 group compared to that in the placebo group (statistical trend; p = 0.073). The elimination rate for major FD symptoms was 17.3 and 35.3% in the placebo and L. gasseri OLL2716 groups respectively (p = 0.048). ***CONCLUSION***: L. gasseri OLL2716 has beneficial effects on FD without H. pylori involvement.

Okada, Y., Tsuzuki, Y., Takeshi, T., Furuhashi, H., Higashiyama, M., Watanabe, C., Shirakabe, K., Kurihara, C., Komoto, S., Tomita, K., Nagao, S., Miura, S., and Hokari, R. Novel probiotics isolated from a Japanese traditional fermented food, Funazushi, attenuates DSS-induced colitis by increasing the induction of high integrin alphav/beta8-expressing dendritic cells. J.Gastroenterol. 6-19-2017; PM: 28631049

ABSTRACT: ***BACKGROUND***: We isolated two novel probiotics strains (s193 and s292) from Funazushi, which is a traditional Japanese fermented food, and evaluated its effects on DSS-induced colitis to determine the possible underlying mechanisms. ***METHODS***: A single colony from homogenized Funazushi was isolated by its ability to suppress TNF-alpha in RAW 264.7. Effect of probiotics on colonic inflammation induced by DSS was evaluated. Effect of probiotics on Treg induction by CD11c+ dendritic cells (DCs) of MLNs were analyzed. ***RESULTS***: Two novel probiotics strains classified into the genus Lactobacillus were isolated (s193 and s292), and those strains showed stronger anti-inflammatory effects on DSS-induced colitis than those of L. gasseri isolated from the gut. mRNA expression beta8 integrin in CD11c+DCs of MLNs and the number of Tregs in the large intestine were significantly increased by s193 and s292 administration compared with L. gasseri administration. Bone marrow DCs treated with s193 and s292 highly increased beta8 integrin, and those cells strongly induced differentiation of CD4+ T cells into Tregs. Differentiation of Tregs was remarkably inhibited by anti-beta8 integrin antibody treatment. ***CONCLUSIONS***: Strains s193 and s292 demonstrate strong anti-inflammatory effects on DSS-induced colitis through induction of beta8 integrin expression on DCs. Our results suggested that Japanese traditional fermented foods are valuable sources for probiotics that are effective for IBD therapy and treatment.

oki-Yoshida, A., Saito, S., Tsuruta, T., Ohsumi, A., Tsunoda, H., and Sonoyama, K. Exosomes isolated from sera of mice fed Lactobacillus strains affect inflammatory cytokine production in macrophages in vitro. Biochem.Biophys.Res.Commun. 7-22-2017; 489(2):248-254; PM: 28559134

ABSTRACT: Orally administered Lactobacillus strains, including L. plantarum No.14 and L. rhamnosus GG, reportedly reduce inflammatory cytokine production in mice. The present study tested our idea that circulating exosomes mediate the action of Lactobacillus strains. The lipopolysaccharide-induced production of TNF-alpha and IL-6 in vitro was attenuated in peritoneal exudate cells (PECs) isolated from C57BL/6N mice that had been fed L. plantarum No.14. When PECs were cultured for 24 h with exosomes isolated from the serum of mice fed L. plantarum No.14 or L. rhamnosus GG, accumulation of both TNF-alpha and of the corresponding mRNA was lowered. Growth in the presence of these exosomes also decreased the production of TNF-alpha and IL-6 by the murine macrophage cell line RAW264.7. In contrast, supplementation with exosome-depleted serum of mice fed L. plantarum No.14 or L. rhamnosus GG failed to affect the production of TNF-alpha and IL-6 by RAW264.7 cells. When PECs and RAW264.7 cells were cultured for 24 h with PKH67-labeled exosomes isolated from murine serum, fluorescent signal was observed inside the cells, suggesting that these cells incorporate serum exosomes. We propose that the anti-inflammatory activity of orally administered L. plantarum No.14 and L. rhamnosus GG is mediated, at least in part, by circulating exosomes.

Olgun, A. "Metformin-resistant" folic acid producing probiotics or folic acid against metformin's adverse effects like diarrhea. Med.Hypotheses. 2017; 106:33-34; PM: 28818268

ABSTRACT: Metformin, first line medication in the treatment of type2 diabetes by millions of patients worldwide, causes gastrointestinal adverse effects (i.e. diarrhea) in approximately 30% of patients, frequently leading to discontinuation. Interestingly, metformin was reported to increase life span in a microscopic worm, Caenorhabditis elegans, by decreasing folate and methionine production of bacteria that this worm uses as a food source. Metformin can be expected to have a similar effect on some microorganisms of human gut microbiota. This can disturb the balance of gut microbiota and cause gastrointestinal adverse effects by altering folate production of some types of bacteria and suppress their growth. Metformin resistant probiotics can be discovered or generated by artificial evolution/selection, and used to prevent these adverse effects. These patients can also be managed with folate supplementation.

Olsen, P., Williamson, M., Traynor, V., and Georgiou, C. The impact of oral probiotics on vaginal Group B Streptococcal colonisation rates in pregnant women: A pilot randomised control study. Women Birth. 6-28-2017; PM: 28668229

ABSTRACT: ***OBJECTIVE***: To perform a pilot project to determine if this research design was appropriate to explore potential causal relationships between oral probiotic use and vaginal Group B Streptococcal (GBS) colonisation rates in pregnant women. ***METHOD***: Thirty-four GBS-positive women at 36 weeks pregnant were recruited. The participants were randomly allocated to the control group, who received standard antenatal care, or to the intervention group, who received standard antenatal care and a daily oral dose of probiotics for three weeks or until they gave birth. A vaginal GBS swab was collected three weeks post consent or during labour. ***FINDINGS***: No significant difference

was found in vaginal GBS rates between the control and intervention groups. Only seven of 21 women in the intervention group completed the entire 21days of probiotics. A subgroup analysis, including only those who had completed 14days or more of probiotics (n=16), also showed no significant difference in vaginal GBS when compared to the control. The findings did show significantly more vaginal commensals in the probiotics group (p=0.048). ***DISCUSSION***: Five possible reasons for the lack of significant results are: the length of the intervention was too short; the dosage of the probiotics was too low; the wrong strains of probiotics were used; the sample size was inadequate; or oral probiotics are ineffective in impacting vaginal GBS. ***IMPLICATIONS***: The finding of a significant increase of vaginal commensals in women who completed 14days or more of probiotics supports the potential of probiotics to impact vaginal GBS in pregnancy.

Pacifici, R. Bone Remodeling and the Microbiome. Cold Spring Harb.Perspect.Med. 8-28-2017; PM: 28847904

ABSTRACT: Exposed surfaces of mammals are colonized with 100 trillion indigenous bacteria, fungi, and viruses, creating a diverse ecosystem known as the microbiome. The gastrointestinal tract harbors the greatest numbers of these microorganisms, which regulate human nutrition, metabolism, and immune system function. Moreover, the intestinal microbiota contains pro- and anti-inflammatory products that modulate immune responses and may play a role in maintaining gut barrier function. Therefore, the community composition of the microbiota has profound effects on the immune status of the host and impacts the development and/or progression of inflammatory diseases. Accordingly, numerous studies have shown differences in the microbiota of patients with and without a given inflammatory condition. There is now strong evidence that the gut microbiome regulates bone homeostasis in health and disease, and that prebiotic and probiotics protect against bone loss. Herein, the evidence supporting the role of the microbiota and the effects of prebiotic and probiotics will be reviewed.

Palaniyandi, S. A., Damodharan, K., Suh, J. W., and Yang, S. H. In Vitro Characterization of Lactobacillus plantarum Strains with Inhibitory Activity on Enteropathogens for Use as Potential Animal Probiotics. Indian J.Microbiol. 2017; 57(2):201-210; PM: 28611498

ABSTRACT: The present study evaluates the probiotic properties of three Lactobacillus plantarum strains MJM60319, MJM60298, and MJM60399 possessing antimicrobial activity against animal enteric pathogens. The three strains did not show bioamine production, mucinolytic and hemolytic activity and were susceptible to common antibiotics. The L. plantarum strains survived well in the simulated orogastrointestinal transit condition and showed adherence to Caco-2 cells in vitro. The L. plantarum strains showed strong antimicrobial activity against enterotoxigenic Escherichia coli, Shiga toxin-producing E. coli, Salmonella enterica subsp. enterica serovar Typhimurium, Choleraesuis and Gallinarum compared to the commercial probiotic strain Lactobacillus rhamnosus GG. The mechanism of antimicrobial activity of the L. plantarum strains appeared to be by the production of lactic acid. Furthermore, the L. plantarum strains tolerated freeze-drying and maintained higher viability in the presence of cryoprotectants than without cryoprotectants. Finally, the three L. plantarum strains tolerated NaCl up to 8% and maintained >60% growth. These characteristics of the three L. plantarum strains indicate that they could be applied as animal probiotic after appropriate in vivo studies.

Pammi, M. and Suresh, G. Enteral lactoferrin supplementation for prevention of sepsis and necrotizing enterocolitis in preterm infants. Cochrane.Database.Syst.Rev. 6-28-2017; 6:CD007137; PM: 28658720

ABSTRACT: ***BACKGROUND***: Lactoferrin, a normal component of human colostrum and milk, can enhance host defenses and may be effective for prevention of sepsis and necrotizing enterocolitis (NEC) in preterm neonates. ***OBJECTIVES***: Primary objective 1. To assess the safety and effectiveness of lactoferrin supplementation to enteral feeds for prevention of sepsis and NEC in preterm neonates Secondary objectives 1. To determine the effects of lactoferrin supplementation to enteral feeds to prevent neonatal sepsis and/or NEC on duration of positive-pressure ventilation, development of chronic lung disease (CLD) or periventricular leukomalacia (PVL), length of hospital stay to discharge among survivors, and adverse neurological outcomes at two years of age or later2. To determine the adverse effects of lactoferrin supplementation for prophylaxis of neonatal sepsis and/or NECWhen data were available, we analyzed the following subgroups.1. Gestational age < 32 weeks and 32 to 36 weeks2. Birth weight < 1000 g (extremely low birth weight (ELBW) infants) and birth weight < 1500 g (very low birth weight (VLBW) infants)3. Type of feeding: breast milk versus formula milk ***SEARCH METHODS***: We used the search strategy of the Cochrane Neonatal Review Group (CNRG) to update our search in December 2016. We searched the databases Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, PREMEDLINE, Embase, and the Cumulative Index to Nursing and Allied Health Literature (CINAHL), as well as trial registries and conference proceedings. ***SELECTION CRITERIA***: Randomized controlled trials (RCTs) evaluating oral lactoferrin at any dose or duration to prevent sepsis or NEC in preterm neonates. ***DATA COLLECTION AND ANALYSIS***: Review authors used standard methods of the CNRG. ***MAIN RESULTS***: This review includes six RCTs. Trial results show that lactoferrin supplementation to enteral feeds decreased late-onset sepsis (typical risk ratio (RR) 0.59, 95% confidence interval (CI) 0.40 to 0.87; typical risk difference (RD) -0.06, 95% CI -0.10 to -0.02; number needed to treat for an additional beneficial outcome (NNTB) 17, 95% CI 10 to 50; six trials, 886 participants; low-quality evidence) and NEC stage II or III (typical RR 0.40, 95% CI 0.18 to 0.86; typical RD -0.04, 95% CI -0.06 to -0.01; NNTB 25, 95% CI 17 to 100; four studies, 750 participants; low-quality evidence). Lactoferrin supplementation did not have an effect on "all-cause mortality" (typical RR 0.65, 95% CI 0.37 to 1.11; typical RD -0.02, 95% CI -0.05 to 0; six studies, 1041 participants; low-quality evidence).Lactoferrin supplementation to enteral feeds with probiotics decreased late-onset sepsis (RR 0.27, 95% CI 0.12 to 0.60; RD -0.13, 95% CI -0.19 to -0.06; NNTB 8, 95% CI 5 to 17; one study, 321 participants; low-quality evidence) and NEC stage II or III (RR 0.04, 95% CI 0.00 to 0.62; RD -0.05, 95% CI -0.08 to -0.03; NNTB 20, 95% CI 12.5 to 33.3; one study, 496 participants; low-quality evidence), but not "all-cause mortality" (low-quality evidence).Lactoferrin supplementation to enteral feeds with or without probiotics decreased bacterial and fungal sepsis but not CLD or length of hospital stay (low-quality evidence). Investigators reported no adverse effects and did not evaluate long-term neurological outcomes and PVL. ***AUTHORS' CONCLUSIONS***: Evidence of low quality suggests that lactoferrin supplementation to enteral feeds with or without probiotics decreases late-onset sepsis and NEC stage II or III in preterm infants without adverse effects. Completed ongoing trials will provide data from more than 6000 preterm neonates, which may enhance the quality of the evidence. Clarification regarding optimal dosing regimens, types of lactoferrin (human or bovine), and long-term outcomes is needed.

Pan, L., Zhao, P. F., Ma, X. K., Shang, Q. H., Xu, Y. T., Long, S. F., Wu, Y., Yuan, F. M., and Piao, X. S. Probiotic supplementation protects weaned pigs against enterotoxigenic Escherichia coli K88 challenge and improves performance similar to antibiotics. J.Anim Sci. 2017; 95(6):2627-2639; PM: 28727032

ABSTRACT: These studies evaluated the effects of probiotics (PB) as a potential substitute for antibiotics (AB) on diarrhea in relation to immune responses and intestinal health in weaned pigs challenged with enterotoxigenic (ETEC) K88 (Exp. 1) and the effects of PB on performance and nutrient digestibility in weaned pigs (Exp. 2). In Exp. 1, 24 weaned barrows (4.9 +/- 0.4 kg initial BW) were randomly assigned to 1 of 4 treatments. The treatments consisted of pigs fed an unsupplemented corn-soybean meal basal diet and not challenged (NON-C) or challenged with ETEC K88 (CHA-C) on d 9 and pigs fed the same basal diet supplemented with AB (100 mg/kg zinc bacitracin, 50 mg/kg colistin sulfate, and 100 mg/kg olaquindox; CHA-AB) or 500 mg/kg PB (and ; CHA-PB) and challenged with ETEC K88 on d 9. In Exp. 2, 108 weaned pigs (7.5 +/- 0.9 kg initial BW) not challenged with ETEC K88 were randomly assigned to 1 of 3 treatments, including an AB-free basal diet (CON) and the basal diet with AB (ABD) or 500 mg/kg PB supplementation (PBD). In Exp. 1, after challenge, CHA-C decreased (< 0.05) ADG and ADFI, whereas CHA-AB and CHA-PB revealed no significant change compared with NON-C. Compared with CHA-C, CHA-AB and CHA-PB improved (< 0.05) ADG and ADFI and decreased (< 0.05) the diarrhea incidence in pigs. Mucosal secretory Ig A contents in the jejunum and ileum were greater in CHA-C than in NON-C (< 0.05) and lower than in CHA-PB (< 0.05). The diet containing PB alleviated the increase in the endotoxin and diamine oxidase concentration and cecal count (< 0.05) and the decrease in intestinal villus height, cecal count, and jejunal mucosal occludin protein abundance (< 0.05). In Exp. 2, dietary supplementation with AB and PB had positive effects on ADG and feed efficiency (< 0.05). Compared with CON, apparent digestibility of nutrients in PBD was improved (< 0.05). Collectively, PB supplementation protected the pigs against ETEC K88 infection by enhancing immune responses and attenuating intestinal damage and improved the performance and nutrient digestibility of weaned pigs. Therefore, PB could be a potential effective alternative to AB for ameliorating diarrhea and improving performance in weaned pigs.

Pan, L. L., Li, J., Shamoon, M., Bhatia, M., and Sun, J. Recent Advances on Nutrition in Treatment of Acute Pancreatitis. Front Immunol. 2017; 8:762; PM: 28713382

ABSTRACT: Acute pancreatitis (AP) is a common abdominal acute inflammatory disorder and the leading cause of hospital admission for gastrointestinal disorders in many countries. Clinical manifestations of AP vary from self-limiting local inflammation to devastating systemic pathological conditions causing significant morbidity and mortality. To date, despite extensive efforts in translating promising experimental therapeutic targets in clinical trials, disease-specific effective remedy remains obscure, and supportive care has still been the primary treatment for this disease. Emerging evidence, in light of the current state of pathophysiology of AP, has highlighted that strategic initiation of nutrition with appropriate nutrient supplementation are key to limit local inflammation and to prevent or manage AP-associated complications. The current review focuses on recent advances on nutritional interventions including enteral versus parenteral nutrition strategies, and nutritional supplements such as probiotics, glutamine, omega-3 fatty acids, and vitamins in clinical AP, hoping to advance current knowledge and practice related to nutrition and nutritional supplements in clinical management of AP.

Pan, W. and Kang, Y. Gut microbiota and chronic kidney disease: implications for novel mechanistic insights and therapeutic strategies. Int.Urol.Nephrol. 8-28-2017; PM: 28849345

ABSTRACT: The complicated communities of microbiota colonizing the human gastrointestinal tract exert a strong function in health maintenance and disease prevention. Indeed, accumulating evidence has indicated that the intestinal microbiota plays a key role in the pathogenesis and development of chronic kidney disease (CKD). Modulation of the gut microbiome composition in CKD may contribute to the accumulation of gut-derived uremic toxins, high circulating level of lipopolysaccharides and immune deregulation, all of which play a critical role in the pathogenesis of CKD and CKD-associated complications. In this review, we discuss the recent findings on the potential impact of gut microbiota in CKD and the underlying mechanisms by which microbiota can influence kidney diseases and vice versa. Additionally, the potential efficacy of pre-, pro- and synbiotics in the restoration of healthy gut microbia is described in detail to provide future directions for research.

Pannek, J. and Wollner, J. Management of urinary tract infections in patients with neurogenic bladder: challenges and solutions. Res.Rep.Urol. 2017; 9:121-127; PM: 28761863

ABSTRACT: ***INTRODUCTION***: Urinary tract infections (UTIs) are one of the most common morbidities in persons with neurogenic lower urinary tract dysfunction (NLUTD). They are associated with a significant morbidity and mortality, and they affect the quality of life of the affected patients. Diagnosis and treatment of UTI in this group of patients are challenging. In this review, the current strategies regarding diagnosis, treatment, and prevention are summarized. ***DIAGNOSTICS***: it is important to correctly diagnose a UTI, as treatment of bacteriuria should strictly be avoided. A UTI is defined as a combination of laboratory findings (leukocyturia and bacteriuria) and symptoms. Laboratory findings without symptoms are classified as asymptomatic bacteriuria. Routine urine screening is not advised. ***TREATMENT***: Only UTI should be treated; treatment of asymptomatic bacteriuria is not indicated. Prior to treatment, urine for a urine culture should be obtained. Antibiotic treatment for ~7 days is advised. ***PREVENTION***: In recurrent UTI, bladder management should be optimized and morphologic causes for UTI should be excluded. If UTIs persist, medical prophylaxis should be considered. Currently, no prophylactic measure with evidence-based efficacy exists. Long-term antibiotic prophylaxis should be used merely as an ultimate measure. Among the various mentioned innovative approaches for UTI prevention, bacteriophages, intravesical instillations, complementary and alternative medicine techniques, and probiotics seem to be most promising. ***CONCLUSION***: Recently, several promising innovative options for UTI prophylaxis have been developed which may help overcome the current therapeutic dilemma. However, further well designed studies are necessary to evaluate the safety and efficacy of these approaches.

Papizadeh, M., Rohani, M., Nahrevanian, H., Javadi, A., and Pourshafie, M. R. Probiotic characters of Bifidobacterium and Lactobacillus are a result of the ongoing gene acquisition and genome minimization evolutionary trends. Microb.Pathog. 8-18-2017; 111:118-131; PM: 28826768

ABSTRACT: Bifidobacterium and Lactobacillus are the main probiotic genera. Collectively, these two genera harbor over 200 species among which are many strains

have been introduced as probiotics. These health-promoting microbes confer health benefits upon the host and so used in food productions and as supplements. Considering the economic importance of probiotics, the biochemistry, genomics, phylogeny and physiology of such genera have been exhaustively studied. According to the genomic data, the probiotic capabilities are strain specific which may be a result of the niche-specialization of the genomes of these bacteria to certain ecological niches like gastrointestinal tract of a diverse range of animals. These microbes have a wide distribution but the culture-based studies and either genomics data suggest selective affinity of some Lactobacillus and either Bifidobacterium species to certain ecological niches. An ongoing genome degradation, which is thought to be a result of passage through an evolutionary bottleneck, is the major trend in the evolution of lactobacilli. Further, evolutionary events resulted into two categories of lactobacilli: habitat generalists and habitat specialists. In place, the main trend in the evolution of bifidobacteria tend to be the gene acquisition. However, probiotic features are the results of a co-evolutionary relationship between these bacteria and their hosts and the aforementioned evolutionary tends have driven the evolution of these probiotic genera.

Park, E., Paik, H. D., and Lee, S. M. Combined effects of whey protein hydrolysates and probiotics on oxidative stress induced by an iron-overloaded diet in rats. Int.J.Food Sci.Nutr. 7-25-2017; 1-10; PM: 28738702

ABSTRACT: Whey proteins possess antioxidant properties, and probiotics have various health-promoting effects. We investigated the effects of whey protein hydrolysates (WPHs) and probiotics in rats exposed to oxidative stress induced by iron-overload diet (IOL). Rats were divided into control (CTRL), IOL (0.2% ferrous sulphate), WPH (10%), probiotic (PB) mixture (Lactococcus lactis NK34 and B. polyfermenticus SCD), and WPH + PB group for 6 weeks. Average leukocytes and colonocytes tail moments were increased in IOL compared to CTRL but decreased in other groups. Conjugated diene was lower in WPH, PB, and WPH + PB than in IOL. Only WPH + PB group could recover glutathione S-transferase (GST) levels. SOD levels were recovered by WPH and PB. PB and WPH + PB increased alpha-tocopherol and only WPH + PB increased gamma-tocopherol. Thus, our data demonstrated that WPH and PB exhibit antioxidant properties in a rat model of high-iron diet-induced oxidative stress and combination of them may provide an enhanced effect.

Park, M. S., Kwon, B., Ku, S., and Ji, G. E. The Efficacy of Bifidobacterium longum BORI and Lactobacillus acidophilus AD031 Probiotic Treatment in Infants with Rotavirus Infection. Nutrients. 8-16-2017; 9(8); PM: 28813007

ABSTRACT: A total of 57 infants hospitalized with rotavirus disease were included in this study. The children were randomly divided into the study's two treatment groups: three days of the oral administration of (i) a probiotics formula containing both Bifidobacterium longum BORI and Lactobacillus acidophilus AD031 (N = 28); or (ii) a placebo (probiotic-free skim milk, N = 29) and the standard therapy for diarrhea. There were no differences in age, sex, or blood characteristics between the two groups. When the 57 cases completed the protocol, the duration of the patients' diarrhea was significantly shorter in the probiotics group (4.38 +/- 1.29, N = 28) than the placebo group (5.61 +/- 1.23, N = 29), with a p-value of 0.001. Symptoms such as duration of fever (p = 0.119), frequency of diarrhea (p = 0.119), and frequency of vomiting (p = 0.331) tended to be ameliorated by the probiotic treatment; however, differences were not statistically significant between

the two groups. There were no serious, adverse events and no differences in the frequency of adverse events in both groups.

Parker, E. A., Roy, T., D'Adamo, C. R., and Wieland, L. S. Probiotics and gastrointestinal conditions: An overview of evidence from the Cochrane Collaboration. Nutrition. 7-6-2017; PM: 28870406

ABSTRACT: Alterations in the composition of the gut microbiota are associated with a number of gastrointestinal (GI) conditions, including diarrhea, inflammatory bowel diseases (IBD), and liver diseases. Probiotics, live microorganisms that may confer a health benefit to the host when consumed, are commonly used as a therapy for treating these GI conditions by means of modifying the composition or activity of the microbiota. The purpose of this review was to summarize the evidence on probiotics and GI conditions available from Cochrane, a nonprofit organization that produces rigorous and high-quality systematic reviews of health interventions. Findings from this review will help provide more precise guidance for clinical use of probiotics and to identify gaps in probiotic research related to GI conditions.

Patel, A. L., Panagos, P. G., and Silvestri, J. M. Reducing Incidence of Necrotizing Enterocolitis. Clin.Perinatol. 2017; 44(3):683-700; PM: 28802346

ABSTRACT: Necrotizing enterocolitis (NEC) is a multifactorial disease that occurs when multiple risk factors and/or stressors overlap, leading to profound inflammation and intestinal injury. Due to its multifactorial nature, there has been much uncertainty in identifying clear strategies for prevention of NEC. Despite these obstacles, the incidence of NEC has gradually been decreasing over the past 10 years, in part due to quality improvement (QI) initiatives to prevent NEC. Current QI strategies primarily target the various predisposing conditions. This article reviews the evidence on which QI interventions to prevent NEC have been based and provides examples of successful QI interventions.

Patole, S. Probiotics for Preterm Infants - The Story Searching for an End. Indian Pediatr. 5-15-2017; 54(5):361-362; PM: 28601850

No Abstract Available.

Pellegrino, M., Berardo, N., Giraudo, J., Nader-Macias, M. E. F., and Bogni, C. Bovine mastitis prevention: humoral and cellular response of dairy cows inoculated with lactic acid bacteria at the dry-off period. Benef.Microbes. 8-24-2017; 8(4):589-596; PM: 28701082

ABSTRACT: The use of lactic acid bacteria (LAB) in animal feed, constitute an alternative tool for bovine mastitis prevention. Previously, two LAB strains were isolated from bovine milk and selected for their probiotics properties. So far, immune response of inoculating LAB in bovine udders at dry-off period has not been investigated. The immunoglobulin isotype levels and memory cell proliferation in blood and milk of animals inoculated with Lactobacillus lactis subsp. lactis CRL1655 and Lactobacillus perolens CRL1724 at dry-off period was studied. Ten animals were inoculated intramammarily with 106 cells of each LAB (IG) and 2 animals used as control (NIG). Milk and blood samples were taken before

inoculation and 1, 2, 4, 6, 12 and 24 h and 7 and 14 days after inoculation. Somatic cell count (SCC) in milk, the presence of bovine mastitis pathogens, the levels of antibodies and lymphocyte proliferation were determined. In the IG, the SCC was <250,000 cells/ml up to 4 h after intramammary inoculation. Six and 12 h after inoculation, the SCC increased up to 600,000 and 2,000,000 cells/ml, respectively. In the NIG, the SCC reached the maximum value 7 days after inoculation. Microbiological analysis showed that all samples were negative for major bovine mastitis pathogens after 24-48 h of incubation. In general, LAB inoculation increased the amount of IgG isotypes in blood and milk, and these antibodies were able to recognise Staphylococcus aureus epitopes. Lymphocytes proliferation was significantly higher in the IG at all time points assayed, following LAB or S. aureus stimulation. The lymphocytes of animals inoculated with LAB do not react in vitro to the presence of S. aureus antigen.. The results showed that probiotic microorganisms could be a natural and effective alternative in the prevention of bovine mastitis at dry-off period and act as immunomodulatory stimulating local and systemic defence lines.

Pelzer, E., Gomez-Arango, L. F., Barrett, H. L., and Nitert, M. D. Review: Maternal health and the placental microbiome. Placenta. 2017; 54:30-37; PM: 28034467

ABSTRACT: Over the past decade, the role of the microbiome in regulating metabolism, immune function and behavior in humans has become apparent. It has become clear that the placenta is not a sterile organ, but rather has its own endogenous microbiome. The composition of the placental microbiome is distinct from that of the vagina and has been reported to resemble the oral microbiome. Compared to the gut microbiome, the placental microbiome exhibits limited microbial diversity. This review will focus on the current understanding of the placental microbiota in normal healthy pregnancy and also in disease states including preterm birth, chorioamnionitis and maternal conditions such as obesity, gestational diabetes mellitus and preeclampsia. Factors known to alter the composition of the placental microbiota will be discussed in the final part of this review.

Pierzchalska, M., Panek, M., Czyrnek, M., Gielicz, A., Mickowska, B., and Grabacka, M. Probiotic Lactobacillus acidophilus bacteria or synthetic TLR2 agonist boost the growth of chicken embryo intestinal organoids in cultures comprising epithelial cells and myofibroblasts. Comp Immunol.Microbiol.Infect.Dis. 2017; 53:7-18; PM: 28750869

ABSTRACT: The intestinal epithelial cells reside in close proximity to myofibroblasts and microbiota, which are supposed to have an impact on intestinal stem cells fate and to influence processes of tissue maturation and regeneration. Mechanism underlying these phenomena and their diversity among vertebrates can be studied in 3D organoid cultures. We investigated the growth of chicken embryo intestinal epithelial organoids in Matrigel with and without Toll-like receptors (TLRs) stimulation. The organoid cultures contained also some myofibroblasts with potential to promote intestinal stem cell survival. Organoid cells, expressing TLR4, TLR2 type 1 and TLR2 type 2 were incubated with their agonists (lipopolysaccharide - LPS and Pam3CSK4) or co-cultured with Lactobacillus acidophilus bacteria (LA-5). Pam3CSK4 and LA-5 promoted organoid growth, which was demonstrated by comparing the morphological parameters (mean number and area of organoids). The profile of prostaglandins (PG), known to promote intestinal regeneration, in supernatants from organoid and fibroblast cultures were evaluated. Both PGE2 and PGD2 were detected. As compared to unstimulated controls, supernatants from the

Pam3CSK4-stimulated organoids contained twice as much of PGE2 and PGD2. The changes in production of prostaglandins and the support of epithelial cell growth by myofibroblasts are factors potentially responsible for stimulatory effect of TLR2 activation.

Pinto, J. M. and Petrova, A. Detection of Acute Gastroenteritis Etiology in Hospitalized Young Children: Associated Factors and Outcomes. Hosp.Pediatr. 2017; 7(9):536-541; PM: 28790133

ABSTRACT: ***BACKGROUND***: The decision to test for the etiology of diarrhea is a challenging question for practicing pediatricians. ***METHODS***: The main goal of this retrospective cohort study was to identify factors associated with testing for and diagnosis of rotavirus, Clostridium difficile, or other bacterial infections, as well as the length of stay (LOS) for children with acute gastroenteritis who were hospitalized at a single institution. Patients aged 6 to 60 months with acute diarrhea (<14 days) and no underlying gastrointestinal conditions were included. Data were analyzed by using multivariate logistic and linear regression models. ***RESULTS***: Stool testing was performed in 73.1% of the 331 patients studied. The majority were tested for multiple pathogens, including rotavirus (65.9%), C difficile (30.8%), and other bacteria (63.4%), with recovery rates of 33.0%, 9.8%, and 6.7%, respectively. Rotavirus was more often identified in older patients with dehydration and vomiting. Although testing for C difficile was more likely with prolonged diarrhea, no vomiting, and recent antibiotic use, no factors were associated with C difficile recovery. Patients who were diagnosed with C difficile were more likely to receive probiotics than those who received negative test results. LOS was not associated with stool testing or recovery of any tested pathogens. ***CONCLUSIONS***: Although children with acute gastroenteritis underwent frequent stool testing for diarrheal etiology, detection of a pathogen was uncommon and not associated with a change in LOS. Experimental research will be needed to make additional conclusions about the efficacy of testing for diarrheal etiology in the inpatient practice of acute pediatric diarrhea.

Piper, A. M., Farnier, K., Linder, T., Speight, R., and Cunningham, J. P. Two Gut-Associated Yeasts in a Tephritid Fruit Fly have Contrasting Effects on Adult Attraction and Larval Survival. J.Chem.Ecol. 8-23-2017; PM: 28836040

ABSTRACT: Yeast-insect interactions have been well characterized in drosophilid flies, but not in tephritid fruit flies, which include many highly polyphagous pest species that attack ripening fruits. Using the Queensland fruit fly (Bactrocera tryoni) as our model tephritid species, we identified yeast species present in the gut of wild-collected larvae and found two genera, Hanseniaspora and Pichia, were the dominant isolates. In behavioural trials using adult female B. tryoni, a fruit-agar substrate inoculated with Pichia kluyveri resulted in odour emissions that increased the attraction of flies, whereas inoculation with Hanseniaspora uvarum, produced odours that strongly deterred flies, and both yeasts led to decreased oviposition. Larval development trials showed that the fruit-agar substrate inoculated with the 'deterrent odour' yeast species, H. uvarum, resulted in significantly faster larval development and a greater number of adult flies, compared to a substrate inoculated with the 'attractive odour' yeast species, P. kluyveri, and a yeast free control substrate. GC-MS analysis of volatiles emitted by H. uvarum and P. kluyveri inoculated substrates revealed significant quantitative differences in ethyl-, isoamyl-, isobutyl-, and phenethyl- acetates, which may be responsible for the yeast-specific olfactory responses of adult flies. We discuss how our seemingly counterintuitive finding that female B. tryoni

flies avoid a beneficial yeast fits well with our understanding of female choice of oviposition sites, and how the contrasting behavioural effects of H. uvarum and P. kluyveri raises interesting questions regarding the role of yeast-specific volatiles as cues to insect vectors. A better understanding of yeast-tephritid interactions could assist in the future management of tephritid fruit fly pests through the formulation of new "attract and kill" lures, and the development of probiotics for mass rearing of insects in sterile insect control programs.

Plaza-Diaz, J., Ruiz-Ojeda, F. J., Vilchez-Padial, L. M., and Gil, A. Evidence of the Anti-Inflammatory Effects of Probiotics and Synbiotics in Intestinal Chronic Diseases. Nutrients. 5-28-2017; 9(6); PM: 28555037

ABSTRACT: Probiotics and synbiotics are used to treat chronic diseases, principally due to their role in immune system modulation and the anti-inflammatory response. The present study reviewed the effects of probiotics and synbiotics on intestinal chronic diseases in in vitro, animal, and human studies, particularly in randomized clinical trials. The selected probiotics exhibit in vitro anti-inflammatory properties. Probiotic strains and cell-free supernatants reduced the expression of pro-inflammatory cytokines via action that is principally mediated by toll-like receptors. Probiotic administration improved the clinical symptoms, histological alterations, and mucus production in most of the evaluated animal studies, but some results suggest that caution should be taken when administering these agents in the relapse stages of IBD. In addition, no effects on chronic enteropathies were reported. Probiotic supplementation appears to be potentially well tolerated, effective, and safe in patients with IBD, in both CD and UC. Indeed, probiotics such as Bifidobacterium longum 536 improved the clinical symptoms in patients with mild to moderate active UC. Although it has been proposed that probiotics can provide benefits in certain conditions, the risks and benefits should be carefully assessed before initiating any therapy in patients with IBD. For this reason, further studies are required to understand the precise mechanism by which probiotics and synbiotics affect these diseases.

Poeta, M., Pierri, L., and Vajro, P. Gut-Liver Axis Derangement in Non-Alcoholic Fatty Liver Disease. Children.(Basel). 8-2-2017; 4(8); PM: 28767077

ABSTRACT: Non-alcoholic fatty liver disease (NAFLD) is the most frequent type of chronic liver disease in the pediatric age group, paralleling an obesity pandemic. A "multiple-hit" hypothesis has been invoked to explain its pathogenesis. The "first hit" is liver lipid accumulation in obese children with insulin resistance. In the absence of significant lifestyle modifications leading to weight loss and increased physical activity, other factors may act as "second hits" implicated in liver damage progression leading to more severe forms of inflammation and hepatic fibrosis. In this regard, the gut-liver axis (GLA) seems to play a central role. Principal players are the gut microbiota, its bacterial products, and the intestinal barrier. A derangement of GLA (namely, dysbiosis and altered intestinal permeability) may promote bacteria/bacterial product translocation into portal circulation, activation of inflammation via toll-like receptors signaling in hepatocytes, and progression from simple steatosis to non-alcoholic steato-hepatitis (NASH). Among other factors a relevant role has been attributed to the farnesoid X receptor, a nuclear transcriptional factor activated from bile acids chemically modified by gut microbiota (GM) enzymes. The individuation and elucidation of GLA derangement in NAFLD pathomechanisms is of interest at all ages and especially in pediatrics to identify new

therapeutic approaches in patients recalcitrant to lifestyle changes. Specific targeting of gut microbiota via pre-/probiotic supplementation, feces transplantation, and farnesoid X receptor modulation appear promising.

Poormontaseri, M., Hosseinzadeh, S., Shekarforoush, S. S., and Kalantari, T. The effects of probiotic Bacillus subtilis on the cytotoxicity of Clostridium perfringens type a in Caco-2 cell culture. BMC.Microbiol. 7-4-2017; 17(1):150; PM: 28676033

ABSTRACT: ***BACKGROUND***: Some Bacillus strains have recently been identified for potential use as probiotics and food additives. The present study evaluated the antimicrobial effects of Bacillus subtilis ATCC 6633 and its metabolite on the enterotoxin and vegetative cells, spore and germinated spore of Clostridium perfringens type A in Caco-2 cells. ***RESULTS***: We used flow cytometry and MTT assays to evaluate the cytotoxicity effect of treatments. According to the results, the most cell survival was found in the 4% crude antimicrobial substance (CAS) with the vegetative form of C. perfringens among co-cultured groups. Furthermore, the apoptosis and necrosis in co-cultured groups were significantly decreased ($P < 0.05$). ***CONCLUSION***: The present results suggested the crucial role of the current probiotic in the control of various forms of C. perfringens type A which was investigated for the first time. Also, the majority of treatments showed higher cell viability in flow cytometry compared to the MTT assay.

Popescu, C. R., Stiemsma, L. T., and Lavoie, P. M. Why haven't the documented benefits of probiotics on preterm babies led to their wider acceptance and use? Acta Paediatr. 8-22-2017; PM: 28833564

No Abstract Available.

Pourramezan, Z., Kasra, Kermanshahi R., Oloomi, M., Aliahmadi, A., and Rezadoost, H. In vitro study of antioxidant and antibacterial activities of Lactobacillus probiotic spp. Folia Microbiol.(Praha). 5-26-2017; PM: 28550367

ABSTRACT: This study investigated the influence of aeration and minimal medium conditions on antioxidant and antibacterial activities of 21 probiotic Lactobacillus strains isolated from dairy products. The probiotic potential of the isolates was evaluated by pH and bile tolerance. Random amplified polymorphic DNA polymerase chain reaction (RAPD-PCR) was used to confirm the phenotypic identification of isolates. Antioxidant producer isolates were screened by resistance to reactive oxygen species (ROS). The antioxidant and antibacterial activities of extracellular materials after 48 h fermentation with antioxidative strains were determined using 2,2-diphenyl-1-picrylhydrazyl (DPPH) and broth microdilution assays, respectively. The results indicate that the antioxidant capacity of supernatants was increased by using of both minimal medium and agitation. The antibacterial activity was increased in minimal medium, but there has nearly no change in the antibacterial properties by using both agitation and minimal medium. The maximum antibacterial activity was observed during mid-exponential phase until the beginning of the early-stationary phase, but the maximum antioxidant activity was detected at the stationary growth phase. There is a significant relationship between antioxidant and antibacterial activities of the cell-free probiotic extracts, and their production rates are closely related to the fermentation type. The bioactive materials

from probiotics could be extracted in a large amount at an appropriate time under a suitable condition.

ppel-da-Silva, M. C., Narvaez, G. A., Perez, L. R. R., Drehmer, L., and Lewgoy, J. Saccharomyces cerevisiae var. boulardii fungemia following probiotic treatment. Med.Mycol.Case.Rep. 2017; 18:15-17; PM: 28794958

ABSTRACT: Probiotics are commonly prescribed as an adjuvant in the treatment of antibiotic-associated diarrhea caused by Clostridium difficile. We report the case of an immunocompromised 73-year-old patient on chemotherapy who developed Saccharomyces cerevisiae var. boulardii fungemia in a central venous catheter during treatment of antibiotic-associated pseudomembranous colitis with the probiotic Saccharomyces cerevisiae var. boulardii. Fungemia was resolved after interruption of probiotic administration without the need to replace the central venous line.

Preveden, T., Scarpellini, E., Milic, N., Luzza, F., and Abenavoli, L. Gut microbiota changes and chronic hepatitis C virus infection. Expert.Rev.Gastroenterol.Hepatol. 2017; 11(9):813-819; PM: 28621554

ABSTRACT: ***INTRODUCTION***: Hepatitis C virus (HCV) infection is a global health problem with 150 million infected people worldwide. Liver can be greatly affected by changes in gut microbiota due to increased intestinal permeability with passage of microbial antigens into the liver through the portal circulation. The concept of 'gut-liver' axis is important to understand the pathophysiology of several liver diseases. Several recent studies also revealed that an altered gut microbiota can be implicated in the pathogenesis of HCV-induced chronic liver disease (CHC). ***Areas covered***: An overview of intestinal microflora composition, host reaction during CHC, and a description of relevant clinical trials on the use of probiotics in this field. ***Expert commentary***: HCV patients gut microbiota composition is stable over liver disease stages. This is a unique example of gut disbiosis stability vs. NAFLD, HBV, HIV, and HCV co-infected patients. The impact of HCV infection on intestinal permeability allows gut disbiosis starting, maintenance and its proinflammatory effect until liver cirrhosis and HCC development. HCV eradication has unraveled the strong impact of gut microbiota unbalance on liver disease development with possible future implications for probiotics use to change the natural history of cirrhosis progression.

Priyodip, P., Prakash, P. Y., and Balaji, S. Phytases of Probiotic Bacteria: Characteristics and Beneficial Aspects. Indian J.Microbiol. 2017; 57(2):148-154; PM: 28611491

ABSTRACT: Probiotics play a vital role in clinical applications for the treatment of diarrhea, obesity and urinary tract infections. Phytate, an anti-nutrient, chelates essential minerals that are vital for human health. In the past few decades, research reports emphasize extensively on phytate degradation in animals. There is a growing need for finding alternate strategies of phytate utilization in human, as they are unable to produce phytase. At this juncture, probiotics can be utilized for phytase production to combat mineral deficiency in humans. The main focus of this review is on improving phosphate bioavailability by employing two approaches: supplementation of (1) fermented food products that contain probiotics and (2) recombinant phytase producing bacteria. In

addition, several factors influencing phytase activity such as bacterial viability, optimal pH, substrate concentration and specificity were also discussed.

Psaltis, A. J. and Wormald, P. J. Therapy of Sinonasal Microbiome in CRS: A Critical Approach. Curr.Allergy Asthma Rep. 2017; 17(9):59; PM: 28785927

ABSTRACT: ***PURPOSE OF REVIEW***: Perturbations in local microbiota have been demonstrated in many chronic inflammatory diseases including chronic rhinosinusitis (CRS). The purpose of this paper is to review the latest microbiome research as it pertains to CRS and establish whether there is any evidence supporting the microbiome hypothesis for CRS. Treatment factors that may influence the sinonasal microbiome as well as the role of probiotics are also discussed. ***RECENT FINDINGS***: Despite significant heterogeneity in study design, tissue sampling, processing and bioinformatics analysis, consistent findings have emerged from the recent literature. Healthy individuals and CRS patients have similar overall bacterial burden of disease and share many common phylum. CRS patients, however, routinely show reductions in markers of biodiversity. Both medical and surgical treatments appear to influence the sinonasal microbiome, with certain bacterial strains associated with better treatment outcomes. The presence of microbial dysbiosis in CRS is now supported by numerous studies. Whether this dysbiosis is a cause or rather an association of the disease process still remains unclear. Although probiotic therapies show early promise, much larger studies are required to establish their real role as a treatment for CRS.

Pu, F., Guo, Y., Li, M., Zhu, H., Wang, S., Shen, X., He, M., Huang, C., and He, F. Yogurt supplemented with probiotics can protect the healthy elderly from respiratory infections: A randomized controlled open-label trial. Clin.Interv.Aging. 2017; 12:1223-1231; PM: 28848330

ABSTRACT: ***PURPOSE***: To evaluate whether yogurt supplemented with a probiotic strain could protect middle-aged and elderly people from acute upper respiratory tract infections (URTI) using a randomized, blank-controlled, parallel-group design. ***PATIENTS AND METHODS***: Two hundred and five volunteers aged >/=45 years were randomly divided into two groups. The subjects in the intervention group were orally administered 300 mL/d of yogurt supplemented with a probiotic strain, Lactobacillus paracasei N1115 (N1115), 3.6x107 CFU/mL for 12 weeks, while those in the control group retained their normal diet without any probiotic supplementation. The primary outcome was the incidence of URTI, and changes in serum protein, immunoglobulins, and the profiles of the T-lymphocyte subsets (total T-cells [CD3+], T-helper cells [CD4+], and T-cytotoxic-suppressor cells [CD8+]) during the intervention were the secondary outcomes. ***RESULTS***: Compared to the control group, the number of persons diagnosed with an acute URTI and the number of URTI events significantly decreased in the intervention group (P=0.038, P=0.030, respectively). The risk of URTI in the intervention group was evaluated as 55% of that in the control group (relative risk =0.55, 95% CI: 0.307-0.969). The change in the percentage of CD3+ cells in the intervention group was significantly higher than in the control group (P=0.038). However, no significant differences were observed in the total protein, albumin, globulin, and prealbumin levels in both groups (P>0.05). ***CONCLUSION***: The study suggested that yogurt with selected probiotic strains such as N1115 may reduce the risk of acute upper tract infections in the elderly. The enhancement of the T-cell-mediated natural immune defense might be one of the important underlying mechanisms for probiotics to express their anti-infective effects.

Radulovic, Z., Miocinovic, J., Mirkovic, N., Mirkovic, M., Paunovic, D., Ivanovic, M., and Seratlic, S. Survival of spray-dried and free-cells of potential probiotic Lactobacillus plantarum 564 in soft goat cheese. Anim Sci.J. 6-19-2017; PM: 28631434

ABSTRACT: A high viability of probiotics in food product, with a living cells threshold of 107 /cfu/g (colony-forming units/g) is a challenge to achieve in food production. Spray drying is an efficient and economic industrial method for probiotic bacterial preservation and its application in food products. In this study, the survival of free and spray-dried cells of potential probiotic strain Lactobacillus plantarum 564 after production and during 8 weeks of storage of soft acid coagulated goat cheese was investigated, as well as compositional and sensory quality of cheese. Total bacterial count of spray-dried Lb. plantarum 564 cells were maintained at the high level of 8.82 log/cfu/g in cheese after 8 weeks of storage, while free-cell number decreased to 6.9 log/cfu/g. However, the chemical composition, pH values and sensory evaluation between control cheese (C1 sample made with commercial starter culture) and treated cheese samples (C2 and C3, made with the same starter, with the addition of free and spray-dried Lb. plantarum 564 cells, respectively) did not significantly differ. High viability of potential probiotic bacteria and acceptable sensory properties indicate that spray-dried Lb. plantarum 564 strain could be successfully used in the production of soft acid coagulated goat cheeses.

Ramakrishnan, V. and Luthria, D. L. Recent applications of NMR in food and dietary studies. J.Sci.Food Agric. 2017; 97(1):33-42; PM: 27435122

ABSTRACT: Over the last decade, a wide variety of new foods have been introduced into the global marketplace, many with health benefits that exceed those of traditional foods. Simultaneously, a wide range of analytical technologies has evolved that allow greater capability for the determination of food composition. Nuclear magnetic resonance (NMR), traditionally a research tool used for structural elucidation, is now being used frequently for metabolomics and chemical fingerprinting. Its stability and inherent ease of quantification have been exploited extensively to identify and quantify bioactive components in foods and dietary supplements. In addition, NMR fingerprints have been used to differentiate cultivars, evaluate sensory properties of food and investigate the influence of growing conditions on food crops. Here we review the latest applications of NMR in food analysis. Published 2016. This article is a U.S. Government work and is in the public domain in the USA.

Ramesh, D., Souissi, S., and Ahamed, T. S. Effects of the potential probiotics Bacillus aerophilus KADR3 in inducing immunity and disease resistance in Labeo rohita. Fish.Shellfish.Immunol. 9-13-2017; PM: 28917486

ABSTRACT: The aim of the present study was to evaluate the dietary administration of Bacillus aerophilus KADR3 on enhancing the immunity and disease resistance against Aeromonas hydrophila infection in Labeo rohita. B. aerophilus culture supernatant exhibited antagonistic activity against fish pathogenic bacteria in an agar well diffusion assay. Four fish groups were fed with either of following diets containing different concentrations of B. aerophilus KADR3 (cfu g-1): 0 (control), 1 x 107 (DI), 1 x 108 (DII), and 1 x 109 (DIII) -cfu g-1. Various innate immune parameters were measured at - 3rd and 6th - week post-feeding. At the end of 6th week, fish were challenged intraperitoneally with A. hydrophila and survival percentage was recorded over 10 days post-challenge.

Studied immunological parameters viz. serum lysozyme, phagocytosis, serum total protein, respiratory bursts, serum IgM levels, superoxide dismutase and alternative complement pathway activities were significantly enhanced ($P < 0.05$) in fish groups fed with B. aerophilus KADR3 supplemented diets, with the highest values were observed in DII (108 cfu g-1) fed group. Further, B. aerophilus supplementation at 108 cfu g-1 exhibited highest post-challenge survivability i.e. 72.83%, followed by DIII (64.19%) and DI (41.97%). Our results collectively suggest that B. aerophilus can potentially be used as probiotic strain in aquaculture to enhance the immunity and disease resistance with an optimal dietary supplementation of 108 cfu g-1.

Rashmi, B. S. and Gayathri, D. Molecular characterization of gluten hydrolysing Bacillus sp. and their efficacy and biotherapeutic potential as probiotics using Caco-2 cell line. J.Appl.Microbiol. 2017; 123(3):759-772; PM: 28637081

ABSTRACT: ***AIM***: To isolate and characterize indigenous gluten hydrolysing bacteria from wheat sourdough and curd samples and further evaluation of their probiotic potentiality. ***METHODS AND RESULTS***: Indigenous gluten hydrolysing isolates GS 33, GS 143, GS 181 and GS 188 were identified as Bacillus sp. by molecular-typing methods and studied extensively for their functional and probiotic attributes. All the tested isolates could survive at pH 2 and toxicity of 0.3% bile and also exhibited cell surface hydrophobicity and autoaggregation phenotype. The isolates were adhered strongly to Caco-2 cells and coaggregated with Escherichia coli MTCC 433 and Listeria monocytogenes MTCC 1143 preventing pathogen invasion into Caco-2 cells in vitro. In addition, the minimum inhibitory concentration of selected antibiotics for all the investigated gluten hydrolysing isolates was within the breakpoint values as recommended by the European Food Safety Authority. ***CONCLUSION***: The indigenous high intensity gluten hydrolysing bacteria exhibited high resistance to gastric and pancreatic stress and possessed antibacterial, aggregation, adhesion and pathogen exclusion properties, and as a potential probiotics, either alone or in consortium would be useful in the development of gluten-free wheat foods. ***SIGNIFICANCE AND IMPACT OF THE STUDY***: Exploring new indigenous gluten hydrolysing bacteria from wheat sourdough and curd samples would be beneficial in developing gluten-free wheat foods using potential indigenous probiotics.

Ray, K. IBS: Mindful of probiotics for psychiatric comorbidities in IBS. Nat.Rev.Gastroenterol.Hepatol. 2017; 14(7):386-387; PM: 28536484

No Abstract Available.

Reda, R. M., Selim, K. M., El-Sayed, H. M., and El-Hady, M. A. In Vitro Selection and Identification of Potential Probiotics Isolated from the Gastrointestinal Tract of Nile Tilapia, Oreochromis niloticus. Probiotics.Antimicrob.Proteins. 8-17-2017; PM: 28819794

ABSTRACT: Fish gut bacteria can be used as probiotics for aquaculture. The aim of this study is to screen and identify beneficial probiotic bacteria from the gut of Nile tilapia, Oreochromis niloticus. Nine out of one hundred thirty-five isolates were non-pathogenic through intraperitoneal injection and had antibacterial activities with at least a strain from the five isolated fish pathogens, Aeromonas sobria, Aeromonas hydrophila, Pseudomonas aeruginosa, Pseudomonas putida, and Staphylococcus aureus. Further tests showed that such isolates can survive in the presence of high bile concentration

(10%) and at different acidic pH values. A strains (14HT) was sensitive to all selected antibiotics, two strains were (9HT and 11HT) resistant to streptomycin and three strains (9HT, 11HT and 38HT) had resistance to two antibiotics. Four isolates (11HT, 33HT, 38HT and 41HT) had an amylase and a protease activities and one strain (47HT) showed only amylase activity. Based on 16S rRNA gene analysis, the isolated strains were identified as follows: Lactococcus lactis (8HT, 9HT, 11HT and 33HT); Enterococcus faecalis (14HT), Lysinibacillus sp. (38HT) and Citrobacter freundii (39HT, 41HT and 47HT).

Redfern, A., Suchodolski, J., and Jergens, A. Role of the gastrointestinal microbiota in small animal health and disease. Vet.Rec. 9-15-2017; PM: 28916525

ABSTRACT: There is a large and emerging interest in the role of the gastrointestinal microbiota in health and disease. This paper serves to review the current knowledge and recommendations of the gastrointestinal microbiota in health and gastrointestinal disease. Further, this review evaluates the current literature and suggests guidelines for faecal microbial transplantation, a novel therapy for dysbiosis in veterinary medicine.

Reid, G., Abrahamsson, T., Bailey, M., Bindels, L. B., Bubnov, R., Ganguli, K., Martoni, C., O'Neill, C., Savignac, H. M., Stanton, C., Ship, N., Surette, M., Tuohy, K., and van, Hemert S. How do probiotics and prebiotics function at distant sites? Benef.Microbes. 8-24-2017; 8(4):521-533; PM: 28726511

ABSTRACT: The realisation that microbes regarded as beneficial to the host can impart effects at sites distant from their habitat, has raised many possibilities for treatment of diseases. The objective of a workshop hosted in Turku, Finland, by the International Scientific Association for Probiotics and Prebiotics, was to assess the evidence for these effects and the extent to which early life microbiome programming influences how the gut microbiota communicates with distant sites. In addition, we examined how probiotics and prebiotics might affect the skin, airways, heart, brain and metabolism. The growing levels of scientific and clinical evidence showing how microbes influence the physiology of many body sites, leads us to call for more funding to advance a potentially exciting avenue for novel therapies for many chronic diseases.

Ren, X., Zhu, Y., Gamallat, Y., Ma, S., Chiwala, G., Meyiah, A., and Xin, Y. E. coli O124 K72 alters the intestinal barrier and the tight junctions proteins of guinea pig intestine. Biomed.Pharmacother. 8-2-2017; 94:468-473; PM: 28779708

ABSTRACT: Our research group previously isolated and identified a strain of pathogenic Escherichia coli from clinical samples called E. coli O124 K72. The present study was aimed at determining the potential effects of E. coli O124 K72 on intestinal barrier functions and structural proteins integrity in guinea pig. Guinea pigs were grouped into three groups; control (CG); E. coli O124 K72 (E. coli); and probiotics Lactobacillus rhamnosus (LGG). Initially, we create intestinal dysbiosis by giving all animals Levofloxacin for 10days, but the control group (CG) received the same volume of saline. Then, the animals received either E. coli O124 K72 (E. coli) or Lactobacillus rhamnosus (LGG) according to their assigned group. E. coli O124 K72 treatment significantly affected colon morphology and distorted intestinal barrier function by up-regulating Claudin2 and down-regulating Occludin. In addition, E. coli upregulated the mRNA expression of MUC1, MUC2, MUC13 and MUC15. Furthermore, suspected tumor was found in the E. coli

treated animals. Our results suggested that E. coli O124 K72 strain has adverse effects on intestinal barrier functions and is capable of altering integrity of structural proteins in guinea pig model while at same time it may have a role in colon carcinogenesis.

revalo-Villena, M., Briones-Perez, A., Corbo, M. R., Sinigaglia, M., and Bevilacqua, A. Biotechnological application of yeasts in food science: Starter cultures, probiotics and enzyme production. J.Appl.Microbiol. 7-26-2017; PM: 28744990

ABSTRACT: This review is an account of experiences of two research teams (from Italy to Spain); the leading idea is the following: yeasts represent valuable sources in food science and microbiology and are a kind of food factories, because of the potentiality of whole cells or for their produced compounds. This review covers three major areas: the first section addresses the role of yeasts as starter cultures with a special focus on wine. The second section is an update on probiotic yeasts. Finally, the focus of the last section is on enzymes produced by yeasts, with a short description of the removal of mycotoxin.

Ribeiro, S. C., Ross, R. P., Stanton, C., and Silva, C. C. G. Characterization and Application of Antilisterial Enterocins on Model Fresh Cheese. J.Food Prot. 2017; 80(8):1303-1316; PM: 28703625

ABSTRACT: Enterococcus faecalis strains isolated from an artisanal cheese were selected based on enterocin production against Listeria monocytogenes. The strains formed biofilms and presented high hydrophobic character and good autoaggregation and coaggregation capacity with L. monocytogenes. Strains L3A21M3 and L3B1K3 presented high survival under gastrointestinal conditions, were able to adhere to human intestinal cells (Caco-2 and HT-29), and blocked the adhesion and invasion of L. monocytogenes. The antilisterial activity of enterocins was not affected by pH (2 to 12), heating (100 degrees C), and chemical and surfactant agents. However, strains L3A21M3 and L3A21M8 produced thermolabile enterocins, which were also sensible to extreme pH values. Enterocins exhibited a bacteriostatic mode of action against L. monocytogenes, and maximum production was observed during the stationary phase. Common enterocin structural genes were not detected by PCR amplification with specific primers, although an exhaustive screening was not performed. The enterocin produced by the L3B1K3 strain was purified and applied to model cheeses contaminated with L. monocytogenes. This enterocin reduced survival of L. monocytogenes on fresh cheeses in a dose-dependent manner. The highest dose tested (2,048 arbitrary units per g of cheese) was effective in reducing the pathogen counts to undetectable values throughout storage (6 to 72 h). These results suggest that these strains have great potential to be used as biopreservatives in the food industry and also as probiotics, with the potential to prevent L. monocytogenes gastrointestinal infection.

Ricoldi, M. S. T., Furlaneto, F. A. C., Oliveira, L. F. F., Teixeira, G. C., Pischiotini, J. P., Moreira, A. L. G., Ervolino, E., de Oliveira, M. N., Bogsan, C. S. B., Salvador, S. L., and Messora, M. R. Effects of the probiotic Bifidobacterium animalis subsp. lactis on the non-surgical treatment of periodontitis. A histomorphometric, microtomographic and immunohistochemical study in rats. PLoS.One. 2017; 12(6):e0179946; PM: 28662142

ABSTRACT: Lactobacillus probiotics have been investigated in periodontitis. However, the effects of the genus Bifidobacterium on periodontitis are hardly known. This study

evaluated the effects of the probiotic (PROB) Bifidobacterium animalis subsp. lactis (B. lactis) HN019 as an adjunct to scaling and root planing (SRP) in rats with experimental periodontitis (EP). At baseline, 32 rats were assigned to 4 groups: C (control), PROB, EP-SRP and EP-SRP-PROB. In groups EP-SRP and EP-SRP-PROB, the mandibular first molars of the animals received a ligature. At day 14, the ligatures were removed and SRP was performed. Animals of groups PROB and EP-SRP-PROB were orally administered with 10 mL/day of 109 colony forming units of B. lactis HN019 for 15 days, starting at day 14. Animals were euthanized at day 29. Histomorphometric, microtomographic and immunohistochemical analyses were performed. Microbiological effects of B. lactis on biofilm were also evaluated. Data were statistically analyzed (ANOVA, Tukey; Kruskal-Wallis, Dunn's; Two-tailed t-test; $p<0.05$). Group EP-SRP-PROB presented reduced alveolar bone resorption and attachment loss when compared with Group EP-SRP ($p<0.05$). Group EP-SRP-PROB showed significantly fewer osteoclasts, increased expression of anti-inflammatory cytokines and reduced expression of proinflammatory cytokines compared with Group EP-SRP ($p<0.05$). B. lactis promoted a higher ratio between aerobic and anaerobic bacteria in biofilm samples ($p<0.05$). B. lactis HN019 may have a role in the treatment of EP in rats, as an adjunct to SRP.

Rigo-Adrover, M., Saldana-Ruiz, S., van, Limpt K., Knipping, K., Garssen, J., Knol, J., Franch, A., Castell, M., and Perez-Cano, F. J. A combination of scGOS/lcFOS with Bifidobacterium breve M-16V protects suckling rats from rotavirus gastroenteritis. Eur.J.Nutr. 2017; 56(4):1657-1670; PM: 27112962

ABSTRACT: ***PURPOSE***: Rotavirus (RV) is the leading cause of severe diarrhoea among infants and young children, and although more standardized studies are needed, there is evidence that probiotics can help to fight against RV and other infectious and intestinal pathologies. On the other hand, the effects of prebiotics have not been properly addressed in the context of an RV infection. The aim of this study was to demonstrate a protective role for a specific scGOS/lcFOS 9:1 prebiotic mixture (PRE) separately, the probiotic Bifidobacterium breve M-16V (PRO) separately and the combination of the prebiotic mixture and the probiotic (synbiotic, SYN) in a suckling rat RV infection model. ***METHODS***: The animals received the intervention from the 3rd to the 21st day of life by oral gavage. On day 7, RV was orally administered. Clinical parameters and immune response were evaluated. ***RESULTS***: The intervention with the PRO reduced the incidence, severity and duration of the diarrhoea ($p < 0.05$). The PRE and SYN products improved clinical parameters as well, but a change in stool consistency induced by the PRE intervention hindered the observation of this effect. Both the PRE and the SYN, but not the PRO, significantly reduced viral shedding. All interventions modulated the specific antibody response in serum and intestinal washes at day 14 and 21 of life. ***CONCLUSIONS***: A daily supplement of a scGOS/lcFOS 9:1 prebiotic mixture, Bifidobacterium breve M-16V or a combination of both is highly effective in modulating RV-induced diarrhoea in this preclinical model.

Rios, A. C., Maurya, P. K., Pedrini, M., Zeni-Graiff, M., Asevedo, E., Mansur, R. B., Wieck, A., Grassi-Oliveira, R., McIntyre, R. S., Hayashi, M. A. F., and Brietzke, E. Microbiota abnormalities and the therapeutic potential of probiotics in the treatment of mood disorders. Rev.Neurosci. 5-8-2017; PM: 28593878

ABSTRACT: Major depressive disorder (MDD) and bipolar disorder (BD) are among the leading causes of burden and disability worldwide. Despite intensified research efforts to

improve the treatment options and remission rates in mood disorders, no disease modifying treatment exists for these disorders. Accumulating evidence implicates the involvement of the gut microbiota in processes relevant to etiopathology of central nervous system-based disorders. The objective of this article was to critically evaluate the evidence supporting the link between gastrointestinal microbiota and mood disorders and to discuss the potential benefits of using probiotics in the treatment of MDD and BD. The concept of psychobiotics, which is bacterial-based interventions with mental health benefit, is emerging in the field. On the other hand, while probiotics might potentially represent a significant advance, specific roles of microbiota in the pathophysiology of mood disorders still need further investigation along with intervention studies.

Rishi, L., Mittal, G., Agarwal, R. K., and Sharma, T. Melioration in Anti-staphylococcal Activity of Conventional Antibiotic(s) by Organic Acids Present in the Cell Free Supernatant of Lactobacillus paraplantarum. Indian J.Microbiol. 2017; 57(3):359-364; PM: 28904422

ABSTRACT: In view of emerging drug resistance in pathogens, there is a need to explore alternative strategies to combat infections. Use of probiotics is one such option. In this regard, efficacy of Lactobacillus plantarum has been reported against Staphylococcus aureus. Here, we propose that cell free supernatant (CFS) of Lactobacillus paraplantarum when used in combination with conventional antibiotics viz. ampicillin and oxacillin [to which the methicillin resistant Staphylococcus aureus (MRSA) strains were originally resistant] reduce the minimum inhibitory concentrations of these antibiotics, rendering the combination either synergistic or additive against the tested MRSA strain. The anti-staphylococcal activity was observed to be due to organic acids (acetic acid and lactic acid as confirmed by HPLC analysis) present in the CFS, as neutralization of the CFS with an alkali, sodium hydroxide (NaOH), caused the complete abrogation of its activity. The role of H2O2 and bacteriocin present in the CFS was also ruled out. The findings of this study suggest that cell free supernatant and ampicillin/oxacillin combination(s) might help in rejuvenating the use of conventional anti-staphylococcal antibiotics for the treatment of multi-drug resistant strains.

Rizzoli, R. and Biver, E. Effects of Fermented Milk Products on Bone. Calcif.Tissue Int. 8-19-2017; PM: 28823001

ABSTRACT: Fermented milk products like yogurt or soft cheese provide calcium, phosphorus, and protein. All these nutrients influence bone growth and bone loss. In addition, fermented milk products may contain prebiotics like inulin which may be added to yogurt, and provide probiotics which are capable of modifying intestinal calcium absorption and/or bone metabolism. On the other hand, yogurt consumption may ensure a more regular ingestion of milk products and higher compliance, because of various flavors and sweetness. Bone mass accrual, bone homeostasis, and attenuation of sex hormone deficiency-induced bone loss seem to benefit from calcium, protein, pre-, or probiotics ingestion, which may modify gut microbiota composition and metabolism. Fermented milk products might also represent a marker of lifestyle promoting healthy bone health.

Robinson, J. L. Probiotics for Modification of the Incidence or Severity of Respiratory Tract Infections. Pediatr.Infect.Dis.J. 7-27-2017; PM: 28767618

No Abstract Available.

Rocha-Ramirez, L. M., Perez-Solano, R. A., Castanon-Alonso, S. L., Moreno Guerrero, S. S., Ramirez, Pacheco A., Garcia, Garibay M., and Eslava, C. Probiotic Lactobacillus Strains Stimulate the Inflammatory Response and Activate Human Macrophages. J.Immunol.Res. 2017; 2017:4607491; PM: 28758133

ABSTRACT: Lactobacilli have been shown to promote health functions. In this study, we analyzed the mechanism by which four different strains of probiotics affected innate immunity, such as regulation of ROS, cytokines, phagocytosis, bactericidal activity, signaling by NF-kappaB pp65, and TLR2 activation. The production of ROS was dependent on the concentration and species of Lactobacillus. The results obtained from the tested strains (Lactobacillus rhamnosus GG, L. rhamnosus KLSD, L. helveticus IMAU70129, and L. casei IMAU60214) showed that strains induced early proinflammatory cytokines such as IL-8,TNF-alpha, IL-12p70, and IL-6. However, IL-1beta expression was induced only by L. helveticus and L. casei strains (after 24 h stimulation). Phagocytosis and bactericidal activity of macrophages against various pathogens, such as S. aureus, S. typhimurium, and E. coli, were increased by pretreatment with Lactobacillus. The nuclear translocation NF-kappaB pp65 and TLR2-dependent signaling were also increased by treatment with the probiotics. Taken together, the experiments demonstrate that probiotic strains of Lactobacillus exert early immunostimulatory effects that may be directly linked to the initial inflammation of the response of human macrophages.

Rochin-Medina, J. J., Ramirez-Medina, H. K., Rangel-Peraza, J. G., Pineda-Hidalgo, K. V., and Iribe-Arellano, P. Use of whey as a culture medium for Bacillus clausii for the production of protein hydrolysates with antimicrobial and antioxidant activity. Food Sci.Technol.Int. 1-1-2017; 1082013217724705; PM: 28816527

ABSTRACT: The use of whey as a natural culture medium to produce hydrolysates with antimicrobial from Bacillus clausii is the objective of this research. The fermentation process was carried out at 25 for five days, where proteolytic activity, soluble peptides quantification, and antimicrobial activity using the disc diffusion method were determined every day. The fermented whey reached values of proteolytic activity between 90 and 260 U ml-1 and a production of soluble peptides between 100 and 2070 microg ml-1. The maximum values were reached after three days of fermentation to all determinations. In addition, the inhibition zone of fermented whey against Salmonella Typhimurium, Escherichia coli, Shigella flexneri, Staphylococcus aureus, Listeria monocytogenes, and Enterococcus faecalis strains were 13.7, 13.2, 14.4, 14.6, 9.8, 15.7 mm, respectively. The hydrolysates inhibited the 2, 2'-azinobis (3-ethylbenzothiazoline- 6-sulfonic acid) (ABTS) and 2, 2-diphenyl-1-picrylhydrazyl (DPPH) radicals by 85 and 80%, respectively. The whey was used to allow the growth of B. clausii and to generate peptides with antioxidant and antimicrobial activity through the hydrolysis of proteins present in the natural culture medium. This process could be used for the development of new dairy products added with probiotics.

Rodklongtan, A. and Chitprasert, P. Combined effects of holy basil essential oil and inlet temperature on lipid peroxidation and survival of Lactobacillus reuteri KUB-AC5 during spray drying. Food Res.Int. 2017; 100(Pt 1):276-283; PM: 28873688

ABSTRACT: Lipid peroxidation induced by oxidative stress plays an important role in reducing probiotic survival during spray drying. In this study, the probiotic Lactobacillus reuteri KUB-AC5 was co-encapsulated with holy basil essential oil, HBEO (0, 6, and 12mg/ml), by spray drying using skim milk at inlet air temperatures of 130, 140, and 150 degrees C. The microcapsule properties in terms of morphology, size, moisture content, water activity, surface oil, microencapsulation efficiency, antioxidant activity, lipid peroxidation, and cell survival were determined. The result showed that the microcapsules with HBEO had much higher antioxidant activity than the ones without HBEO. The optimal condition of HBEO (6mg/ml) with inlet temperature (130 degrees C) was effective in reducing malondialdehyde (MDA) level and enhancing survival of probiotics. This study indicates the potential role of HBEO in decreasing oxidative stress in probiotics during spray drying, which contributed to an increase in cell survival and health benefits.

Rodrigues, F. J., Omura, M. H., Cedran, M. F., Dekker, R. F. H., Barbosa-Dekker, A. M., and Garcia, S. Effect of natural polymers on the survival of Lactobacillus casei encapsulated in alginate microspheres. J.Microencapsul. 2017; 34(5):431-439; PM: 28618877

ABSTRACT: Linseed and okra mucilages, the fungal exopolysaccharide botryosphaeran, and commercial fructo-oligosaccharides (FOS) were used to microencapsulate Lactobacillus casei LC-01 and L. casei BGP 93 in sodium alginate microspheres by the extrusion technique in calcium chloride. The addition of carbohydrate biopolymers from linseed, okra and the fungal exocellular (1 --> 3)(1 --> 6)-beta-D-glucan, named botryosphaeran provided higher encapsulation efficiency (EE) (>93% and >86%) for L. casei LC 01 and L. casei BGP 93, respectively. The use of linseed, okra and botryosphaeran improved the stability of probiotics encapsulated in the microspheres during the storage period over 15 d at 5 degrees C when compared to microspheres formulated with sodium alginate alone as the main encapsulating agent (p </= 0.05). In in vitro gastrointestinal simulation tests, the use of FOS combined with linseed mucilage was shown to be more effective in protecting L. casei cells LC-01 and L. casei BGP 93.

Rodriguez-Nogales, A., Algieri, F., Garrido-Mesa, J., Vezza, T., Utrilla, M. P., Chueca, N., Garcia, F., Olivares, M., Rodriguez-Cabezas, M. E., and Galvez, J. Differential intestinal anti-inflammatory effects of Lactobacillus fermentum and Lactobacillus salivarius in DSS mouse colitis: impact on microRNAs expression and microbiota composition. Mol.Nutr.Food Res. 7-28-2017; PM: 28752563

ABSTRACT: ***SCOPE***: To compare the intestinal anti-inflammatory effects of two probiotics Lactobacillus fermentum and Lactobacillus salivarius in mouse colitis, focusing on their impact on selected miRNAs and microbiota composition. ***METHODS AND RESULTS***: Male C57BL/6J mice were randomly assigned to four groups (n = 10): non-colitic, DSS colitic and two colitic groups treated with probiotics (5 x 108 CFU/mouse/day). Both probiotics ameliorated macroscopic colonic damage. They improved the colonic expression of markers involved in the immune response, and the expression of miR-155 and miR-223. L. fermentum also restored miR-150 and miR-143 expression, also linked to the preservation of the intestinal barrier function. Besides, these beneficial effects were associated with

the amelioration of the microbiota dysbiosis and a recovery of the SCFAs- and lactic acid-producing bacterial populations, although only L. fermentum improved Chao richness, Pielou evenness and Shannon diversity. Moreover, L. fermentum also restored the Treg cell population in MLNs and the Th1/Th2 cytokine balance. ***CONCLUSION***: Both probiotics exerted intestinal anti-inflammatory effects in DSS-mouse colitis, maybe due to their ability to restore the intestinal microbiota homeostasis and modulate the immune response. L. fermentum showed a greater beneficial effect compared to L. salivarius, which makes it more interesting for future studies.

Rodriguez-Palacios, A., Staempfli, H. R., and Weese, J. S. High Doses of Halotolerant Gut-Indigenous Lactobacillus plantarum Reduce Cultivable Lactobacilli in Newborn Calves without Increasing Its Species Abundance. Int.J.Microbiol. 2017; 2017:2439025; PM: 28596790

ABSTRACT: To elucidate the ecological effect of high oral doses of halotolerant (resistant to table salt) indigenous-gut bacteria on other commensals early in life, we conducted a culture-based study to quantify the effect of intestinal Lactobacillus plantarum strain of bovine origin (with remarkable aerobic growth capabilities and inhibitory activity against Escherichia coli O157:H7 and F5) on clinical health and gut lactobacilli/coliforms in newborn calves. In a double-blind placebo-randomized trial twelve colostrum-fed calves, consecutively born at a farm, were fed L. plantarum within 12 hours from birth at low (107-8 CFU/day) or high concentrations (1010-11) or placebo (q24 h, 5 d; 10 d follow-up). We developed a 2.5% NaCl-selective culture strategy to facilitate the enumeration of L. plantarum-strain-B80, and tested 384 samples (>1,152 cultures). L. plantarum-B80-like colonies were detected in a large proportion of calves (58%) even before their first 24 hours of life indicating endemic presence of the strain in the farm. In contrast to studies where human-derived Lactobacillus LGG or rhamnosus had notoriously high, but short-lived, colonization, we found that L. plantarum colonized stably with fecal shedding of 6 +/- 1 log10.g-1 (irrespective of dose, $P > 0.2$). High doses significantly reduced other fecal lactic acid bacteria (e.g., lactobacilli, $P < 0.01$) and slightly reduced body weight gain in calves after treatment. For the first time, a halotolerant strain of L. plantarum with inhibitory activity against a human pathogen has the ability to inhibit other lactobacilli in vivo without changing its species abundance, causing transintestinal translocation, or inducing clinical disease. The future selection of probiotics based on halotolerance may expand therapeutic product applicability.

Rondanelli, M., Faliva, M. A., Perna, S., Giacosa, A., Peroni, G., and Castellazzi, A. M. Using probiotics in clinical practice: Where are we now? A review of existing meta-analyses. Gut Microbes. 6-22-2017; 1-23; PM: 28640662

ABSTRACT: The scientific literature has demonstrated that probiotics have a broad spectrum of activity, although often the results are contradictory. This study provides a critical overview of the current meta-analyses that have evaluated the efficacy of probiotics in physiologic and pathological conditions, such as metabolic disease, antibiotic-associated and Clostridium difficile-associated diarrhea, IBS, constipation, IBD, chemotherapy-associated diarrhea, respiratory tract infection, ventilator-associated pneumonia, NAFLD, liver encephalopathy, periodontitis, depression, vaginosis, urinary tract infections, pancreatitis, incidence of ventilator-associated pneumonia, hospital infection and stay in ICU, mortality of post-trauma patients, necrotising enterocolitis in premature infants. Only for antibiotic- and Clostridium difficile-associated diarrhea, and

respiratory tract infections the effects of probiotics are considered "evidence-based." Concerning other fields, meta-analyses lacks to define type and biologic effect of probiotic strains, as well as the outcome in a disease state. Therefore, the results presented should be a stimulus for further studies which will provide clinical recommendations.

Rosales-Bravo, H., Morales-Torres, H. C., Vazquez-Martinez, J., Molina-Torres, J., Olalde-Portugal, V., and Partida-Martinez, L. P. Novel consortium of Klebsiella variicola and Lactobacillus species enhances the functional potential of fermented dairy products by increasing the availability of branched-chain amino acids and the amount of distinctive volatiles. J.Appl.Microbiol. 8-17-2017; PM: 28815819

ABSTRACT: ***AIMS***: Identify novel bacterial taxa that could increase the availability of branched-chain amino acids and the amount of distinctive volatiles during skim milk fermentation. ***METHODS AND RESULTS***: We recovered 344 bacterial isolates from stool samples of healthy and breastfed infants. Five were selected based on their ability to produce branched-chain amino acids. Three strains were identified as Escherichia coli, one as Klebsiella pneumoniae and other as Klebsiella variicola by molecular and biochemical methods. HPLC and solid-phase microextraction with GC-MS were used for the determination of free amino acids and volatile compounds respectively. The consortium formed by K. variicola and four Lactobacillus species showed the highest production of Leu and Ile in skim milk fermentation. In addition, the production of volatile compounds, such as acetoin, ethanol, 2-nonanone, and acetic, hexanoic and octanoic acids, increased in comparison to commercial yogurt, Emmental and Gouda cheese. Also, distinctive volatiles, such as 2,3-butanediol, 4-methyl-2- hexanone and octanol, were identified. ***CONCLUSION***: The use of K. variicola in combination with probiotic Lactobacillus species enhances the availability of Leu and Ile and the amount of distinctive volatiles during skim milk fermentation. ***SIGNIFICANCE AND IMPACT OF THE STUDY***: The identified consortium increases the functional potential of fermented dairy products.

Rungsri, P., Akkarachaneeyakorn, N., Wongsuwanlert, M., Piwat, S., Nantarakchaikul, P., and Teanpaisan, R. Effect of fermented milk containing Lactobacillus rhamnosus SD11 on oral microbiota of healthy volunteers: A randomized clinical trial. J.Dairy Sci. 8-9-2017; PM: 28803012

ABSTRACT: The aims of this study were to evaluate whether short-term consumption of fermented milk containing Lactobacillus rhamnosus SD11 affected levels of oral microbiota in vivo and whether L. rhamnosus SD11 could colonize in the human mouth. We also monitored for potential side effects of the probiotic. The applicability of using L. rhamnosus SD11 compared with Lactobacillus bulgaricus as a starter culture for fermented milk was evaluated. After informed consent, 43 healthy young adults were recruited and randomly assigned to either the probiotic or control group and received fermented milk containing L. rhamnosus SD11 or L. bulgaricus, respectively, once daily for 4 wk. The numbers of mutans streptococci, lactobacilli, and total bacteria in saliva were counted at baseline and then after 4 and 8 wk. An oral examination was performed at baseline and after 8 wk. The persistence of L. rhamnosus SD11 was investigated by DNA fingerprinting using arbitrary primer-PCR. Results demonstrated that statistically significant reductions in mutans streptococci and total bacteria were observed in the probiotic group compared with the control group, and the number of lactobacilli was significantly

increased in both groups after receiving fermented milks. Lactobacillus rhamnosus SD11 could be detected (in >80% of subjects) up to 4 wk following cessation of dosing among subjects in the probiotic group. No side effects were reported. Thus, L. rhamnosus SD11 could be used as a starter culture for fermented milk. Daily consumption of L. rhamnosus SD11-containing fermented milk for 4 wk may have beneficial effects on oral health by reducing salivary levels of mutans streptococci. The probiotic was apparently able to colonize the oral cavity for a longer time than previously reported. However, the potential benefits of probiotic L. rhamnosus SD11 on oral health require further evaluation with a larger group of volunteers in a longer-term study.

Sabatini, S., Lauritano, D., Candotto, V., Silvestre, F. J., and Nardi, G. M. Oral probiotics in the management of gingivitis in diabetic patients: a double blinded randomized controlled study. J.Biol.Regul.Homeost.Agents. 2017; 31(2 Suppl 1):197-202; PM: 28691473

ABSTRACT: Diabetic patients are more prone to develop infections such as periodontal diseases. Bacteriotherapy with the concept of using good bacterial strains to replace the pathogenic ones emerged as a fascinating field due to the increasing incidence of antibiotic resistance. The aim of this study was to evaluate if a particular combination of probiotics (Lactobacillus Reuteri DSM 17938 and Lactobaciullus Reuteri ATCC PTA 5289) is useful in treating gingivitis in diabetic patients. Eighty adult patients with diagnosis of controlled diabetes type II and gingivitis were enrolled for this study and randomized in two groups. Only oral hygiene instructions were given. Bacteriotherapy (Lactobacillus Reuteri) was administered to test group. Outcome measures were presence of Plaque (P.I.) and Bleeding on Probing (B.O.P.). Data were collected at baseline and after 30 days. At 30 days, both groups showed a statistically significant clinical indexes reduction from baseline. More reduction was present in the test group for P.I. (14%+/-6) and for B.O.P. (18%+/-4) and was statistically significant (p less than 0.05). Within the limitations of this study, bacteriotherapy can be considered effective in reducing plaque and BOP in patients with controlled diabetes type II and gingivitis.

Sadaf, H., Raza, S. I., and Hassan, S. W. Role of gut microbiota against calcium oxalate. Microb.Pathog. 2017; 109:287-291; PM: 28624518

ABSTRACT: Nephrolithiasis is a condition marked by the presence or formation of stones in kidneys. Several factors contribute to kidney stones development such as environmental conditions, type of dietary intake, gender and gastrointestinal flora. Most of the kidney stones are composed of calcium phosphate and calcium oxalate, which enter in to the body through diet. Both sources of oxalates become dangerous when normal flora of gastrointestinal tract is disturbed. Oxalobacter and Lactobacillus species exist symbiotically in the human gut and prevent stone formation by altering some biochemical pathways through production of specific enzymes which help in the degradation of oxalate salts. Both Oxalobacter and Lactobacillus have potential probiotic characteristics for the prevention of kidney stone formation and this avenue should be further explored.

Saldanha, L. G., Dwyer, J. T., Andrews, K. W., Brown, L. L., Costello, R. B., Ershow, A. G., Gusev, P. A., Hardy, C. J., and Pehrsson, P. R. Is Nutrient Content and Other Label Information for Prescription Prenatal Supplements Different from Nonprescription Products? J.Acad.Nutr.Diet. 2017; 117(9):1429-1436; PM: 28571654

ABSTRACT: ***BACKGROUND***: Prenatal supplements are often recommended to pregnant women to help meet their nutrient needs. Many products are available, making it difficult to choose a suitable supplement because little is known about their labeling and contents to evaluate their appropriateness. ***OBJECTIVE***: To determine differences between prescription and nonprescription prenatal supplements available in the United States regarding declared nutrient and nonnutrient ingredients and the presence of dosing and safety-related information. ***DESIGN***: Using two publicly available databases with information about prenatal supplement products, information from prescription and nonprescription product labels were extracted and evaluated. For the 82 prescription and 132 nonprescription products, declared label amounts of seven vitamins and minerals, docosahexaenoic acid (DHA), the presence of other nonnutrient components, and the presence of key safety and informational elements as identified in two Department of Health and Human Services Office of Inspector General (OIG)'s 2003 reports were compiled and compared. ***RESULTS***: Compared with nonprescription products, prescription products contained significantly fewer vitamins (9+/-0.2 vs 11+/-0.3; P</=0.05) and minerals (4+/-0.1 vs 8+/-0.3; P</=0.05). Declared amounts of folic acid were higher in prescription products, whereas vitamin A, vitamin D, iodine, and calcium were higher in the nonprescription products. Amounts of iron, zinc, and DHA were similar. Virtually all products contained levels of one or more nutrients that exceeded the Recommended Dietary Allowances for pregnant and/or lactating women. Product type also influenced ingredients added. Fewer prescription products contained botanical ingredients (6% prescription vs 33% nonprescription) and probiotics (2% prescription vs 8% nonprescription). Only prescription products contained the stool softener docusate sodium. ***CONCLUSIONS***: Our analysis of prenatal supplements indicates that prescription and nonprescription supplements differ in terms of declared composition and nutrient strength, but have labels that are similarly sparse regarding aspects of use such as dosing information.

Saliu, E. M., Vahjen, W., and Zentek, J. Types and prevalence of extended-spectrum beta-lactamase producing Enterobacteriaceae in poultry. Anim Health Res.Rev. 2017; 18(1):46-57; PM: 28641596

ABSTRACT: For several billion years, bacteria have developed mechanisms to resist antibacterial substances. In modern time, antibiotics are frequently used in veterinary and human medicine for prevention and treatment of diseases, globally still also for their growth promoting effects as feed additives. This complex situation has evolved in accelerating development and prevalence of multi-drug resistant bacteria in livestock and people. Extended-spectrum beta-lactamase (ESBL) producing bacteria are resistant to a wide range of ss-lactam antibiotics. They are currently considered as one of the main threats for the treatment of infections in humans and animals. In livestock and animal products, poultry and poultry products show the highest prevalence of ESBL-producers with CTX-M-1, TEM-52 and SHV-12 being the most common ESBL-types in poultry. Escherichia coli and Salmonella spp. are the bacteria in poultry, which carry ESBL-genes most frequently. ESBL-producing bacteria are present at every level of the poultry production pyramid and can be detected even in the meconium of newly hatched chicks. The environment close to poultry barns shows high prevalence rates of these bacteria and contributes to an ongoing infection pressure with further ESBL-types. Probiotics have been shown to successfully reduce ESBL-producers in chicken, as well as ESBL-gene transfer. Other feed additives, such as zinc and copper, increase the prevalence of ESBL-producing bacteria when fed to animals. To our best knowledge, this

is the first publication presenting a comparative overview of the prevalence of ESBL-types using data from different countries. To reduce the hazard for public health from poultry carrying high numbers of ESBL-producers, preventive measurements must include the surrounding environment and avoidance of antibiotic usage at all levels of the production pyramid. The first results, of the research on the impact of feed additives on the spread of ESBL-genes, indicate the diet as a further, possible magnitude of influence.

Salvetti, E. and O'Toole, P. W. The Genomic Basis of Lactobacilli as Health-Promoting Organisms. Microbiol.Spectr. 2017; 5(3); PM: 28643623

ABSTRACT: Lactobacilli occupy a unique position in human culture and scientific history. Like brewer's and baker's yeast, lactobacilli have been associated with food production and preservation for thousands of years. Lactobacillus species are used in mixed microbial cultures, such as the classical Lactobacillus bulgaricus/Streptococcus thermophilus inoculum for yogurt fermentation, or combinations of diverse lactobacilli/yeasts in kefir grains. The association of lactobacilli consumption with greater longevity and improved health formed the basis for developing lactobacilli as probiotics, whose market has exploded worldwide in the past 10 years. The decade that followed the determination of the first genome sequence of a food-associated species, Lactobacillus plantarum, saw the application to lactobacilli of a full range of functional genomics methods to identify the genes and gene products that govern their distinctive phenotypes and health associations. In this review, we will briefly remind the reader of the range of beneficial effects attributed to lactobacilli, and then explain the phylogenomic basis for the distribution of these traits across the genus. Recognizing the strain specificity of probiotic effects, we review studies of intraspecific genomic variation and their contributions to identifying probiotic traits. Finally we offer a perspective on classification of lactobacilli into new genera in a scheme that will make attributing probiotic properties to clades, taxa, and species more logical and more robust.

Sander, R. Use of probiotics for infection prevention in trauma patients. Nurs.Older.People. 6-30-2017; 29(6):11; PM: 28664800

ABSTRACT: Probiotics is a general term to describe the different species of healthy microbes that are usually found in our gastrointestinal tract and support our immune system. When ingested in adequate amounts, probiotics can provide health benefits to the host. Their ingestion is thought to replenish microbiota that may have been depleted from injury, medication or diet. When there is a depletion of microbiota, pathogenic bacteria can flourish and cause disease.

Sauer, M., Russmayer, H., Grabherr, R., Peterbauer, C. K., and Marx, H. The Efficient Clade: Lactic Acid Bacteria for Industrial Chemical Production. Trends Biotechnol. 2017; 35(8):756-769; PM: 28549804

ABSTRACT: Lactic acid bacteria are well known to be beneficial for food production and, as probiotics, they are relevant for many aspects of health. However, their potential as cell factories for the chemical industry is only emerging. Many physiological traits of these microorganisms, evolved for optimal growth in their niche, are also valuable in an industrial context. Here, we illuminate these features and describe why the distinctive adaptation of lactic acid bacteria is particularly useful when developing a microbial

process for chemical production from renewable resources. High carbon uptake rates with low biomass formation combined with strictly regulated simple metabolic pathways, leading to a limited number of metabolites, are among the key factors defining their success in both nature and industry.

Schachter, J., Martel, J., Lin, C. S., Chang, C. J., Wu, T. R., Lu, C. C., Ko, Y. F., Lai, H. C., Ojcius, D. M., and Young, J. D. Effects of obesity on depression: a role for inflammation and the gut microbiota. Brain Behav.Immun. 9-6-2017; PM: 28888668

ABSTRACT: Depression is a mental disorder associated with environmental, genetic and psychological factors. Recent studies indicate that chronic neuro-inflammation may affect brain physiology and alter mood and behavior. Consumption of a high-fat diet leads to obesity and chronic systemic inflammation. The gut microbiota mediates many effects of a high-fat diet on human physiology and may also influence the mood and behavior of the host. We review here recent studies suggesting the existence of a link between obesity, the gut microbiota and depression, focusing on the mechanisms underlying the effects of a high-fat diet on chronic inflammation and brain physiology. This body of research suggests that modulating the composition of the gut microbiota using prebiotics and probiotics may produce beneficial effects on anxiety and depression.

Schei, K., Avershina, E., Oien, T., Rudi, K., Follestad, T., Salamati, S., and Odegard, R. A. Early gut mycobiota and mother-offspring transfer. Microbiome. 8-24-2017; 5(1):107; PM: 28837002

ABSTRACT: ***BACKGROUND***: The fungi in the gastrointestinal tract, the gut mycobiota, are now recognised as a significant part of the gut microbiota, and they may be important to human health. In contrast to the adult gut mycobiota, the establishment of the early gut mycobiota has never been described, and there is little knowledge about the fungal transfer from mother to offspring. ***METHODS***: In a prospective cohort, we followed 298 pairs of healthy mothers and offspring from 36 weeks of gestation until 2 years of age (1516 samples) and explored the gut mycobiota in maternal and offspring samples. Half of the pregnant mothers were randomised into drinking probiotic milk during and after pregnancy. The probiotic bacteria included Lactobacillus rhamnosus GG (LGG), Bifidobacterium animalis subsp. lactis Bb-12 and Lactobacillus acidophilus La-5. We quantified the fungal abundance of all the samples using qPCR of the fungal internal transcribed spacer (ITS)1 segment, and we sequenced the 18S rRNA gene ITS1 region of 90 high-quantity samples using the MiSeq platform (Illumina). ***RESULTS***: The gut mycobiota was detected in most of the mothers and the majority of the offspring. The offspring showed increased odds of having detectable faecal fungal DNA if the mother had detectable fungal DNA as well (OR = 1.54, p = 0.04). The fungal alpha diversity in the offspring gut increased from its lowest at 10 days after birth, which was the earliest sampling point. The fungal diversity and fungal species showed a succession towards the maternal mycobiota as the child aged, with Debaryomyces hansenii being the most abundant species during breast-feeding and Saccharomyces cerevisiae as the most abundant after weaning. Probiotic consumption increased the gut mycobiota abundance in pregnant mothers (p = 0.01). ***CONCLUSION***: This study provides the first insight into the early fungal establishment and the succession of fungal species in the gut mycobiota. The results support the idea that the fungal host phenotype is transferred from mother to offspring. ***TRIAL REGISTRATION***: Clinicaltrials.gov NCT00159523.

Scheri, G. C., Fard, S. N., Schietroma, I., Mastrangelo, A., Pinacchio, C., Giustini, N., Serafino, S., De, Girolamo G., Cavallari, E. N., Statzu, M., Laghi, L., Vullo, A., Ceccarelli, G., Vullo, V., and d'Ettorre, G. Modulation of Tryptophan/Serotonin Pathway by Probiotic Supplementation in Human Immunodeficiency Virus-Positive Patients: Preliminary Results of a New Study Approach. Int.J.Tryptophan.Res. 2017; 10:1178646917710668; PM: 28607543

ABSTRACT: ***BACKGROUND***: To date, no data are available regarding the effects of probiotics on the pathway of tryptophan/serotonin metabolism among human immunodeficiency virus (HIV) 1-infected individuals. Because a condition of dysbiosis might be responsible for the altered use of tryptophan described in this population, the aim of this study was to investigate the link between probiotic supplementation and serotonin levels in combined antiretroviral therapy-treated patients and the subsistence of an interplay with inflammation. ***METHODS***: We conducted a pilot study that included 8 HIV-positive subjects. We collected blood and fecal samples before and after 6 months of probiotic supplementation, to measure the level of serotonin in serum and tryptophan in stool, the expression of CD38 and HLA-DR on peripheral CD4+ T lymphocytes (as immune activation markers), the expression of indoleamine 2,3-dioxygenase 1 messenger RNA (mRNA) and IFN-gamma mRNA (as markers of tryptophan metabolism and systemic inflammation). ***RESULTS***: After probiotic supplementation, we observed a significant increase in concentration of serum serotonin (P = .008) and a decreased level of tryptophan in plasma. Moreover, a significant reduction in CD38 and HLA-DR expression on the surface of peripheral CD4+ T cells (P = .008) and a reduced expression of indoleamine 2,3-dioxygenase 1 mRNA on peripheral blood mononuclear cells (P = .04) were observed. ***CONCLUSIONS***: Considering that this probiotic (Vivomixx(R) in EU; Visbiome(R) in USA) has an influence on tryptophan metabolism, larger studies on this topic are needed.

Seghouani, H., Garcia-Rangel, C. E., Fuller, J., Gauthier, J., and Derome, N. Walleye Autochthonous Bacteria as Promising Probiotic Candidates against Flavobacterium columnare. Front Microbiol. 2017; 8:1349; PM: 28769909

ABSTRACT: Walleye (Sander vitreus) is the second most fished freshwater species in Canada. While much sought by anglers, walleye also supports substantial commercial fisheries. To cope with the recent decline of wild walleye populations, fish farmers produce juveniles for lake stocking. However, walleye breeding is particularly tedious, mostly due to high disease susceptibility at larval and juvenile developmental stages. The main threat is the columnaris disease, which is caused by Flavobacterium columnare, an opportunistic bacteria. As F. columnare strains exhibit increasing antibiotic resistance, there is a strong need to develop efficient and sustainable alternative strategies to control columnaris disease. Bacterial probiotics have been shown to mitigate infections either by enhancing host immune response or by inhibiting pathogen growth. Being successfully assessed in many fish/pathogen combinations, we developed a tailored probiotic strategy for walleye to prevent and treat columnaris disease. Thirty-seven endogenous bacterial strains were isolated from healthy walleye's skin and gut, were tested in vitro against F. columnare. Significant antagonistic effect against F. columnare was measured for 2 out of 37 endogenous strains. These two probiotic strains were identified as Pseudomonas fluorescens. The antagonistic effect of these two successful probiotics was further validated in vivo during a 2-month stress trial: groups receiving probiotic treatments showed on average 53.74% survival improvement.

Seidel, D. V., zcarate-Peril, M. A., Chapkin, R. S., and Turner, N. D. Shaping functional gut microbiota using dietary bioactives to reduce colon cancer risk. Semin.Cancer Biol. 7-1-2017; PM: 28676459

ABSTRACT: Colon cancer is a multifactorial disease associated with a variety of lifestyle factors. Alterations in the gut microbiota and the intestinal metabolome are noted during colon carcinogenesis, implicating them as critical contributors or results of the disease process. Diet is a known determinant of health, and as a modifier of the gut microbiota and its metabolism, a critical element in maintenance of intestinal health. This review summarizes recent evidence demonstrating the role and responses of the intestinal microbiota during colon tumorigenesis and the ability of dietary bioactive compounds and probiotics to impact colon health from the intestinal lumen to the epithelium and systemically. We first describe changes to the intestinal microbiome, metabolome, and epithelium associated with colon carcinogenesis. This is followed by a discussion of recent evidence indicating how specific classes of dietary bioactives, prebiotics, or probiotics affect colon carcinogenesis. Lastly, we briefly address the prospects of using multiple 'omics' techniques to integrate the effects of diet, host, and microbiota on colon tumorigenesis with the goal of more fully appreciating the interconnectedness of these systems and thus, how these approaches can be used to advance personalized nutrition strategies and nutrition research.

Seifi, K., Karimi-Torshizi, M. A., and Deldar, H. Probiotics intake from proximal or distal gastrointestinal tract: The investigation on intestinal morphology and performance of Japanese quail. J.Anim Physiol Anim Nutr.(Berl). 7-10-2017; PM: 28691244

ABSTRACT: The aim of the present study was to investigate the efficacy of early single-dose probiotics administered from proximal or distal gastrointestinal tract on quails' performance and small intestinal morphology. A total of 120 Japanese quail (Coturnix coturnix japonica) 1-d-old chicks were divided into the following experimental groups before being transferred to the raising room: (i) control (no probiotic administered); (ii) oral group (received probiotics via oesophageal gavage); and (iii) vent lip group (received probiotics directly into vent). Four replicates of 10 chicks per cage were considered for each treatment and birds were raised up to 35 days in the same conditions with ad libitum access to feed and water. A commercial probiotics (Protexin, Somerset, UK) used in this study contained 2 x 109 cfu/g of nine different micro-organisms. On day 35, all birds were weighed and then three birds in every pen were killed via cervical dislocation. Two cm of mid-point of duodenum and ileum were cut for histomorphology assays. Both probiotics-treated groups had higher body weight and body weight gain than control ($p < .01$). Ileum was longer in probiotics-treated groups than in the control ($p < .01$). Orally treated birds had the highest duodenum villus height and crypt depth ($p < .01$). In the cloacally treated quails, ileum villus length was higher than the both other groups, and crypts' depth was deeper than the control ($p < .01$). The numbers of both types of goblet cells (acidic mucin producer and neutral mucin producer) were higher in the birds receiving probiotics than control birds ($p < .01$). Although there were no statistical differences in performance values between the different ways of probiotics entrance into gut, some intestinal histomorphometric parameters were improved in ileum of the birds receiving probiotics through distal gut that is cloaca ($p < .01$).

Selma, M. V., Beltran, D., Luna, M. C., Romo-Vaquero, M., Garcia-Villalba, R., Mira, A., Espin, J. C., and Tomas-Barberan, F. A. Isolation of Human Intestinal Bacteria Capable of Producing the Bioactive Metabolite Isourolithin A from Ellagic Acid. Front Microbiol. 2017; 8:1521; PM: 28824607

ABSTRACT: Urolithins are intestinal microbial metabolites produced from ellagitannin- and ellagic acid-containing foods such as walnuts, strawberries, and pomegranates. These metabolites, better absorbed than their precursors, can contribute significantly to the beneficial properties attributed to the polyphenols ellagitannins and ellagic acid (EA). However, both the ability of producing the final metabolites in this catabolism (urolithins A, B and isourolithin A) and the health benefits associated with ellagitannin consumption differ considerably among individuals depending on their gut microbiota composition. Three human urolithin metabotypes have been previously described, i.e., metabotype 0 (urolithin non-producers), metabotype A (production of urolithin A as unique final urolithin) and metabotype B (urolithin B and/or isourolithin A are produced besides urolithin A). Although production of some intermediary urolithins has been recently attributed to intestinal species from Eggerthellaceae family named Gordonibacter urolithinfaciens and Gordonibacter pamelaeae, the identification of the microorganisms responsible for the complete transformation of EA into the final urolithins, especially those related to metabotype B, are still unknown. In the present research we illustrate the isolation of urolithin-producing strains from human feces of a healthy adult and their ability to transform EA into different urolithin metabolites, including isourolithin A. The isolates belong to a new genus from Eggerthellaceae family. EA transformation and urolithin production arisen during the stationary phase of the growth of the bacteria under anaerobic conditions. The HPLC-DAD-MS analyses demonstrated the sequential appearance of 3,8,9,10-tetrahydroxy-urolithin (urolithin M6), 3,8,9-trihydroxy-urolithin (urolithin C) and 3,9-dihydroxy-urolithin (isourolithin A) while 3,8-dihydroxy-urolithin (urolithin A) and 3-hydroxy-urolithin (urolithin B) were not detected. For the first time isourolithin A production capacity of pure strains has been described. The biological activity attributed to urolithins A and B and isourolithin A (anti-inflammatory, anti-carcinogenic, cardioprotective, and neuroprotective properties) explains the relevance of identifying these urolithin-producing bacteria as potential novel probiotics with applications in the development of functional foods and nutraceuticals. Their human administration could improve the health benefits upon ellagitannin consumption, especially in metabotype 0 individuals. However, further research is necessary to probe well-established beneficial effects on the host and safety requirements before being considered among the next-generation probiotics.

Shaaban, S. Y., El Gendy, Y. G., Mehanna, N. S., El-Senousy, W. M., El-Feki, H. S. A., Saad, K., and El-Asheer, O. M. The role of probiotics in children with autism spectrum disorder: A prospective, open-label study. Nutr.Neurosci. 7-7-2017; 1-6; PM: 28686541

ABSTRACT: ***OBJECTIVE***: There are limited data on the efficacy of probiotics in children with ASD, therefore, this study aims to evaluate the efficacy and tolerability of probiotics in an Egyptian cohort of children with ASD. ***METHODS***: Gastrointestinal (GI) flora were assessed by quantitative real-time PCR of stool samples of 30 autistic children from 5 to 9 years old. GI symptoms of autistic children were assessed with a modified six-item Gastrointestinal Severity Index (6-GSI) questionnaire, and autistic symptoms were assessed with Autism Treatment Evaluation Checklist (ATEC) before and after 3 months of supplementation of probiotics nutritional supplement formula (each gram contains 100 x 106 colony forming units of three probiotic strains; Lactobacillus acidophilus,

Lactobacillus rhamnosus and Bifidobacteria longum). ***RESULTS***: After probiotic supplementation, the stool PCR of autistic children showed increases in the colony counts of Bifidobacteria and Lactobacilli levels, with a significant reduction in their body weight as well as significant improvements in the severity of autism (assessed by the ATEC), and gastrointestinal symptoms (assessed by the 6-GSI) compared to the baseline evaluated at the start of the study. ***CONCLUSIONS***: We concluded that probiotics have beneficial effects on both behavioral and GI manifestations of ASD. Probiotics (a non-pharmacological and relatively risk-free option) could be recommended for children with ASD as an adjuvant therapy. At this stage, this study is a single center with a small number of patients and a great deal of additional wide-scale randomized controlled trials are needed to critically confirm the efficacy of probiotics in ASD. ***TRIAL REGISTRATION NUMBER***: UMIN-CTR Study Design: Trial Number UMIN000026157.

Shanahan, F. Editorial: probiotics in inflammatory bowel disease-wrong organisms, wrong disease, or flawed concepts? Aliment.Pharmacol.Ther. 2017; 46(6):632-633; PM: 28805324

No Abstract Available.

Shang, M. and Sun, J. Vitamin D/VDR, Probiotics, and Gastrointestinal Diseases. Curr.Med.Chem. 2017; 24(9):876-887; PM: 27915988

ABSTRACT: Vitamin D is an important factor in regulating inflammation, immune responses, and carcinoma inhibition via action of its receptor, vitamin D receptor (VDR). Recent studies have demonstrated the role of vitamin D/VDR in regulating host-bacterial interactions. Probiotics are beneficial bacteria with the power of supporting or favoring life on the host. In the current review, we will discuss the recent progress on the roles of vitamin D/VDR in gut microbiome and inflammation. We will summarize evidence of probiotics in modulating vitamin D/VDR and balancing gut microbiota in health and gastrointestinal diseases. Moreover, we will review the clinical application of probiotics in prevention and therapy of IBD or colon cancer. Despite of the gains, there remain several barriers to advocate broad use of probiotics in clinical therapy. We will also discuss the limits and future direction in scientific understanding of probiotics, vitamin D/VDR, and host responses.

Shariaty, Z., Mahmoodi Shan, G. R., Farajollahi, M., Amerian, M., and Behnam, Pour N. The effects of probiotic supplement on hemoglobin in chronic renal failure patients under hemodialysis: A randomized clinical trial. J.Res.Med.Sci. 2017; 22:74; PM: 28717371

ABSTRACT: ***BACKGROUND***: Chronic inflammation is one of the causes of anemia in chronic renal failure patients under hemodialysis. Probiotics probably establish a balance between pro- and anti-inflammatory cytokines. The study was conducted to determine the effects of probiotic supplementation on hemoglobin (Hb) in hemodialysis patients. ***MATERIALS AND METHODS***: A parallel clinical trial was conducted in which patients were randomly allocated into two groups. The intervention group (n = 18) was given a 500 mg probiotic supplement (a capsule) every day whereas the control group (n = 18) received placebo (a capsule), both for 3 months. Hb levels and C-reactive protein (CRP) levels were measured for three periods. The data were analyzed in SPSS-16 using statistical tests including the t-test and repeated-measures ANOVA. ***RESULTS***: In the probiotic supplementation group, the mean Hb was 9.22 +/- 1.04 mg/dl before the intervention

and reached 10.85 +/- 1.177 mg/dl afterward, while in the placebo group, the mean Hb level was 9.38 +/- 0.97 mg/dl before the intervention and reached 10.03 +/- 1.97 mg/dl afterward (P > 0.05). During the study, the placebo caused to increase of Hb temporary, but in longer term, the effect of probiotic was more manifested. Hb levels increased in both groups although the change was not statistically significant (P > 0.05). The findings showed no significant differences between the two groups in either the pre- or post-intervention CRP levels (P = 0.239). ***CONCLUSION***: Probiotic supplementation decreased Hb fluctuations in hemodialysis patients but did not result in a significant increase in Hb levels. Similar studies are therefore recommended to be conducted with a prolonged duration of the study or an increased probiotic dose with larger sample size to complete the results of the present study.

Sharifuzzaman, S. M., Rahman, H., Austin, D. A., and Austin, B. Properties of Probiotics Kocuria SM1 and Rhodococcus SM2 Isolated from Fish Guts. Probiotics.Antimicrob.Proteins. 6-5-2017; PM: 28585158

ABSTRACT: This study characterized probiotics Kocuria SM1 and Rhodococcus SM2, which were recovered from the intestinal microbiota of rainbow trout (Oncorhynchus mykiss, Walbaum). The cultures were Gram-positive, non-motile, catalase-positive and oxidase-negative cocci or rods. Cell multiplication of SM1 and SM2 was observed at 4-37 degrees C (45 degrees C for SM1), in 0-20% (w/v) NaCl and at pH 2-11. The viability was not affected when exposed to pepsin at pH 2.0 and 3.0, and pancreatin at pH 8.0. Neither isolates were chrome azurol S-positive for siderophore production. Of the 19 common enzymes analysed using the API-ZYM system, only 8 were evident in the culture of SM1 compared to 11 enzymes for SM2. The secondary metabolites of both probiotics were inhibitory to Acinetobacter baumannii, Vibrio anguillarum and V. ordalii; SM2 inhibited Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa and Staphylococcus aureus. SM2 was resistant to penicillin and sulphatriad, out of six antimicrobial agents; SM1 was resistant to sulphatriad. These results suggest that Kocuria SM1 and Rhodococcus SM2 are able to grow over a wide range of temperature, salinity and pH, including in conditions that mimic the gastrointestinal environment of fish and produce extracellular enzymes that may have a role in the host digestive processes. Importantly, Rhodococcus SM2 displays a high degree of bacteriocinogenic potential against multi-drug-resistant human pathogens that have never been documented among the gut microbiota of fish.

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.

Sharma, S., Puri, S., and Kurpad, A. V. Potential of Probiotics in Hypercholesterolemia: A Review of In Vitro and In Vivo Findings. Altern.Ther.Health Med. 6-23-2017; PM: 28646806

ABSTRACT: Context * Coronary heart disease (CHD) is a major public health problem in developing and developed countries. Elevated cholesterol levels, especially low-density lipoprotein (LDL) cholesterol, and the emergence of CHD, have been positively correlated in many clinical and epidemiological studies. The health benefits of probiotics have received a great deal of attention, including their blood cholesterol-lowering

effects on humans. Objective * The research team intended to determine the current state of research examining the effects of various probiotic strains on lipid profiles, including measures in serum of total cholesterol, LDL cholesterol, triglycerides, and high-density lipoprotein (HDL) cholesterol. Design * The review examined studies, in both animal and human models and focused on the potential of various probiotic strains to be dietary adjuncts in lowering levels of serum cholesterol with the aim of reducing the risk of cardiovascular disease (CVD) and CHD. Articles were reviewed systematically from Web search bases including PubMed and Cochrane Clinical Trial Registry. Articles meeting the inclusion search criteria were selected for further review and analysis. Only randomized controlled trials evaluating the effects of probiotics on lipid profiles in animals or humans were considered for inclusion in the review. Setting * The selection of articles and further inclusion in the review was performed in Institute of Home Economics, University of Delhi (New Delhi, India). Results * Some of the studies, in both animal and human models, have revealed that several strains were able to improve at least 1 lipid fraction. Although the results from animal studies have been fairly consistent, the findings from studies on humans have varied. Some strains when evaluated in human studies have shown insignificant effects on lipid fractions. Conclusions * Although several mechanisms for cholesterol removal by probiotics have been proposed, they need further investigation to be validated.

Shazer, A., Stewart, D., Deng, K., and Tortorello, M. Approaches toward Identification of Surrogates To Validate Antimicrobial Washes as Preventive Controls for Fresh-Cut Leafy Greens. J.Food Prot. 8-30-2017; 1600-1604; PM: 28853631

ABSTRACT: In fresh-cut produce production, antimicrobials may be used during washing to control the risk of cross-contamination by microbial hazards. Surrogate microorganisms have long been used to validate processes, but none have been identified for validating the efficacy of antimicrobial washing of fresh-cut produce. The objective of this study was to develop procedures by which surrogates may be identified for use in validating the control of cross-contamination for fresh-cut lettuce operations. Four microbial characteristics, which may be important factors in cross-contamination events, were quantitatively evaluated in potential surrogate microorganisms for comparison to a reasonably foreseeable hazard, Escherichia coli O157:H7: sensitivity to chlorine in solution, sensitivity to chlorine on lettuce leaf surfaces, shedding from contaminated lettuce leaves into the water during washing, and cross-contamination from inoculated to uninoculated lettuce leaves during chorine washing. A procedure of practical quantitative experiments for comparing the characteristics reduced the original pool of 80 potential strains, which consisted of lactic acid bacteria, probiotics, and isolates obtained from lettuce enrichment cultures, to five strains: Lactobacillus plantarum, Pediococcus pentosaceus, probiotic 22C, and two lettuce enrichment isolates. These strains may be evaluated in additional studies involving comparisons to other reasonably foreseeable hazards and including other potential process variables that should be understood and controlled to prevent cross-contamination in fresh-cut lettuce operations.

She, R., Li, T. T., Luo, D., Li, J. B., Yin, L. Y., Li, H., Liu, Y. M., Li, X. Z., and Yan, Q. G. Changes in the Intestinal Microbiota of Gibel Carp (Carassius gibelio) Associated with Cyprinid herpesvirus 2 (CyHV-2) Infection. Curr.Microbiol. 7-26-2017; PM: 28748273

ABSTRACT: Gut microbiota are integral to the host, and have received increased

attention in recent years. However, information regarding the intestinal microbiota of many aquaculture animals is insufficient; elucidating the dynamics of the intestinal microbiota can be beneficial for nutrition, immunity, and disease control. In this study, we used 16S rRNA sequencing to observe changes in the intestinal microbiota of gibel carp (Carassius auratus gibelio) associated with cyprinid herpesvirus 2 (CyHV-2) infection. Our results indicate that the diversity of the intestinal microbiota was strongly reduced, and the composition was dramatically altered following CyHV-2 infection. The most dominant species in healthy fish were Cetobacterium, Rhodobacter, and Crenothrix; meanwhile, Cetobacterium, Plesiomonas, Bacteroides, and Flavobacterium were the most abundant species in sick fish. Plesiomonas was highly abundant in infected samples, and could be used as a microbial biomarker for CyHV-2 infection. Chemical properties of the aquaculture water were significantly correlated with the microbial community structure; however, it is difficult to determine whether these changes are a cause or consequence of infection. However, it may be possible to use probiotics or prebiotics to restore the richness of the host intestinal microbiota in infected animals to maintain host health.

Sheikhi, A., Giti, H., Heibor, M. R., Jafarzadeh, A., Shakerian, M., Baharifar, N., Niruzad, F., Moghaddam, A. S., Kokhaei, P., and Baghaeifar, M. Lactobacilus Delbrueckii subsp. Bulgaricus Modulates the Secretion of Th1/Th2 and Treg Cell-Related Cytokines by PBMCs from Patients with Atopic Dermatitis. Drug Res.(Stuttg). 9-12-2017; PM: 28898911

ABSTRACT: Background Atopic dermatitis (AD) is an inflammatory skin disease which may be due to the imbalance between Th1-, Th2 and Treg cell-related immune responses. Evidences suggest that appropriate stimulation with probiotics may correct the skewed immune response in children with AD. The aim was to determine the effects of the yogurt culture lactobacillus Bulgaricus on the secretion of Th1/Th2/Treg type cytokines by PBMCs from children with AD. MethodsL. Bulgaricus was cultivated on MRS broth. The PBMCs from 20 children with AD were separated by Ficoll-Hypaque centrifugation and co-cultured with different concentrations of UV killed bacteria in RPMI-1640 plus 10% FCS for 48/72 h. The levels of IL-10, IL-4, IL-12 and IFN-gamma were measured in supernatant of PBMCs by ELISA. ResultsL. Bulgaricus significantly up-regulated the secretion of IL-10, IL-12 and IFN-gamma, whereas decreased the secretion of IL-4 by PBMCs at both incubation times 48 h/72 h and both bacteria:PBMCs ratios 100:1/50:1, compared to control ($p<0.05$). There were no significant differences between incubation times 48 h and 72 h regarding the secretion levels of IL-12, IFN-gamma and IL-4. However, the secretion of IL-10 by L. Bulgaricus-stimulated PBMCs at incubation time 72 h and in the presence of bacteria:PBMCs ratio 100:1 was significantly higher than in incubation time 48 h and in the presence of bacteria:PBMCs ratio 50:1 ($P<0.000$ and $P<0.00$, respectively). Conclusion These data show that L. Bulgaricus may modulate the secretion of Th1-, Th2-Treg-related cytokines in AD patients. Therefore, the possible potential therapeutic of L. Bulgaricus for treatment of AD should be consider in further investigation.

Shen, Z., Zhu, C., Quan, Y., Yuan, W., Wu, S., Yang, Z., Luo, W., Tan, B., and Wang, X. Update on intestinal microbiota in Crohn's disease 2017: Mechanisms, Clinical application, Adverse reactions and Outlook. J.Gastroenterol.Hepatol. 7-5-2017; PM: 28677158

ABSTRACT: The pathogenesis of CD is complex and it is thought to be associated with the environment, immune, hereditary, microbe and other factors. If the balance between the host and the intestinal microbes in CD patients was broken, immune-inflammatory response of susceptible individuals might be triggered. Probiotics could improve the

intestinal microbial flora balance and treat human effectively. There are several new mechanisms which might explain the role of probiotics. Fecal microbiota transplantation (FMT) is becoming more and more attractive in treating a large amount of digestive system diseases which are related to the dysbiosis of intestinal microbiota. FMT has been widely used in recurrent clostridium difficile infection (RCDI). More and more attention has been paid on the clinical application of FMT in CD.While the exact mechanism is still a mystery. So in this review, we explore the mechanism, clinical application and adverse reactions of intestinal microbiota in CD so that we can use the tool to cure more diseases. Enteric microbiota leads to new therapeutic strategies for CD.

Sheng, L., Jena, P. K., Hu, Y., Liu, H. X., Nagar, N., Kalanetra, K. M., French, S. W., French, S. W., Mills, D. A., and Wan, Y. Y. Hepatic inflammation caused by dysregulated bile acid synthesis is reversible by butyrate supplementation. J.Pathol. 9-11-2017; PM: 28892150

ABSTRACT: Dysregulated bile acid (BA) synthesis or reduced farnesoid x receptor (FXR) levels are found in patients having metabolic diseases, autoimmune hepatitis, and liver cirrhosis or cancer. The objective of this study was to establish the relationship between butyrate and dysregulated BA synthesis-induced hepatitis as well as the effect of butyrate in reversing the liver pathology. Wild type (WT) and FXR knockout (KO) male mice were placed on control (CD) or Western diet (WD) for 15 months. In the presence or absence of butyrate supplementation, feces obtained from 15-month-old WD-fed FXR KO mice, which had severe hepatitis and liver tumors, were transplanted to 7-month-old WD-fed FXR KO for 3 months. Hepatic phenotypes, microbiota profile, and BA composition were analyzed. Butyrate-generating bacteria and colonic butyrate concentration were reduced due to FXR inactivation and further reduced by WD intake. In addition, WD-fed FXR KO male mice had the highest concentration of hepatic beta-muricholic acid (beta-MCA) and bacteria-generated deoxycholic acid (DCA) accompanied by serious hepatitis. Moreover, dysregulated BA and reduced SCFA signaling coexisted in both human liver cancers and WD-fed FXR KO mice. Microbiota transplantation using butyrate-deficient feces derived from 15-month-old WD-fed FXR KO mice increased hepatic lymphocyte numbers as well as hepatic beta-MCA and DCA concentrations. Furthermore, butyrate supplementation reduced hepatic beta-MCA as well as DCA and eliminated hepatic lymphocyte infiltration. In conclusion, reduced butyrate contributes to the development of hepatitis in the FXR KO mouse model. In addition, butyrate reverses dysregulated BA synthesis and its associated hepatitis.

Sherf-Dagan, S., Zelber-Sagi, S., Zilberman-Schapira, G., Webb, M., Buch, A., Keidar, A., Raziel, A., Sakran, N., Goitein, D., Goldenberg, N., Mahdi, J. A., Pevsner-Fischer, M., Zmora, N., Dori-Bachash, M., Segal, E., Elinav, E., and Shibolet, O. Probiotics administration following sleeve gastrectomy surgery: A randomized double-blind trial. Int.J.Obes.(Lond). 8-30-2017; PM: 28852205

ABSTRACT: ***BACKGROUND***: Probiotics are commonly used after bariatric surgery; however uncertainty remains regarding their efficacy. Our aim was to compare the effect of probiotics vs. placebo on hepatic, inflammatory and clinical outcomes following laparoscopic sleeve gastrectomy (LSG). ***METHODS***: This randomized, double-blind, placebo-controlled, trial of 6-months treatment with probiotics (Bio-25;Supherb) vs. placebo and 6-months of additional follow-up was conducted among 100 morbidly obese non-alcoholic fatty liver disease (NAFLD) patients who underwent LSG surgery. The primary-outcome was a reduction in liver fat content, measured by abdominal-

ultrasound, and secondary-outcomes were improvement of fibrosis, measured by shear-wave elastography, metabolic and inflammatory parameters, anthropometrics and quality of life (QOL). Fecal samples were collected and analyzed for microbial composition. ***RESULTS***: One-hundred patients (60% women, mean age of 41.9+/-9.8 years and BMI of 42.3+/-4.7 kg/m2) were randomized, 80% attended the 6-month visit and 77% completed the 12-month follow-up. Fat content and NAFLD remission rate were similarly reduced in the probiotics and placebo groups at 6-months post-surgery (-0.9+/-0.5 vs -0.7+/-0.4 score; P=0.059 and 52.5 vs 40%; P=0.262, respectively) and at 12-months post-surgery. Fibrosis, liver-enzymes, C-Reactive Protein (CRP), leptin, cytokeratin-18 (CK-18) levels were significantly reduced and QOL significantly improved within-groups (P0.014 for all), but not between-groups (P0.173 for all) at 6 and 12-months post-surgery. Within-sample microbiota diversity (alpha-diversity) increased at 6-months post-surgery compared to baseline in both study-arms (P0.008) and decreased again at 12-months post-surgery compared to 6-months post-surgery (P0.004), but did not reach baseline values. ***CONCLUSIONS***: Probiotics administration does not improve hepatic, inflammatory and clinical outcomes 6 and 12-months post-LSG.International Journal of Obesity accepted article preview online, 30 August 2017. doi:10.1038/ijo.2017.210.

Shin, J. H., Nam, M. H., Lee, H., Lee, J. S., Kim, H., Chung, M. J., and Seo, J. G. Amelioration of obesity-related characteristics by a probiotic formulation in a high-fat diet-induced obese rat model. Eur.J.Nutr. 6-12-2017; PM: 28608319

ABSTRACT: ***PURPOSE***: Obesity is a major public health concern. Despite its multi-factorial etiology, alterations in intestinal microbiota and the immune system are frequently observed. We investigated the effect of Duolac Gold (DG), a probiotic formulation containing 2 Lactobacillus strains (L. acidophilus LA1 and L. rharmnosus LR5), 3 Bifidobacterium (B. bifidum BF3, B. lactis BL3, and B. longum BG7), and Streptococcus thermophilus ST3, on morphometric and metabolic parameters, intestinal microbiota, and intestinal immune responses in a high-fat diet (HFD)-induced obese rat model. ***METHODS***: Rats received either a conventional balanced diet or HFD with or without water containing DG for 8 weeks. HFD-induced adiposity, intestinal microbiota, and changes in inflammatory cytokine, chemokine, and metabolite levels in serum were evaluated. ***RESULTS***: DG administration effectively decreased HFD-induced body weight and modulated morphometric and metabolic parameters. Quantitative analysis of fecal microbiota showed that obese rats given DG exhibited significantly increased levels of Bacteroidetes, Lactobacillus, and Bifidobacterium, with significant decreases in the level of Firmicutes. Serum levels of the inflammatory cytokines and the chemokine were also altered. Serum metabolite analysis revealed that DG administration modulated HFD-induced changes in serum metabolites, including fatty acids (FA), lysophosphatidylcholine, lysophosphatidylethanolamine, phosphatidylcholine (PC), and triacylglycerol (TAG). ***CONCLUSIONS***: DG administration appears to have the potential to alleviate HDF-induced obesity through the modulation of intestinal microbiota, immune responses, and host metabolism, which supports the use of probiotics to treat obesity.

Silva, H. L. A., Balthazar, C. F., Esmerino, E. A., Vieira, A. H., Cappato, L. P., Neto, R. P. C., Verruck, S., Cavalcanti, R. N., Portela, J. B., Andrade, M. M., Moraes, J., Franco, R. M., Tavares, M. I. B., Prudencio, E. S., Freitas, M. Q., Nascimento, J. S., Silva, M. C., Raices, R. S. L., and Cruz, A. G. Effect of sodium reduction and flavor enhancer addition on probiotic Prato cheese processing. Food Res.Int. 2017; 99(Pt 1):247-255; PM: 28784481

ABSTRACT: The effect of partial substitution of NaCl with KCl and the flavor enhancers addition (arginine, yeast extract and oregano extract) on Probiotic Prato cheese processing with (L. casei 01, 7logCFU/mL) was investigated. Microbiological (lactic acid bacteria and probiotic counts), physicochemical (proximate composition, pH, proteolysis), bioactivity (antioxidant and angiotensin I-converting enzyme inhibitory activity), rheological (uniaxial compression and creep tests), water mobility (time domain low field magnetic resonance), microstructure (scanning electron microscopy) and sensory evaluation (consumer test) were performed. Sodium reduction and flavor enhancers addition did not constitute an obstacle to the survival of lactic and probiotic bacteria. Proximate composition, antioxidant and angiotensin I-converting enzyme inhibitory activity, and the rheological parameters were affected by the addition of flavor enhancer. No change in the fatty acid profile of cheeses was observed while good performance in the consumer test was obtained by the addition of yeast extract and oregano extract. Prato cheese can be an adequate carrier of probiotics and the addition of different flavor enhancers can contribute developing this functional product in the cheese industry.

Sirtori, C. R., Pavanello, C., Calabresi, L., and Ruscica, M. Nutraceutical approaches to metabolic syndrome. Ann.Med. 8-22-2017; 1-20; PM: 28786719

ABSTRACT: Metabolic Syndrome (MetS), affecting at least 30% of adults in the Western World, is characterized by three out of five variables, from high triglycerides, to elevated waist circumference and blood pressure. MetS is not characterized by elevated cholesterolemia, but is rather the consequence of a complex interaction of factors generally leading to increased insulin resistance. Drug treatments are of difficult handling, whereas well-characterized nutraceuticals may offer an effective alternative. Among these, functional foods, e.g. plant proteins, have been shown to improve insulin resistance and reduce triglyceride secretion. Pro- and pre-biotics, that are able to modify intestinal microbiome, reduce absorption of specific nutrients and improve the metabolic handling of energy-rich foods. Finally, specific nutraceuticals have proven to be of benefit, in particular, red-yeast rice, berberine, curcumin as well as vitamin D. All these can improve lipid handling by the liver as well as ameliorate insulin resistance. While lifestyle approaches, such as with the Mediterranean diet, may prove to be too complex for the single patient, better knowledge of selected nutraceuticals and more appropriate formulations leading to improved bioavailability will certainly widen the use of these agents, already in large use for the management of these very frequent patient groups. Key messages Functional foods, e.g. plant proteins, improve insulin resistance. Pro- and pre-biotics improve the metabolic handling of energy-rich foods. Nutraceutical can offer a significant help in handling MetS patients being part of lifestyle recommendations.

Skorka, A., Piescik-Lech, M., Kolodziej, M., and Szajewska, H. To add or not to add probiotics to infant formulae? An updated systematic review. Benef.Microbes. 8-31-2017; 1-10; PM: 28856907

ABSTRACT: We updated evidence on the effects of the administration of probiotic-supplemented infant formulae (IF) compared with unsupplemented IF. Five databases were searched up to September 2016 for randomised controlled trials. Twenty publications were identified, including five new RCTs. Supplementation of IF with

Bifidobacterium lactis Bb12, either alone or with Streptococcus thermophilus, had no effect on growth, respiratory illness, antibiotic use, stool frequency or consistency. However, there was a significant reduction in the number of episodes of gastrointestinal infections (Bb12) and a lower frequency of colic or irritability (when both strains were used). Lactobacillus johnsonii La1 had no effect on growth, gastrointestinal infections, or respiratory illness episodes. There were no effects of supplementation of IF with Bifidobacterium longum BL999, alone or with Lactobacillus rhamnosus LPR. L. rhamnosus GG was associated with better growth; it had no effect on colic/crying, or irritability, and it was associated with greater indexes of loose stools and a higher defecation frequency. Lactobacillus reuteri ATCC 55730 had no effect on growth, colic, crying, irritability, respiratory illness, antibiotic use, stool frequency, or stool consistency; however, it reduced the number of episodes of diarrhoea. L. reuteri DSM 17938 had no effect on growth, night-time sleeping, or flatulence, but it reduced the number of spitting episodes. Lactobacillus salivarius CEC5713 had no effect on growth, colic, crying, or irritability; however, it resulted in a significant reduction in the rate of diarrhoea and the number of episodes of respiratory symptoms. In conclusion, the administration of probiotic-supplemented formulae to healthy infants does not raise safety concerns with regard to growth and adverse effects. Some beneficial clinical effects are possible; however, there is no existing robust evidence to recommend their routine use. The latter conclusion may reflect the small amount of data on a specific probiotic strain(s) and outcomes, rather than a genuine lack of an effect.

Smarkusz, J., Ostrowska, L., and Witczak-Sawczuk, K. Probiotic strains as the element of nutritional profile in physical activity - new trend or better sports results? Rocz.Panstw.Zakl.Hig. 2017; 68(3):229-235; PM: 28895388

ABSTRACT: A diet, individually customized to the needs of sportsmen and sportswomen prepares them better for competition and achievement of better sports results. However, disorders of the gastrointestinal tract and frequently recurrent upper respiratory tract infections pose a common problem observed among athletes of disciplines such as triathlon, cycling and marathon. Diarrhea, splashing in the intestines or gastrointestinal bleeding make it difficult to start and win in the race. Recently researchers have paid special attention to the therapeutic effect of probiotic strains on the human body. Various probiotic strains may have a beneficial effect on elimination of disorders mentioned above among athletes of these disciplines. Still, researchers continue looking for answers to the question how a specific probiotic strain is able to reduce the risk of the gastrointestinal tract and the respiratory system disorders appearing during training or competition. Attention is also drawn to the possible impact of probiotics on the physical capacity athletes and their athletic performance. Probiotic strains properly applied may have a positive influence on the athletes' bodies, but still randomized controlled trials are required to prove this thesis.

Smilowitz, J. T., Moya, J., Breck, M. A., Cook, C., Fineberg, A., Angkustsiri, K., and Underwood, M. A. Safety and tolerability of Bifidobacterium longum subspecies infantis EVC001 supplementation in healthy term breastfed infants: a phase I clinical trial. BMC.Pediatr. 5-30-2017; 17(1):133; PM: 28558732

ABSTRACT: ***BACKGROUND***: Historically, bifidobacteria were the dominant intestinal bacteria in breastfed infants. Still abundant in infants in developing nations, levels of intestinal bifidobacteria are low among infants in developed nations. Recent studies have described an intimate relationship between human milk and a specific subspecies

of Bifidobacterium, B. longum subsp. infantis (B. infantis), yet supplementation of breastfed, healthy, term infants with this organism, has not been reported. The IMPRINT Study, a Phase I clinical trial, was initiated to determine the safety and tolerability of supplementing breastfed infants with B. infantis (EVC001). ***METHODS***: Eighty mother-infant dyads were enrolled in either lactation support plus B. infantis supplementation (BiLS) or lactation support alone (LS). Starting with Day 7 postnatal, BiLS infants were fed 1.8-2.8 x 1010 CFU B. infantis EVC001 daily in breast milk for 21 days. Mothers collected fecal samples, filled out health questionnaires, and kept daily logs about their infants' feeding and gastrointestinal symptoms from birth until Day 61 postnatal. Safety and tolerability were determined from maternal reports. ***RESULTS***: There were no differences in the mean gestational age at birth, weight 1 and 2 months postnatal, and breast milk intake between groups. The mean Log10 change in fecal Bifidobacterium from Day 6 to Day 28 was higher ($p = 0.0002$) for BiLS (6.6 +/- 2.8 SD) than for LS infants (3.5 +/- 3.5 SD). Daily stool number was higher ($p < 0.005$) for LS and lower ($p < 0.05$) for BiLS infants during supplementation than at Baseline. During supplementation, watery stools decreased and soft stools increased by 36% over baseline in BiLS infants ($p < 0.05$) with no significant changes in stool consistency for the LS infants. None of the safety and tolerability endpoints, including flatulence, bloody stool, body temperature, ratings of gastrointestinal symptoms, use of antibiotics or gas-relieving medications, infant colic, jaundice, number of illnesses, sick doctor visits, or diagnoses of eczema were different for the groups at any point. ***CONCLUSIONS***: The B. infantis EVC001 supplement was safely consumed and well-tolerated. Stools were fewer and better formed in infants in the BiLS group compared with LS group. Adverse events were those expected in healthy infants and not different between groups. ***TRIAL REGISTRATION***: ClinicalTrials.gov NCT02457338 . Registered May 27, 2015.

Sohn, K. and Underwood, M. A. Prenatal and postnatal administration of prebiotics and probiotics. Semin.Fetal Neonatal Med. 2017; 22(5):284-289; PM: 28720399

ABSTRACT: Colonization of the neonatal gut by beneficial bacteria is important for the establishment and maintenance of the mucosal barrier, thus protecting the neonate from enteric pathogens and local and systemic inflammation. The neonatal microbiome is influenced by infant diet, environment, and the maternal microbiome. Dysbiosis in pregnancy increases the risk of pre-eclampsia, diabetes, infection, preterm labor, and later childhood atopy. Dysbiosis of the neonatal gut plays an important role in colic in the term infant, in the disease processes which plague preterm infants, including necrotizing enterocolitis and sepsis, and in the long-term outcomes of neonates. Administration of enteral prebiotics, probiotics, and synbiotics during pregnancy, lactation, and postnatal life appears to be a safe and feasible method to alter the maternal and neonatal microbiome, thus improving pregnancy and neonatal outcomes.

Song, X., Huang, H., Xiong, Z., Ai, L., and Yang, S. CRISPR-Cas9D10A Nickase-Assisted Genome Editing in Lactobacillus casei. Appl.Environ.Microbiol. 9-1-2017; PM: 28864652

ABSTRACT: Lactobacillus casei has drawn increasing attention as health-promoting probiotics, while effective genetic manipulation tools are often not available, e.g. the single gene knockout in L. casei still depends on the classic homologous recombination-dependent double crossover strategy that is quite labor intensive and time-requiring. In the present study, a rapid and precise genome editing plasmid pLCNICK was established for L. casei genome engineering based on CRISPR-Cas9D10A In addition to the P23-

Cas9D10A and Pldh-sgRNA (single guide RNA) expression cassettes, pLCNICK includes the homologous arms of the target gene as repair templates. The ability and efficiency of chromosomal engineering using pLCNICK were evaluated by in-frame deletions of four independent genes and chromosomal insertion of an enhanced green fluorescent protein (eGFP) expression cassette at the LC2W_1628 locus. The efficiencies associated with in-frame deletions and chromosomal insertion is 25-62%. The pLCNICK has been proved to be an effective, rapid and precise tool for genome editing in L. casei and its potential application in other members of Lactic acid bacteria (LAB) was also discussed in this study.Importance The lack of efficient genetic tools has limited the investigation and biotechnological application of many LAB. The CRISPR-Cas9D10A nickase-based genome editing in Lactobacillus casei, an important food industrial microorganism, was demonstrated in this study. This genetic tool allows efficient single gene deletion and insertion to be accomplished by one-step transformation and the cycle time is reduced to 9 days. It facilitates a rapid and precise chromosomal manipulation in L. casei and overcomes some limitations of previous methods. This editing system can serve as a basic technological platform and offer the possibility to start a comprehensive investigation on L. casei As a broad host-range plasmid, pLCNICK has the potential to be adapted to other Lactobacillus species for genome editing.

Soukoulis, C., Behboudi-Jobbehdar, S., Macnaughtan, W., Parmenter, C., and Fisk, I. D. Stability of Lactobacillus rhamnosus GG incorporated in edible films: Impact of anionic biopolymers and whey protein concentrate. Food Hydrocoll. 2017; 70:345-355; PM: 28867864

ABSTRACT: The incorporation of probiotics and bioactive compounds, via plasticised thin-layered hydrocolloids, within food products has recently shown potential to functionalise and improve the health credentials of processed food. In this study, choice of polymer and the inclusion of whey protein isolate was evaluated for their ability to stabalise live probiotic organisms. Edible films based on low (LSA) and high (HSA) viscosity sodium alginate, low esterified amidated pectin (PEC), kappa-carrageenan/locust bean gum (kappa-CAR/LBG) and gelatine (GEL) in the presence or absence of whey protein concentrate (WPC) were shown to be feasible carriers for the delivery of L. rhamnosus GG. Losses of L. rhamnosus GG throughout the drying process ranged from 0.87 to 3.06 log CFU/g for the systems without WPC, losses were significantly reduced to 0 to 1.17 log CFU/g in the presence of WPC. Storage stability (over 25d) of L. rhamnosus GG at both tested temperatures (4 and 25 degrees C), in descending order, was kappa-CAR/LBG > HSA > GEL > LSA = PEC. In addition, supplementation of film forming agents with WPC led to a 1.8- to 6.5-fold increase in shelf-life at 4 degrees C (calculated on the WHO/FAO minimum requirements of 6 logCFU/g), and 1.6-4.3-fold increase at 25 degrees C. Furthermore probiotic films based on HSA/WPC and kappa-CAR/LBG/WPC blends had both acceptable mechanical and barrier properties.

Spinler, J. K., Auchtung, J., Brown, A., Boonma, P., Oezguen, N., Ross, C. L., Luna, R. A., Runge, J., Versalovic, J., Peniche, A., Dann, S. M., Britton, R. A., Haag, A., and Savidge, T. C. Next-generation probiotics targeting Clostridium difficile through precursor-directed antimicrobial biosynthesis. Infect.Immun. 7-31-2017; PM: 28760934

ABSTRACT: Integration of antibiotic and probiotic therapy has the potential to lessen the public health burden to antimicrobial-associated diseases. Clostridium difficile infection (CDI) represents an important example where rational design of next generation

probiotics is being actively pursued to prevent disease recurrence. Because intrinsic resistance to clinically relevant CDI antibiotics (vancomycin, metronidazole, and fidaxomicin) is a desired trait in such probiotic species, we screened several bacteria and identified Lactobacillus reuteri as a promising candidate for adjunct therapy. Human-derived L. reuteri convert glycerol to the broad-spectrum antimicrobial compound, reuterin. When supplemented with glycerol, strains carrying the pocR gene locus were potent reuterin producers with L. reuteri 17938 inhibiting C. difficile growth on a par with vancomycin. Targeted pocR mutations and complementation studies identified reuterin as the precursor-induced antimicrobial agent. Pathophysiological relevance was demonstrated when co-delivery of L. reuteri with glycerol was effective against C. difficile colonization in complex human fecal microbial communities, whereas treatment with either glycerol or L. reuteri alone was ineffective. Global unbiased microbiome and metabolomics analysis independently confirmed that glycerol precursor delivery with L. reuteri elicited changes in human microbial community composition and function that preferentially targets C. difficile outgrowth and toxicity, a finding consistent with glycerol fermentation and reuterin production. Antimicrobial resistance has thus been successfully exploited in the natural design of the human microbiome evasion of C. difficile and may provide a prototypic precursor-directed probiotic approach. Antibiotic resistance and substrate bioavailability may therefore represent critical new determinants for probiotic efficacy in clinical trials.

Srinivasan, S., Nandlal, B., and Rao, M. V. S. Assessment of plaque regrowth with a probiotic toothpaste containing Lactobacillus paracasei: A spectrophotometric study. J.Indian Soc.Pedod.Prev.Dent. 2017; 35(4):307-311; PM: 28914242

ABSTRACT: ***BACKGROUND***: Probiotics are live microorganisms which when administered in adequate amounts confer health benefits on the host. Commonly, most of the organisms ascribed as having probiotic properties belong to the genera Lactobacillus and Bifidobacterium and milk is the most commonly used vehicle. ***OBJECTIVES***: The study was aimed at analyzing the biofilm formation by plaque regrowth method upon the usage of a probiotic toothpaste containing Lactobacillus paracasei by measuring the optical density using a spectrophotometer. ***MATERIALS AND METHODS***: A commercially available probiotic toothpaste, PerioBiotic (spearmint flavored) from the company Designs for Health, has been tested. The toothpaste contains the strain L. paracasei, which has been found to co-aggregate with Streptococcus mutans (MS). The Plaque Glycolysis and Regrowth Method (PGRM) was used for the evaluation of the antimicrobial effects on plaque metabolism in vivo. PGRM is based on the observation that natural fasted dental plaque, sampled from different quadrants of the dentition, exhibits similar metabolic and regrowth properties when suspended at equal "biomass" in standardized media. ***CONCLUSION***: The results suggest that L. paracasei-based toothpaste, PerioBiotic, is effective in the reduction of MSmonospecies biofilm, but the activity appears short lived when high sucrose exposure is administered.

Srisapoome, P. and Areechon, N. Efficacy of viable Bacillus pumilus isolated from farmed fish on immune responses and increased disease resistance in Nile tilapia (Oreochromis niloticus): Laboratory and on-farm trials. Fish.Shellfish.Immunol. 2017; 67:199-210; PM: 28602733

ABSTRACT: Applications of viable Bacillus pumilus AQAHBS01 isolated from Nile tilapia

farms as probiotics were studied in both laboratory and farm conditions. In the laboratory, feeding fish (approximately 50 g) with feed containing viable B. pumilus at concentrations of 1 x 107-109 colony forming units (CFU)/kg elevated fish immune responses, as indicated by their phagocytic activity and superoxide anion levels, and led to more effective disease resistance against Streptococcus agalactiae. However, when these concentrations were applied to Nile tilapia cultures growing in cage culture systems, only B. pumilus AQAHBS01 at concentrations of 1 x 108 and 109 CFU/kg diet could effectively enhance disease resistance against S. agalactiae during the critical period of early to middle April when the temperature reached 33 degrees C, whereas control fish and fish that consumed B. pumilus AQAHBS01 at concentrations of 1 x 107 CFU/kg showed very rapid streptococcosis-induced mortality. However, in late April, massive levels of organic matter-containing water flowed into the culture areas, causing all fish groups to become infected with Flavobacterium columnare. Moreover, the dissolved oxygen levels in the river declined to critical levels of approximately 1.0-1.5 mg/L, causing anorectic effects in fish for long periods of time. This effect may have also gradually killed the cultured fish until the end of the experiment. This information strongly demonstrates the effective application of B. pumilus as a probiotic for streptococcosis resistance in both laboratory and field culture conditions. For on-farm cage culture practices, however, fluctuations in water quality remain a significant constraint for probiotic application, as they usually induce negative effects on fish health. This decline in health makes fish more fragile and more susceptible to problems from both infectious and non-infectious diseases, which farmers must consider carefully.

Starosila, D., Rybalko, S., Varbanetz, L., Ivanskaya, N., and Sorokulova, I. Anti-influenza Activity of a Bacillus subtilis Probiotic Strain. Antimicrob.Agents Chemother. 2017; 61(7); PM: 28416546

ABSTRACT: Among Bacillus bacteria, B. subtilis is the species that produces the most antimicrobial compounds. In this study, we analyzed the activity of probiotic strain B. subtilis 3 against the influenza virus. The antiviral effect of this strain has been demonstrated in vitro and in vivo A new peptide, P18, produced by the probiotic strain was isolated, purified, chemically synthesized, and characterized. Cytotoxicity studies demonstrated no toxic effect of P18 on Madin-Darby canine kidney (MDCK) cells, even at the highest concentration tested (100 mug/ml). Complete inhibition of the influenza virus in vitro was observed at concentrations of 12.5 to 100 mug/ml. The protective effect of P18 in mice was comparable to that of oseltamivir phosphate (Tamiflu). Further study will assess the potential of peptide P18 as an antiviral compound and as a promising candidate for the development of new antiviral vaccines.

Stavropoulou, E. and Bezirtzoglou, E. Human microbiota in aging and infection: A review. Crit Rev.Food Sci.Nutr. 9-14-2017; 0PM:28910544¶

ABSTRACT: In most developed countries, ageing of the population started more than a century ago and it seems to be emerged in a wide range of developing countries as well. Moreover, research into ageing has moved forward in extremely rapidly rhythms nowadays, and the scientific area is of great interest, as implications for nearly all sectors of society, including work, social, economic features, in addition to nutrition and health issues which are involved. The fragile elder population is affected and experienced more frequently infections than the younger population. Infections in elderly patients are of

major medical importance because of hormonal changes, increased production of pro-inflammatory cytokines and chemokines, abnormalities of the telomeres which could cause a dysfunction of the immune system called immunosenescence and malnutrition.

Strompfova, V., Kubasova, I., and Laukova, A. Health benefits observed after probiotic Lactobacillus fermentum CCM 7421 application in dogs. Appl.Microbiol.Biotechnol. 2017; 101(16):6309-6319; PM: 28721546

ABSTRACT: The importance of the intestinal microbiota has attracted much interest in recent years particularly with respect to ways in which the microbiota can be manipulated in order to improve health. Improving gut health through the use of probiotic microorganisms has become an area of research activity in both human and animal nutrition. However, the amount of research using companion animals is insufficient. The present review evaluates and compares the effects achieved after application of canine-derived probiotic strain Lactobacillus fermentum CCM 7421 to healthy dogs as well as to dogs suffering from gastrointestinal disorders. The experiments involved varying duration of application (4 days-14 days), dosage (107-109 CFU), form of application (fresh culture or lyophilized from) or combination with natural substances. Results from nine independent studies show the ability of probiotic strains to establish themselves in the canine gastrointestinal tract, alter the composition of intestinal microbiota and metabolites (organic acids), and modulate the physiology (serum biochemical parameters) and immunity parameters in dogs. Almost all observed effects were irrespective of dose or duration of probiotic administration.

Su, Y., Chen, X., Liu, M., and Guo, X. Effect of three lactobacilli with strain-specific activities on the growth performance, faecal microbiota and ileum mucosa proteomics of piglets. J.Anim Sci.Biotechnol. 2017; 8:52; PM: 28616225

ABSTRACT: ***BACKGROUND***: The beneficial effects of Lactobacillus probiotics in animal production are often strain-related. Different strains from the same species may exert different weight-gain effect on hosts in vivo. Most lactobacilli are selected based on their in vitro activities, and their metabolism and regulation on the intestine based on strain-related characters are largely unexplored. The objective of the present study was to study the in vivo effects of the three lactobacilli on growth performance and to compare the differential effects of the strains on the faecal microbiota and ileum mucosa proteomics of piglets. ***METHODS***: Three hundred and sixty piglets were assigned to one of four treatments, which included an antibiotics-treated control and three experimental groups supplemented with the three lactobacilli, L. salivarius G1-1, L. reuteri G8-5 and L. reuteri G22-2, respectively. Piglets were weighed and the feed intake was recorded to compare the growth performance. The faecal lactobacilli and coliform was quantified using quantitative PCR and the faecal microbiota was profiled by denaturing gradient gel electrophoresis (DGGE). The proteomic approach was applied to compare the differential expression of proteins in the ileum mucosa. ***RESULTS***: No statistical difference was found among the three Lactobacillus-treated groups in animal growth performance compared with the antibiotics-treated group ($P > 0.05$). Supplementation of lactobacilli in diets significantly increased the relative 16S rRNA gene copies of Lactobacillus genus on both d 14 and d 28 ($P < 0.05$)., and the bacterial community profiles based on DGGE from the lactobacilli-treated groups were distinctly different from the antibiotics-treated group ($P < 0.05$). The ileum mucosa of piglets responded to all Lactobacillus supplementation by producing more newly expressed proteins and the identified

proteins were all associated with the functions beneficial for stabilization of cell structure. Besides, some other up-regulated and down-regulated proteins in different Lactobacillus-treated groups showed the expression of proteins were partly strain-related. ***CONCLUSIONS***: All the three lactobacilli in this study show comparable effects to antibiotics on piglets growth performance. The three lactobacilli were found able to modify intestinal microbiota and mucosa proteomics. The regulation of protein expression in the intestinal mucosa are partly associated with the strains administrated in feed.

Succi, M., Tremonte, P., Pannella, G., Tipaldi, L., Cozzolino, A., Romaniello, R., Sorrentino, E., and Coppola, R. Pre-cultivation with Selected Prebiotics Enhances the Survival and the Stress Response of Lactobacillus rhamnosus Strains in Simulated Gastrointestinal Transit. Front Microbiol. 2017; 8:1067; PM: 28659890

ABSTRACT: In our study, we dwelled upon combinations of lactobacilli/prebiotics, considering four different strains belonging to the Lactobacillus rhamnosus species, including Lactobacillus rhamnosus GG (LGG), and different prebiotics often found in commercial synbiotic products, such as inulin, lactulose and polyols mannitol and sorbitol. In the first step of the research, the survival, the growth kinetic parameters and the protein expression of Lb. rhamnosus strains cultivated in presence of the different prebiotics as a unique carbon source were evaluated. In the second step, the influence of pre-cultivation in medium added of metabolizable prebiotics on the strains survival to simulated gastrointestinal (GI) transit, assayed without prebiotics addition, was estimated. Our results showed that the presence in the medium of certain low fermented prebiotics, specific for each strain, represents a stress factor that significantly affects the growth of Lb. rhamnosus strains, inducing the up-regulation of several proteins. In detail, all added prebiotics used as unique carbon source caused a growth retard compared with glucose, as testified by increased values of the lag phase and decreased values of the mumax. Mannitol evidenced intermediate mumax values between those registered with glucose and those detected with the other assayed prebiotics. Moreover, the cultivation with prebiotics induced the over expression of 7 protein bands. Interestingly, we found a correlation between the up-regulation of two specific stress proteins, called P4 (ATP-binding subunit ClpX) and P7 (GrpE), and the death kinetic parameters (resistance and cells viability) registered during the simulated GI transit of strains pre-cultivated with specific, low fermented prebiotics. Specifically, the highest resistance and gastric-vitality scores were highlighted for the strain AT195 when pre-cultivated in presence of sorbitol. Conversely, the lowest values were found in the case of DSM20021 pre-cultivated with mannitol. Among the up-regulated stress proteins, P7 resulted involved in the response to the starvation. Finally, it is possible to conclude that the pre-cultivation with certain prebiotics as a unique carbon source represents a strain-specific, sub-lethal stress able to enhance the resistance of Lb. rhamnosus strains and consequently their viability under simulated GI transit.

Sujlana, A., Goyal, R., Pannu, P., Opal, S., and Bansal, P. Visual pedagogy and probiotics for hearing impaired children: A pilot study. J.Indian Soc.Pedod.Prev.Dent. 2017; 35(4):353-358; PM: 28914249

ABSTRACT: ***CONTEXT***: Oral health care for children with special needs remains largely unmet. It is important that we should focus on preventive strategies for special children to

help curtail and prevent oral diseases. AIM: This study aimed to assess the effect of visual pedagogy and probiotic mouth rinse on the periodontal health of hearing impaired children. ***MATERIALS AND METHODOLOGY***: The study cohort consisted of twenty children with hearing impairment (HI) and 20 age-matched healthy children. The gingival index (GI), plaque index (PI), and salivary pH for all children were assessed at baseline, 15 days after oral hygiene training using visual pedagogy, 15 days after probiotic mouth rinse introduction, and at the end of the test period, i.e., 2 months after discontinuing probiotics. ***STATISTICAL ANALYSIS***: Comparison of means was carried out using the Student's t-test. Intragroup parameters were assessed using the one-way ANOVA, followed by the post hoc Scheffe test. Value for statistical significance was fixed at 0.05. ***RESULTS***: The GI and PI scores did not improve significantly after oral hygiene training in either of the two groups. The use of probiotic mouth rinse significantly reduced GI scores (<0.01) and PI scores (<0.01) and increased salivary pH above the critical pH in both groups. ***CONCLUSION***: The use of visual pedagogy coupled with probiotic mouth rinsing may improve the periodontal status of children with HI and should be explored as a preventive procedure for children with special health-care needs.

Sun, J., Marwah, G., Westgarth, M., Buys, N., Ellwood, D., and Gray, P. H. Effects of Probiotics on Necrotizing Enterocolitis, Sepsis, Intraventricular Hemorrhage, Mortality, Length of Hospital Stay, and Weight Gain in Very Preterm Infants: A Meta-Analysis. Adv.Nutr. 2017; 8(5):749-763; PM: 28916575

ABSTRACT: Probiotics are increasingly used as a supplement to prevent adverse health outcomes in preterm infants. We conducted a systematic review, meta-analysis, and subgroup analysis of findings from randomized controlled trials (RCTs) to assess the magnitude of the effect of the probiotics on health outcomes among very-low-birth-weight (VLBW) infants. Relevant articles from January 2003 to June 2017 were selected from a broad range of databases, including Medline, PubMed, Scopus, and Embase. Studies were included if they used an RCT design, involved a VLBW infant (birthweight <1500 g or gestational age <32 wk) population, included a probiotic intervention group, measured necrotizing enterocolitis (NEC) as a primary outcome, and measured sepsis, mortality, length of hospital stay, weight gain, and intraventricular hemorrhage (IVH) as additional outcomes. The initial database search yielded 132 potentially relevant articles and 32 (n = 8998 infants) RCTs were included in the final meta-analysis. Subgroup analysis was used to evaluate the effects of the moderators on the outcome variables. In the probiotics group, it was found that NEC was reduced by 37% (95% CI: 0.51%, 0.78%), sepsis by 37% (95% CI: 0.72%, 0.97%), mortality by 20% (95% CI: 0.67%, 0.95%), and length of hospital stay by 3.77 d (95% CI: -5.94, -1.60 d). These findings were all significant when compared with the control group. There was inconsistent use of strain types among some of the studies. The results indicate that probiotic consumption can significantly reduce the risk of developing medical complications associated with NEC and sepsis, reduce mortality and length of hospital stay, and promote weight gain in VLBW infants. Probiotics are more effective when taken in breast milk and formula form, consumed for <6 wk, administered with a dosage of <109 CFU/d, and include multiple strains. Probiotics are not effective in reducing the incidence of IVH in VLBW infants.

Sungur, T., Aslim, B., Karaaslan, C., and Aktas, B. Impact of Exopolysaccharides (EPSs) of Lactobacillus gasseri strains isolated from human vagina on cervical tumor cells (HeLa). Anaerobe. 5-26-2017; 47:137-144; PM: 28554813

ABSTRACT: Lactobacilli, commonly used as probiotics, have been shown to maintain vaginal health and contribute to host microbiota interaction. Exopolysaccharides (EPSs) produced by lactobacillus have been found to have an important role in probiotic activity; however, there is limited knowledge concerning their impact on cervical cancer and urogenital health. The objective of this study is to investigate and compare EPSs of L. gasseri strains (G10 and H15), isolated from a healthy human vagina, for their capability to inhibit cervical cancer cell (HeLa) growth and modulate immune response. HeLa cells were treated with live culture at approximately 108 CFU/ml or increasing concentration of lyophilized EPS (L-EPS) (100, 200, or 400 mug/ml) of L. gasseri strains and their ability to adhere to host cells, inhibit proliferation, and modulate immune response were evaluated. Additionally, monosaccharide composition of the L-EPSs produced by L. gasseri strains was determined by HPLC. The sugar component was the same; however, relative proportions of the individual monosaccharides except mannose were different. Although they both produce similar amount of EPS, the most adhesive strain was G10. Both live and L-EPS of L. gasseri strains were capable of inhibiting the cell proliferation of HeLa cells with the impact of L-EPS being strain specific. L-EPSs of L. gasseri strains induced apoptosis in HeLa cells in a strain dependent manner. The ability to induce apoptosis by G10 associated with an upregulation of Bax and Caspase 3. L. gasseri strains showed an anti-inflammatory impact on HeLa cells by decreasing the production of TNF-alpha and increasing the IL-10 production. In conclusion, diversity in sugar composition of EPS might contribute to adhesion and proliferation properties. Although our results suggest a relationship between the ability of a strain to induce apoptosis and its sugar composition of EPS, further research is required to determine the probiotic mechanisms of action by which L. gasseri strains result in strain specific anti-proliferative activity.

Suzuki, Y., Ikeda, K., Sakuma, K., Kawai, S., Sawaki, K., Asahara, T., Takahashi, T., Tsuji, H., Nomoto, K., Nagpal, R., Wang, C., Nagata, S., and Yamashiro, Y. Association between Yogurt Consumption and Intestinal Microbiota in Healthy Young Adults Differs by Host Gender. Front Microbiol. 2017; 8:847; PM: 28553274

ABSTRACT: Human intestinal microbiota are influenced by various factors viz. diet, environment, age, gender, geographical, and socioeconomic situation, etc. among which diet has the most profound impact. However, studies investigating this impact have mostly included subjects from diverse geographic/socioeconomic backgrounds and hence the precise effects of dietary factors on gut microbiota composition remain largely confounded. Herein, with an aim to evaluate the association between dietary habits, specifically yogurt consumption, and the gut microbiota in healthy young adults sharing similar age, lifestyle routine, geographical setting, etc., we conducted a cross-sectional study wherein 293 collegiate freshmen answered a questionnaire about their frequency of yogurt consumption over the last 2 months and provided stool specimens for microbiota analysis. Fecal microbiota were analyzed by highly sensitive reverse-transcription-quantitative-PCR assays targeting bacterial 16S rRNA molecules. Fecal organic acids were measured by HPLC. Overall, the gut microbiota were predominated (97.1 +/- 8.6%) by Clostridium coccoides group, Clostridium leptum subgroup, Bacteroides fragilis group, Bifidobacterium and Atopobium cluster. Interestingly, after adjusting the data for yogurt consumption, females were found to have higher total bacterial ($P = 0.013$) and Bifidobacterium ($P = 0.046$) count and fecal pH ($P = 0.007$) and lower fecal concentration of total organic acids ($P = 0.030$), succinic acid ($P = 0.007$) and formic acid ($P = 0.046$) as compared to males. Altogether, yogurt consumption showed

positive linear association with Lactobacillus and Lactobacillus gasseri subgroup in both male and female subjects; however, several gender-specific disparities were also detected in this yogurt-microbiota association. Yogurt consumption demonstrated a negative association with L. sakei subgroup, Enterobacteriaceae and Staphylococcus in males but shared a positive association with L. casei subgroup and succinic acid in female subjects. The study manifests the association between yogurt consumption and gut microbiota in a healthy homogeneous cohort and show how this association can differ by host gender. The findings should be helpful for prospective studies investigating the diet-microbiome interaction in human health and disease.

Szymanski, H. and Szajewska, H. Efficacy of Lactobacillus Reuteri DSM 17938 for the Treatment of Acute Gastroenteritis in Children: Protocol of a Randomized Controlled Trial. JMIR.Res.Protoc. 8-23-2017; 6(8):e164; PM: 28835355

ABSTRACT: ***BACKGROUND***: Acute gastroenteritis (AGE) is one of the most common diseases among children. Oral rehydration therapy is the key treatment. However, despite proven efficacy, it remains underused. This is because oral rehydration solution neither reduces the frequency of bowel movements and fluid loss nor shortens the duration of illness. Hence, there is interest in adjunctive treatments. According to the 2014 guidelines developed by the European Society for Paediatric Gastroenterology, Hepatology and Nutrition, the use of the following probiotics may be considered in the management of children with AGE in addition to rehydration therapy: Lactobacillus rhamnosus GG (low quality of evidence; strong recommendation) and Saccharomyces boulardii (low quality of evidence; strong recommendation). Less compelling evidence is available for Lactobacillus reuteri DSM 17938 (very low quality of evidence; weak recommendation). ***OBJECTIVE***: Considering that evidence on L reuteri remains limited, the goal of the study is to assess the effectiveness of L reuteri DSM 17938 in the treatment of AGE in children. Children vaccinated and not vaccinated against rotavirus will be evaluated separately. ***METHODS***: This will be a double-blind, placebo-controlled, randomized trial. Children between 1 and 60 months of age with AGE, defined as a change in stool consistency to loose or liquid form (according to the Bristol Stool Form scale or Amsterdam Stool Form scale) and/or an increase in the frequency of evacuations (typically >/=3 in 24 h) lasting for no longer than 5 days, will be recruited. A total of 72 children will receive either L reuteri DSM 17938 at a dose of 2x108colony-forming units twice daily or matching placebo for 5 consecutive days. A similar sample size for rotavirus vaccinated and nonvaccinated children is planned. The primary outcome measure is the duration of diarrhea. Two separate studies and reports for rotavirus vaccinated and nonvaccinated children are planned. ***RESULTS***: The recruitment started in January 2017 and is planned to be finalized in June 2018 for rotavirus nonvaccinated children. The recruitment of rotavirus-vaccinated children may be slower due to a relatively low coverage rate in Poland. Data analysis and submission to a peer-reviewed journal is expected within 3 months after completion of the study. ***CONCLUSION***: This study will add to current knowledge on the efficacy of L reuteri DSM 17938 for the management of AGE. ***TRIAL REGISTRATION***: ClinicalTrials.gov NCT02989350; https://clinicaltrials.gov/ct2/show/NCT02989350 (Archived by WebCite at http://www.webcitation.org/6slOFkyTH).

Tada, H., Masaki, C., Tsuka, S., Mukaibo, T., Kondo, Y., and Hosokawa, R. The effects of Lactobacillus reuteri probiotics combined with azithromycin on peri-implantitis: A randomized placebo-controlled study. J.Prosthodont.Res. 7-26-2017; PM: 28756115

ABSTRACT: ***PURPOSE***: The aim of this randomized placebo-controlled clinical study was to investigate the effects of a probiotic tablet containing Lactobacillus reuteri in peri-implantitis patients. ***METHODS***: Subjects comprised 30 patients with mild to moderate peri-implantitis. A baseline clinical examination and microbiological assessment were conducted, followed by an antibiotics treatment (azithromycin, 500mg, once a day for 3 days). Subjects were divided into probiotic and placebo groups. The clinical examination and bacterial sampling were performed 0, 4, 12 and 24 weeks after the intake of probiotics. The clinical examination included probing pocket depth (PPD), bleeding on probing (BOP), the modified plaque index (mPI), and modified bleeding index (mBI). The number of bacteria was assessed using the PCR-invader method. The Wilcoxon rank-sum test and Wilcoxon signed-rank test with Bonferroni corrections were used for data analyses. ***RESULTS***: Although the number of bacteria decreased after the administration of azithromycin in both groups, they increased again thereafter. No significant difference was observed in bacterial numbers between the two groups. Although PPD in the probiotics group was significantly lower at 4 and 24 weeks than at 0 weeks ($p<0.05$), a significant decrease did not occur in the placebo group. The mBI score at 24 weeks was significantly lower in the probiotics group than in the placebo group ($p<0.05$). No significant difference was observed in BOP or mPI between the two groups. ***CONCLUSION***: These results suggested that probiotics prevent inflammation by affecting host responses rather than improving microbial flora in peri-implant sulci in peri-implantitis patients.

Tao, L., Wang, B., Zhong, Y., Pow, S. H., Zeng, X., Qin, C., Zhang, P., Chen, S., He, W., Tan, Y., Liu, H., Jiang, Y., Chen, W., and Chen, Y. Z. Database and Bioinformatics Studies of Probiotics. J.Agric.Food Chem. 9-6-2017; 65(35):7599-7606; PM: 28727425

ABSTRACT: Probiotics have been widely explored for health benefits, animal cares, and agricultural applications. Recent advances in microbiome, microbiota, and microbial dark matter research have fueled greater interests in and paved ways for the study of the mechanisms of probiotics and the discovery of new probiotics from uncharacterized microbial sources. A probiotics database named PROBIO was developed to facilitate these efforts and the need for the information on the known probiotics, which provides the comprehensive information about the probiotic functions of 448 marketed, 167 clinical trial/field trial, and 382 research probiotics for use or being studied for use in humans, animals, and plants. The potential applications of the probiotics data are illustrated by several literature-reported investigations, which have used the relevant information for probing the function and mechanism of the probiotics and for discovering new probiotics. PROBIO can be accessed free of charge at http://bidd2.nus.edu.sg/probio/homepage.htm.

Tavares Estevam, A. C., de Almeida, M. C., de Oliveira, T. A., Florentino, E. R., onso Buriti, F. C., and Porto, A. L. F. Comparison of dairy desserts produced with a potentially probiotic mixed culture and dispersions obtained from Gracilaria birdiae and Gracilaria domingensis seaweeds used as thickening agents. Food Funct. 7-26-2017; PM: 28745749

ABSTRACT: Dairy desserts have emerged as interesting options for the incorporation of

probiotics, bioactive ingredients and alternative sources of thickeners. This shows an opportunity to investigate the use of Gracilaria seaweeds in the formulation of potentially probiotic dairy desserts. This study aimed to compare the effects of dispersions obtained from Gracilaria domingensis and Gracilaria birdiae used as thickening agents on texture properties of dairy desserts fermented with SAB 440-A, composed of the starter Streptococcus thermophilus and the potential probiotics Bifidobacterium animalis and Lactobacillus acidophilus, and also to study their physicochemical characteristics, microbial viability and sensory acceptability. No significant differences between desserts with G. birdiae or G. domingensis dispersions regarding total solids, ash and fat content, as well as pH, titratable acidity, the viability of the microorganisms of the mixed culture and sensory acceptability were verified ($P > 0.05$). Nonetheless, the dessert with G. domingensis dispersion showed higher dietary fibre content and significantly increased firmness than the one produced with G. birdiae ($P < 0.05$). Moreover, B. animalis was able to maintain higher populations, above 7 log cfu g-1 during 21 days of storage of desserts, in the presence of either G. birdiae or G. domingensis dispersions, despite the fact that L. acidophilus has shown low viability in the final products. Therefore, the G. domingensis dispersion is suitable to be used as a thickening agent to produce dairy desserts with enhanced firmness and good sensory acceptability, it being also advisable to use only B. animalis as a probiotic for this product.

Taverniti, V., Dalla, Via A., Minuzzo, M., Del, Bo' C., Riso, P., Frokiaer, H., and Guglielmetti, S. In vitro assessment of the ability of probiotics, blueberry and food carbohydrates to prevent S. pyogenes adhesion on pharyngeal epithelium and modulate immune responses. Food Funct. 9-11-2017; PM: 28891576

ABSTRACT: Group A streptococci (GAS) cause 20-30% of pediatric pharyngitis episodes, which are a major cause of ambulatory care visits. Therefore, a strategy to prevent GAS dissemination in children could significantly benefit public healthcare. Contextually, we assessed the possibility of employing alternative food-grade strategies to be used with the oral probiotic L. helveticus MIMLh5 for the prevention of pharyngeal infections. First, we demonstrated through an antagonism-by-exclusion assay that guaran may potentially prevent S. pyogenes adhesion on pharyngeal cells. Subsequently, we showed that an anthocyanin-rich fraction extracted from wild blueberry (BbE) exerts anti-inflammatory effects on the human macrophage cell line U937. Finally, we showed that BbE reduces interferon-beta expression in MIMLh5-stimulated murine dendritic cells, resulting in a reduction in the pro-inflammatory cytokines IL-12 and TNF-alpha. In conclusion, this proof-of-concept study indicates that different food-grade strategies may be concomitantly adopted to potentially prevent GAS colonization and modulate local immune defences.

The, H. C., Florez de, Sessions P., Jie, S., Pham, Thanh D., Thompson, C. N., Nguyen Ngoc, Minh C., Chu, C. W., Tran, T. A., Thomson, N. R., Thwaites, G. E., Rabaa, M. A., Hibberd, M., and Baker, S. Assessing gut microbiota perturbations during the early phase of infectious diarrhea in Vietnamese children. Gut Microbes. 8-2-2017; 1-17; PM: 28767339

ABSTRACT: Diarrheal diseases remain the second most common cause of mortality in young children in developing countries. Efforts have been made to explore the impact of diarrhea on bacterial communities in the human gut, but a thorough understanding has been impeded by inadequate resolution in bacterial identification and the examination of only few etiological agents. Here, by profiling an extended region of the 16S rRNA

gene in the fecal microbiome, we aimed to elucidate the nature of gut microbiome perturbations during the early phase of infectious diarrhea caused by various etiological agents in Vietnamese children. Fecal samples from 145 diarrheal cases with a confirmed infectious etiology before antimicrobial therapy and 54 control subjects were analyzed. We found that the diarrheal fecal microbiota could be robustly categorized into 4 microbial configurations that either generally resembled or were highly divergent from a healthy state. Factors such as age, nutritional status, breastfeeding, and the etiology of the infection were significantly associated with these microbial community structures. We observed a consistent elevation of Fusobacterium mortiferum, Escherichia, and oral microorganisms in all diarrheal fecal microbiome configurations, proposing similar mechanistic interactions, even in the absence of global dysbiosis. We additionally found that Bifidobacterium pseudocatenulatum was significantly depleted during dysenteric diarrhea regardless of the etiological agent, suggesting that further investigations into the use of this species as a dysentery-orientated probiotic therapy are warranted. Our findings contribute to the understanding of the complex influence of infectious diarrhea on gut microbiome and identify new opportunities for therapeutic interventions.

Therio, S. R., Dadone, L. I., Garner, M. M., Arble, J., Lalonde, C. J., Baesl, T. J., Siegel, M., Marta, J. A., Pikaart, D. P., and Johnston, M. S. SUCCESSFUL MANAGEMENT OF CECAL PERFORATION AND FOCAL PERITONITIS IN A GORILLA (GORILLA GORILLA GORILLA). J.Zoo.Wildl.Med. 2017; 48(2):540-543; PM: 28749298

ABSTRACT: An 18-yr-old female Western lowland gorilla (Gorilla gorilla gorilla) presented with acute-onset severe lethargy, bloody vaginal discharge, decreased appetite, and an abnormal posture. The gorilla was diagnosed with a ruptured cecal blind sac with severe adhesions to the right ovary. A typhlectomy and unilateral ovariectomy were performed. Histologic examination identified a severe transmural circumferential typhlitis with rupture and adhesions to the infundibulum and chronic typhlitis. Postoperative management included antibiotics, analgesics, short-term dietary modifications, and probiotics for suspect oral candidiasis. The gorilla made a full clinical recovery and was pregnant within 1 yr of surgery. To the authors' knowledge, this is the first case of successful management of typhlitis in a gorilla. Typhlitis and intestinal rupture should be considered as a differential diagnosis for acute onset severe abdominal pain in gorillas.

Thongaram, T., Hoeflinger, J. L., Chow, J., and Miller, M. J. Human milk oligosaccharide consumption by probiotic and human-associated bifidobacteria and lactobacilli. J.Dairy Sci. 8-2-2017; PM: 28780103

ABSTRACT: Human milk contains high concentrations of nondigestible complex oligosaccharides (human milk oligosaccharides; HMO) that reach the colon and are subsequently fermented by the infant gut microbiota. Using a high-throughput, low-volume growth determination, we evaluated the ability of 12 lactobacilli and 12 bifidobacteria strains, including several commercial probiotics, to ferment HMO and their constituent monomers. Of the 24 strains tested, only Bifidobacterium longum ssp. infantis ATCC 15697 and Bifidobacterium infantis M-63 were able to ferment 3'-sialyllactose, 6'-sialyllactose, 2'-fucosyllactose, and 3'-fucosyllactose. Bifidobacterium infantis M-63 degraded almost 90% of the 2'-fucosyllactose but left most of the fucose in the supernatant, as detected by HPLC. Among bifidobacteria, only the B. infantis strains and Bifidobacterium breve ATCC 15700 were able to ferment lacto-N-neotetraose (LNnT). Among lactobacilli, Lactobacillus acidophilus NCFM was found to be the most efficient

at utilizing LNnT. The extracellular beta-galactosidase (lacL, LBA1467) of L. acidophilus NCFM cleaves the terminal galactose of LNnT for growth, leaving lacto-N-triose II in the media as detected by HPLC. Inactivation of lacL abolishes growth of L. acidophilus NCFM on LNnT. These results contribute to our knowledge of HMO-microbe interactions and demonstrate the potential for synbiotic combinations of pre- and probiotics.

Tian, H., Shen, Y., Yu, H., He, Y., and Chen, C. Effects of 4 Probiotic Strains in Coculture with Traditional Starters on the Flavor Profile of Yogurt. J.Food Sci. 2017; 82(7):1693-1701; PM: 28598540

ABSTRACT: To study the influence of probiotics on the flavor profile of yogurt, 4 probiotics, including Lactobacillus acidophilus, Lactobacillus plantarum, Lactobacillus rhamnosus, and Lactobacillus casei, were cofermented with traditional starters. The changes of bacterial growth, acid contents and volatile compounds of yogurt were investigated during fermentation and refrigerated storage. The strains that exhibited a low growth rate in milk did not significantly affect the bacterial population dynamics, acidity, or organic acid content during fermentation and storage. However, high viability and enhancement of postacidification were clearly observed in the samples that contained strains with a high growth rate in milk, particularly L. casei. A total of 45 volatile compounds, detected in most samples, were identified by headspace solid-phase micro-extraction followed by gas chromatography-mass spectrometry. Among these compounds, ketones and aldehydes were the most abundant. The presence of either L. rhamnosus or L. plantarum did not significantly affect the major volatile compounds, while contributions of L. casei and L. acidophilus were found in the formation of minor volatile metabolites. Electronic nose measurements exhibited a good discrimination of samples that contained different probiotics during refrigerated storage.

Tiani, K. A., Yeung, T. W., McClements, D. J., and Sela, D. A. Extending viability of Lactobacillus plantarum and Lactobacillus johnsonii by microencapsulation in alginate microgels. Int.J.Food Sci.Nutr. 7-6-2017; 1-10; PM: 28683582

ABSTRACT: ***AIM***: To investigate whether microencapsulation of Lactobacillus in alginate microbeads will lead to increased longevity during refrigerated storage or simulated digestion. ***MATERIALS AND METHODS***: Microscopy was used to confirm that Lactobacillus plantarum ATCC BAA-793 and Lactobacillus johnsonii ATCC 33200 were immobilised within the microbeads and laser scattering analysis was used to determine the mean diameter of the microbeads. The number of viable cells were enumerated throughout refrigerated storage and simulated digestion experiments. ***RESULTS***: Microencapsulation was shown to have differing effects on viability depending on the species, but led to extended viability during refrigerated storage and simulated digestion in L. johnsonii and L. plantarum respectively. ***CONCLUSION***: Fermented functional foods contain microbes beneficial to human health. However, extended shelf storage and the harsh environment of the GI tract significantly reduces the number of viable microbes reaching the consumer. Microencapsulation allows beneficial microbes to reach the gut of the consumer in higher numbers, and thus confer greater health benefits.

Tidjani, Alou M., Million, M., Traore, S. I., Mouelhi, D., Khelaifia, S., Bachar, D., Caputo, A., Delerce, J., Brah, S., Alhousseini, D., Sokhna, C., Robert, C., Diallo, B. A., Diallo, A., Parola, P., Golden, M., Lagier, J. C., and Raoult, D. Gut Bacteria Missing in Severe Acute Malnutrition,

Can We Identify Potential Probiotics by Culturomics? Front Microbiol. 2017; 8:899; PM: 28588566

ABSTRACT: Severe acute malnutrition is the world-leading cause of children under-five's death. Recent metagenomics studies have established a link between gut microbiota and severe acute malnutrition, describing an immaturity with a striking depletion in oxygen-sensitive prokaryotes. Amoxicillin and therapeutic diet cure most of the children with severe acute malnutrition but an irreversible disruption of the gut microbiota is suspected in the refractory and most severe cases. In these cases, therapeutic diet may be unable to reverse the microbiota alteration leading to persistent impaired development or death. In addition, as enteric sepsis is a major cause of death in this context, identification of missing gut microbes to be tested as probiotics (live bacteria that confer a benefit to the host) to restore rapidly the healthy gut microbiota and prevent the gut pathogenic invasion is of foremost importance. In this study, stool samples of malnourished patients with kwashiorkor and healthy children were collected from Niger and Senegal and analyzed by culturomics and metagenomics. We found a globally decreased diversity, a decrease in the hitherto unknown diversity (new species isolation), a depletion in oxygen-sensitive prokaryotes including Methanobrevibacter smithii and an enrichment in potentially pathogenic Proteobacteria, Fusobacteria and Streptococcus gallolyticus. A complex of 12 species identified only in healthy children using culturomics and metagenomics were identified as probiotics candidates, providing a possible, defined, reproducible, safe, and convenient alternative to fecal transplantation to restore a healthy gut microbiota in malnourished children. Microbiotherapy based on selected strains has the potential to improve the current treatment of severe acute malnutrition and prevent relapse and death by reestablishing a healthy gut microbiota.

Toh, M. and Liu, S. Q. Influence of commercial inactivated yeast derivatives on the survival of probiotic bacterium Lactobacillus rhamnosus HN001 in an acidic environment. AMB.Express. 2017; 7(1):156; PM: 28747041

ABSTRACT: This study evaluated the influence of three inactivated yeast derivatives (IYDs) used in wine production, namely OptiRed(R), OptiWhite(R) and Noblesse(R), on the viability of the probiotic strain Lactobacillus rhamnosus HN001 in an acidic environment. Addition of the IYDs at 3 g/L significantly enhanced the survival of the probiotic bacteria by 2.75-4.05 log cycles after 10-h exposure in a pH 3.0 buffer. Acid stress assay with IYD components obtained after centrifugation and filtration revealed that water-soluble compounds were responsible for improving the acid tolerance of L. rhamnosus HN001 for all three preparations. Differences in protective effect amongst the IYDs on L. rhamnosus HN001 were observed when permeates and retentates of the water-soluble extracts, obtained through ultrafiltration with a 2 kDa membrane, were assayed against the lactic acid bacterium. Chemical analysis of the water-soluble components suggests that low molecular weight polysaccharides, specific free amino acids and/or antioxidants in the 2 kDa permeates could have contributed to the enhanced survival of L. rhamnosus HN001 during acid stress. The contrast amongst the 2 kDa retentates' viability enhancing property may have been attributed to the differences in size and structure of the higher molecular weight carbohydrates and proteins, as the survival of the probiotic did not relate to the concentration of these compounds. These results suggests that oenological IYDs could potentially be applied to probiotic foods for enhancing the acid tolerance of the beneficial microorganisms, and consequently prolonging the shelf life of these products.

Toh, S. L., Boswell-Ruys, C. L., Lee, B. S. B., Simpson, J. M., and Clezy, K. R. Probiotics for preventing urinary tract infection in people with neuropathic bladder. Cochrane.Database.Syst.Rev. 9-8-2017; 9:CD010723; PM: 28884476

ABSTRACT: ***BACKGROUND***: Neuropathic or neurogenic bladder describes a process of dysfunctional voiding as the result of injury in the brain, spinal cord or nerves innervating the bladder. People with neuropathic bladder, such as from spinal cord injury (SCI), are at significant risk of morbidity from urinary tract infections (UTI). Effective methods to prevent UTI in people with SCI have been sought for many years. Probiotics (micro-organisms that exert beneficial health effects in the host) have been recommended for bacterial interference of the urological tract to reduce colonisation by uropathogen and to manage the dual problems of infection and antibiotic resistance. ***OBJECTIVES***: This review looked at the benefits and harms of probiotics in preventing symptomatic UTI in people with neuropathic bladder compared with placebo, no therapy, or non-antibiotic prophylaxis (cranberry juice, methenamine hippurate, topical oestrogen). ***SEARCH METHODS***: We searched the Cochrane Kidney and Transplant Specialised Register up to 10 March 2017 through contact with the Information Specialist using search terms relevant to this review. Studies in the Specialised Register are identified through searches of CENTRAL, MEDLINE, and EMBASE, conference proceedings, the International Clinical Trials Register (ICTRP) Search Portal, and ClinicalTrials.gov. ***SELECTION CRITERIA***: All randomised controlled trials (RCTs), quasi-RCTs and cross-over RCTs looking at the use of probiotics for the prophylaxis of UTI in people with neuropathic bladders was considered for inclusion. Men, women and children of all ages with neuropathic bladders from neurological injury such as suprapontine, supra sacral and sacral aetiologies was included. All bladder management types, including reflex voiding, time voiding, indwelling and intermittent catheterization were eligible for this review.Studies comparing probiotics to placebo, no treatment or other non-antibiotic prophylaxis was included. Studies comparing probiotics with antibiotics or in combination with antibiotics were excluded. ***DATA COLLECTION AND ANALYSIS***: Summary estimates of effect were obtained using a random-effects model, and results were expressed as risk ratios (RR) and their 95% confidence intervals (CI) for dichotomous outcomes, and mean difference (MD) or standardised mean difference (SMD) and 95% CI were planned for continuous outcomes. ***MAIN RESULTS***: This review includes a total of three studies (one cross-over and two parallel RCTs) which involved 110 participants. All three studies looked at intravesical instillation of a low virulent Escherichia coli (E. coli) strain in reducing the risk of symptomatic UTI in participants with neuropathic bladder, predominantly from SCI. Two studies used the E. coli 83972 strain and one study used the E. coli HU2117 strain.We did not find any RCTs involving other probiotics or other routes of administration for preventing UTI in people with neuropathic bladder.There was consistency in definition of symptomatic UTI in all three studies. Symptoms that all studies considered were relevant to diagnose UTI were adequately defined. All three studies defined microbiological diagnosis of symptomatic UTI.Asymptomatic bacteriuria was not considered an outcome measure in any of the included studies; however it was defined in two studies to establish successful inoculation.It is uncertain if the risk of symptomatic UTI is reduced with bladder inoculation using E. coli because the certainty of the evidence is very low (3 studies, 110 participants: RR 0.32, 95% CI 0.08 to 1.19; I2 = 82%).Two studies reported adverse events. One study reported one episode of autonomic dysreflexia. One study reported three symptomatic UTI occurring in two patients, and two studies mentioned the absence of septicaemia and pyelonephritis. Intravesical instillation was reported as "generally safe". One study reported high attrition rates in participants due to the need to adhere to strict instillation protocols.The overall quality of the studies was poor. All three studies had high

risk of attrition bias due to failure of an intention-to-treat analysis which undermines the randomisation process and weakened the results of the studies. All three studies also had high risk of reporting bias. ***AUTHORS' CONCLUSIONS***: In this review, there were no studies identified addressing oral probiotics in preventing UTI in people with neuropathic bladder. It is uncertain if the risk of symptomatic UTI is reduced in people with neuropathic bladders via intravesical instillation of non-pathogenic E. coli as data were derived from small studies with high risk of bias.Although very minimal levels of harm was reported with this procedure, due to variable success rates, the need for strict adherence to instillation protocols together with high attrition rates in these studies, it is doubtful bladder instillation will be a widely accepted intervention in its current form.It is recommended that further appropriately powered RCTs with more robust methodological reporting be carried out.

Tomlinson, J. A. P. and Wheeler, D. C. The role of trimethylamine N-oxide as a mediator of cardiovascular complications in chronic kidney disease. Kidney Int. 8-11-2017; PM: 28807612

ABSTRACT: Patients with chronic kidney disease (CKD) have an enhanced risk of cardiovascular (CV) morbidity and mortality when compared with age- and gender-matched individuals with normal kidney function. Trimethlyamine N-oxide (TMAO) is a gut-derived amine oxide that has been implicated in the causation of CV diseases. Plasma TMAO is cleared by the kidney, and TMAO levels are elevated in CKD. Experimental studies have identified pathogenic mechanisms by which TMAO may contribute to CV disease through dysregulation of lipid metabolism, enhanced macrophage foam cell formation, and platelet dysfunction. Safe and well-tolerated therapeutic interventions such as pre- and probiotics, which modify the gut microbiome, offer the opportunity for interventional studies. This review examines the pathogenicity of TMAO, its value as a biomarker, and its potential as a therapeutic target in the context of CKD.

Toscano, M., De, Grandi R., Pastorelli, L., Vecchi, M., and Drago, L. A consumer's guide for probiotics: 10 golden rules for a correct use. Dig.Liver Dis. 8-1-2017; PM: 28830747

ABSTRACT: Probiotics are used all over the world as their beneficial effects on the human organism have been widely demonstrated. Certain probiotics can down-regulate production of pro-inflammatory cytokines and promote intestinal epithelial barrier functions, increasing an anti-inflammatory response and contributing to the host's overall health. The main mechanisms by which probiotic microorganisms can interact with the host are by modulating the immune system and the epithelial cell functions and interacting with intestinal gut microbiota. To date, hundreds of different microorganisms are used for the formulation of numerous probiotic products; therefore, it is very difficult to choose the best probiotic product for specific or more general needs. Therefore, physicians are getting more and more confused due to the high number of commercial products which are often lacking healthy effects on the host. Therefore, the aim of this paper is to demonstrate the main characteristics that probiotic microorganisms and products should possess to have a positive impact on the host's health. To this purpose, this review suggests "10 golden rules" or "commandments" that clinicians should follow to properly select the optimal probiotic product and avoid misidentifications, mislabelling and "pie in the sky" stories.

Tremellen, K. and Pearce, K. Probiotics to improve testicular function (Andrology 5:439-444, 2017) - a comment on mechanism of action and therapeutic potential of probiotics beyond reproduction. Andrology. 2017; 5(5):1052-1053; PM: 28914502

No Abstract Available.

Tse, J. K. Y. Gut Microbiota, Nitric Oxide, and Microglia as Prerequisites for Neurodegenerative Disorders. ACS Chem.Neurosci. 7-19-2017; 8(7):1438-1447; PM: 28640632

ABSTRACT: Regulating fluctuating endogenous nitric oxide (NO) levels is necessary for proper physiological functions. Aberrant NO pathways are implicated in a number of neurological disorders, including Alzheimer's disease (AD) and Parkinson's disease. The mechanism of NO in oxidative and nitrosative stress with pathological consequences involves reactions with reactive oxygen species (e.g., superoxide) to form the highly reactive peroxynitrite, hydrogen peroxide, hypochloride ions and hydroxyl radical. NO levels are typically regulated by endogenous nitric oxide synthases (NOS), and inflammatory iNOS is implicated in the pathogenesis of neurodegenerative diseases, in which elevated NO mediates axonal degeneration and activates cyclooxygenases to provoke neuroinflammation. NO also instigates a down-regulated secretion of brain-derived neurotrophic factor, which is essential for neuronal survival, development and differentiation, synaptogenesis, and learning and memory. The gut-brain axis denotes communication between the enteric nervous system (ENS) of the GI tract and the central nervous system (CNS) of the brain, and the modes of communication include the vagus nerve, passive diffusion and carrier by oxyhemoglobin. Amyloid precursor protein that forms amyloid beta plaques in AD is normally expressed in the ENS by gut bacteria, but when amyloid beta accumulates, it compromises CNS functions. Escherichia coli and Salmonella enterica are among the many bacterial strains that express and secrete amyloid proteins and contribute to AD pathogenesis. Gut microbiota is essential for regulating microglia maturation and activation, and activated microglia secrete significant amounts of iNOS. Pharmacological interventions and lifestyle modifications to rectify aberrant NO signaling in AD include NOS inhibitors, NMDA receptor antagonists, potassium channel modulators, probiotics, diet, and exercise.

Tunapong, W., Apaijai, N., Yasom, S., Tanajak, P., Wanchai, K., Chunchai, T., Kerdphoo, S., Eaimworawuthikul, S., Thiennimitr, P., Pongchaidecha, A., Lungkaphin, A., Pratchayasakul, W., Chattipakorn, S. C., and Chattipakorn, N. Chronic treatment with prebiotics, probiotics and synbiotics attenuated cardiac dysfunction by improving cardiac mitochondrial dysfunction in male obese insulin-resistant rats. Eur.J.Nutr. 6-12-2017; PM: 28608320

ABSTRACT: ***PURPOSE***: In metabolic syndrome, the composition of gut microbiota has been disrupted, and is associated with left ventricular (LV) dysfunction. Several types of prebiotics, probiotics, and synbiotics have been shown to exert cardioprotection by restoring gut microbiota from dysbiosis and reducing systemic inflammation. However, the effects of prebiotics such as xylooligosaccharides (XOS); probiotics such as Lactobacillus paracasei STII01 HP4, and synbiotics on metabolic and LV function in obese insulin-resistant rats have not been investigated. In this study, we hypothesized that prebiotics and probiotics improve metabolic parameters, heart rate variability (HRV), blood pressure (BP), and LV function by attenuating cardiac mitochondrial dysfunction,

systemic inflammation, and oxidative stress, and that synbiotics provide greater efficacy than a single regimen in obese insulin resistance. ***METHODS***: Rats were fed with either normal diet or high-fat diet (HFD) for 12 weeks and then rats in each dietary group were randomly subdivided into four subgroups to receive either a vehicle, prebiotics, probiotics, or synbiotics for another 12 weeks. Metabolic parameters, BP, HRV, LV function, cardiac mitochondrial function, systemic inflammation, and oxidative stress were determined. ***RESULTS***: HFD-fed rats had obese insulin resistance with markedly increased systemic inflammatory marker [Serum LPS; ND; 0.6 +/- 0.1 EU/ml vs. HFD; 5.7 +/- 1.2 EU/ml ($p < 0.05$)], depressed HRV, and increased BP and LV dysfunction [%ejection fraction; ND; 93 +/- 2% vs. HFD; 83 +/- 2% ($p < 0.05$)]. Prebiotics, probiotics, and synbiotics attenuated insulin resistance by improving insulin sensitivity and lipid profiles. All interventions also improved HRV, BP, LV function [%ejection fraction; HFV; 81 +/- 2% vs. HFPE; 93 +/- 3%, HFPO; 92 +/- 1%, HFC; 92 +/- 2% ($p < 0.05$)] by attenuating mitochondrial dysfunction, oxidative stress, and systemic inflammation in obese insulin-resistant rats. ***CONCLUSION***: Prebiotics, probiotics, and synbiotics shared similar efficacy in reducing insulin resistance and LV dysfunction in obese insulin-resistant rats.

Uchiyama-Tanaka, Y. Case Study of Homeopathic Bowel Nosode Remedies for Dysbiotic Japanese Patients. J.Altern.Complement Med. 8-14-2017; PM: 28805460

ABSTRACT: ***BACKGROUND***: The composition of intestinal microbiota is very important in human health. Gastrointestinal disturbances are among the symptoms commonly reported by individuals diagnosed with chronic diseases, such as inflammatory bowel disease, autism, and chronic fatigue syndrome. The effects of probiotics and prebiotics for dysbiosis have been reported in many studies. Bowel nosodes are homeopathic remedies made from human gut microbiota. ***OBJECTIVE***: Bowel nosodes made from the intestinal bacteria of European patients from the 1900s were administered to Japanese patients suffering from gastrointestinal disturbances, such as constipation and diarrhea, to determine their therapeutic efficacy. ***METHODS***: Twenty-eight outpatients from Yoko Clinic (11 males, 17 females; age range, 4-72 years) were enrolled in this study. One nosode remedy was selected for each case. Patients took six pills for 2 days. After a month, the effect of each treatment was evaluated using the Glasgow Homeopathic Hospital Outcome Scale (grade +4 to -4). ***RESULTS***: Patient number of each grade was +4 (N = 2), +3 (N = 4), +2 (N = 7), +1 (N = 3), 0 (N = 7), with no negative grades. Of the 23 patients analyzed, 69.6% showed some type of improvement, and no harmful effects from taking bowel nosodes were observed; 26% of patients showed major improvement or were "cured." ***CONCLUSION***: It is difficult to find correct constitutional remedies as they often require high-level techniques and time. Since there are only 11 main bowel nosode remedies, they are easier to choose from and cheaper to use and develop than classical constitutional remedies. Herein, 69.6% of dysbiotic patients taking bowel nosodes showed improvements, and no harmful effects were reported by any patient. These results suggest that the homeopathic bowel nosodes are a useful method for controlling gastrointestinal disturbances.

Van, Raay T. and Ien-Vercoe, E. Microbial Interactions and Interventions in Colorectal Cancer. Microbiol.Spectr. 2017; 5(3); PM: 28643625

ABSTRACT: Recently, several lines of evidence that indicate a strong link between the development of colorectal cancer (CRC) and aspects of the gut microbiota have become apparent. However, it remains unclear how changes in the gut microbiota

might influence carcinogenesis or how regional organization of the gut might influence the microbiota. In this review, we discuss several leading theories that connect gut microbial dysbiosis with CRC and set this against a backdrop of what is known about proximal-distal gut physiology and the pathways of CRC development and progression. Finally, we discuss the potential for gut microbial modulation therapies, for example, probiotics, antibiotics, and others, to target and improve gut microbial dysbiosis as a strategy for the prevention or treatment of CRC.

Vandenplas, Y. Prevention and Management of Cow's Milk Allergy in Non-Exclusively Breastfed Infants. Nutrients. 7-10-2017; 9(7); PM: 28698533

ABSTRACT: ***Introduction***: The prevention and management of cow milk allergy (CMA) is still debated. Since CMA is much less frequent in breastfed infants, breastfeeding should be stimulated. Method: Literature was searched using databases to find original papers and reviews on this topic. ***Results***: Hydrolysates with a clinical proof of efficacy are recommended in the prevention and treatment of CMA. However, not all meta-analyses conclude that hydrolysates do prevent CMA or other atopic manifestations such as atopic dermatitis. There are pros and cons to consider partially hydrolysed protein as an option for starter infant formula for each non-exclusively breastfed infant. A challenge test is still recommended as the most specific and sensitive diagnostic test, although a positive challenge test does not proof that the immune system is involved. The Cow Milk Symptom Score (CoMiSS) is an awareness tool that enables healthcare professionals to better recognize symptoms related to the ingestion of cow milk, but it still needs validation as diagnostic tool. The current recommended elimination diet is a cow milk based extensive hydrolysate, although rice hydrolysates or soy infant formula can be considered in some cases. About 10 to 15% of infants allergic to cow milk will also react to soy. Mainly because of the higher cost, amino acid based formula is reserved for severe cases. There is no place for infant formula with intact protein from other animals as cross-over allergenicity is high. During recent years, attention focused also on the bifidogenic effect of prebiotics and more recently also on human milk oligosaccharides. A bifidogenic gastrointestinal microbiome may decrease the risk to develop allergic disease. The addition of probiotics and prebiotics to the elimination diet in treatment may enhance the development of tolerance development. ***Conclusion***: Breastfeeding is the best way to feed infants. Cow milk based extensive hydrolysates remain the first option for the treatment of CMA for the majority of patients, while amino acid formulas are reserved for the most severe cases. Rice hydrolysates and soy infant formula are second choice options. Partial hydrolysates with clinical proof of efficacy are recommended in some guidelines in the prevention of CMA and allergic disease in at risk infants, and may be considered as an option as protein source in starter infant formula.

Vazquez, G. H., Camino, S., Tondo, L., and Baldessarini, R. J. Potential Novel Treatments for Bipolar Depression: Ketamine, Fatty Acids, Anti-inflammatory Agents, and Probiotics. CNS.Neurol.Disord.Drug Targets. 7-28-2017; PM: 28758582

ABSTRACT: ***BACKGROUND***: Treatments for depression in bipolar disorder (BD) are far less well developed than for unipolar major depressive disorder. Several innovative and experimental approaches have been emerging recently, including use of the dissociative anesthetic ketamine and other antagonists of central NMDA glutamate receptors, as well as unsaturated fatty acids, anti-inflammatory agents, and possibly probiotic methods. ***METHODS***: We reviewed relevant reports from the past decade.

FINDINGS: Ketamine, a phencyclidine-like NMDA-glutamate receptor antagonist, has emerged as a highly innovative, experimental treatment for treatment-resistant unipolar major depression, possibly in bipolar depression, and with brief antisuicidal effects. Its limitations include poor bioavailability, rapid but short-lived effects, and little information about long-term benefits and safety of repeated administration. Polyunsaturated fatty acids critical for the structure and functioning of neuronal and other cell membranes have some evidence of benefit as experimental treatments for depression including in BD. There also is evidence of altered expression of peptides associated with inflammation in mood disorder patients, encouraging experimental treatment with anti-inflammatory agents; of these, the COX-II inhibitor celecoxib has shown some evidence of benefit. The concept of altering intestinal flora with probiotic treatments to treat mood disorders remains speculative. ***CONCLUSIONS***: Ketamine represents an innovative, rapidly acting, experimental treatment for bipolar depression with practical limitations. Unsaturated fatty acids and anti-inflammatory agents have inconsistent support; probiotic treatments lack evidence. These innovative approaches require much more clinical investigation.

Vena, G. A., Maurer, M., Cassano, N., and Zuberbier, T. Alternative treatments for chronic spontaneous urticaria beyond the guideline algorithm. Curr.Opin.Allergy Clin.Immunol. 2017; 17(4):278-285; PM: 28537934

ABSTRACT: ***PURPOSE OF REVIEW***: The international EAACI/GALEN/EDF/WAO guideline suggests a stepwise approach for the therapeutic management of chronic spontaneous urticaria (CSU), outlined in an algorithm. The aim of this article is to summarize and review the evidence available on alternative treatment options for CSU outside of this algorithm. ***RECENT FINDINGS***: Although CSU is a common disease, there are a limited number of high-quality studies, and only antihistamines and omalizumab are licensed for its treatment. Most studies regarding alternative therapies for CSU show methodological limitations and a high risk of bias. For many therapies, only case reports and uncontrolled studies exist. Recent publications on alternative treatments for chronic urticaria/CSU include reports on the use of adalimumab, rituximab, vitamin D, probiotics, histaglobulin, injection of autologous whole blood or serum, and phototherapy. ***SUMMARY***: Numerous treatments beyond the guideline algorithm have been evaluated in patients with refractory CSU. The global level of evidence to support their efficacy in CSU is low or very low. Further research is needed to assess the efficacy and safety of alternative therapies of CSU to manage adequately those patients who do not respond to the treatments included in the algorithm.

Venkatasubramanian, P. B., Toydemir, G., de, Wit N., Saccenti, E., Martins, Dos Santos, V, van, Baarlen P., Wells, J. M., Suarez-Diez, M., and Mes, J. J. Use of Microarray Datasets to generate Caco-2-dedicated Networks and to identify Reporter Genes of Specific Pathway Activity. Sci.Rep. 7-28-2017; 7(1):6778; PM: 28755007

ABSTRACT: Intestinal epithelial cells, like Caco-2, are commonly used to study the interaction between food, other luminal factors and the host, often supported by microarray analysis to study the changes in gene expression as a result of the exposure. However, no compiled dataset for Caco-2 has ever been initiated and Caco-2-dedicated gene expression networks are barely available. Here, 341 Caco-2-specific microarray samples were collected from public databases and from in-house experiments pertaining to Caco-2 cells exposed to pathogens, probiotics and several food compounds. Using these datasets, a gene functional association network specific

for Caco-2 was generated containing 8937 nodes 129711 edges. Two in silico methods, a modified version of biclustering and the new Differential Expression Correlation Analysis, were developed to identify Caco-2-specific gene targets within a pathway of interest. These methods were subsequently applied to the AhR and Nrf2 signalling pathways and altered expression of the predicted target genes was validated by qPCR in Caco-2 cells exposed to coffee extracts, known to activate both AhR and Nrf2 pathways. The datasets and in silico method(s) to identify and predict responsive target genes can be used to more efficiently design experiments to study Caco-2/intestinal epithelial-relevant biological processes.

Vientos-Plotts, A. I., Ericsson, A. C., Rindt, H., and Reinero, C. R. Oral Probiotics Alter Healthy Feline Respiratory Microbiota. Front Microbiol. 2017; 8:1287; PM: 28744273

ABSTRACT: Probiotics have been advocated as a novel therapeutic approach to respiratory disease, but knowledge of how oral administration of probiotics influences the respiratory microbiota is needed. Using 16S rRNA amplicon sequencing of bacterial DNA our objective was to determine whether oral probiotics changed the composition of the upper and lower airway, rectal, and blood microbiota. We hypothesized that oral probiotics would modulate the respiratory microbiota in healthy cats, demonstrated by the detection and/or increased relative abundance of the probiotic bacterial species and altered composition of the microbial population in the respiratory tract. Six healthy young research cats had oropharyngeal (OP), bronchoalveolar lavage fluid (BALF), rectal, and blood samples collected at baseline and 4 weeks after receiving oral probiotics. 16S rRNA gene amplicon libraries were sequenced, and coverage, richness, and relative abundance of representative operational taxonomic units (OTUs) were determined. Hierarchical and principal component analyses (PCA) demonstrated relatedness of samples. Mean microbial richness significantly increased only in the upper and lower airways. The number of probiotic OTUs (out of 5 total) that significantly increased in relative abundance vs. baseline was 5 in OP, 3 in BAL and 2 in feces. Using hierarchical clustering, BALF and blood samples grouped together after probiotic administration, and PERMANOVA supported that these two sites underwent significant changes in microbial composition. PERMANOVA revealed that OP and rectal samples had microbial population compositions that did not significantly change. These findings were visualized via PCA, which revealed distinct microbiomes in each site; samples clustered more tightly at baseline and had more variation after probiotic administration. This is the first study describing the effect of oral probiotics on the respiratory microbiota via detection of probiotic species in the airways. Finding bacterial species present in the oral probiotics in the upper and lower airways provides pilot data suggesting that oral probiotics could serve as a tool to target dysbiosis occurring in inflammatory airway diseases such as feline asthma, a disease in which cats serve as an important comparative and translational model for humans.

Walter, J., Maldonado-Gomez, M. X., and Martinez, I. To engraft or not to engraft: an ecological framework for gut microbiome modulation with live microbes. Curr.Opin.Biotechnol. 8-31-2017; 49:129-139; PM: 28866242

ABSTRACT: Strategies aimed at modulating the gut microbiota by using live microbes range from single strains (probiotics or live biotherapeutics) to whole non-defined fecal transplants. Although often clinically efficacious, our understanding on how microbial-based strategies modulate gut microbiome composition and function is vastly

incomplete. In this review, we present a framework based on ecological theory that provides mechanistic explanations for the findings obtained in studies that attempted to modulate the gut microbiota of humans and animals using live microbes. We argue that an ecological perspective grounded in theory is necessary to interpret and predict the impact of microbiome-modulating strategies and thus advance our ability to develop improved and targeted approaches with enhanced therapeutic efficiency.

Wang, F., Feng, J., Chen, P., Liu, X., Ma, M., Zhou, R., Chang, Y., Liu, J., Li, J., and Zhao, Q. Probiotics in Helicobacter pylori eradication therapy: Systematic review and network meta-analysis. Clin.Res.Hepatol.Gastroenterol. 2017; 41(4):466-475; PM: 28552432

ABSTRACT: ***BACKGROUND***: Several probiotics were effective in the eradication treatment for Helicobacter pylori (Hp), but their comparative efficacy was unknown. AIM: To compare the efficacy of different probiotics when supplemented in Hp eradication therapy. ***METHODS***: A comprehensive search was conducted to identify all relevant studies in multiple databases and previous meta-analyses. Bayesian network meta-analysis was performed to combine direct and indirect evidence and estimate the relative effects. ***RESULTS***: One hundred and forty studies (44 English and 96 Chinese) were identified with a total of 20,215 patients, and more than 10 probiotic strategies were supplemented in Hp eradication therapy. The rates of eradication and adverse events were 84.1 and 14.4% in probiotic group, while 70.5 and 30.1% in the control group. In general, supplementary probiotics were effective in improving the efficacy of Hp eradication and decreasing the incidence of adverse events, despite of few ineffective subtypes. In triple eradication therapy, there was no significant difference among the effective probiotics, and combined probiotics did not show a better efficacy and tolerance than single use. In triple therapy of 7 days and 14 days, Lactobacillus acidopilus was a slightly better choice, while Saccharomyces boulardii was more applicable for 10-day triple therapy. ***CONCLUSIONS***: Compared to placebo, most probiotic strategies were effective when supplemented in Hp eradication therapy. In triple eradication therapy, no probiotic showed a superior efficacy to the others. Compared to single use, combined probiotics could not improve the efficacy or tolerance significantly.

Wang, G., Li, X., Zhao, J., Zhang, H., and Chen, W. Lactobacillus casei CCFM419 attenuates type 2 diabetes via a gut microbiota dependent mechanism. Food Funct. 8-7-2017; PM: 28782784

ABSTRACT: Probiotics, as dietary supplements, transmit their major effects through the regulation of gut microbiota. According to a previous study, one possible mechanism of Lactobacillus casei CCFM419 protection against diabetes may involve gut flora. To test this hypothesis, high fat and streptozotocin-induced C57BL/6J mice were fed L. casei CCFM419 at 108, 109, and 1010 colony forming units (CFU). Compared to untreated mice, 109 CFU of L. casei CCFM419 attenuated several symptoms of diabetes, including fasting blood glucose, postprandial blood glucose, glucose intolerance, and insulin resistance. In addition, this CFU level also decreased the levels of the inflammatory markers tumor necrosis factor-alpha and interleukin-6 and increased intestinal glucagon-like peptide-1 (GLP-1) levels, which are associated with the production of short chain fatty acids (SCFAs). The 16S rRNA gene sequencing of fecal samples demonstrated that 109 CFU of L. casei CCFM419 dramatically increased the abundance of Bacteroidetes and decreased the proportion of Firmicutes at the phylum level, and enriched

Bifidobacterium, Lactobacillus, and SCFA-producing bacteria, including Allobaculum and Bacteroides. These findings suggested that L. casei CCFM419 modified the gut flora-SCFA-inflammation/GLP-1 mechanism to ameliorate type 2 diabetes.

Wang, H., Ni, X., Qing, X., Zeng, D., Luo, M., Liu, L., Li, G., Pan, K., and Jing, B. Live Probiotic Lactobacillus johnsonii BS15 Promotes Growth Performance and Lowers Fat Deposition by Improving Lipid Metabolism, Intestinal Development, and Gut Microflora in Broilers. Front Microbiol. 2017; 8:1073; PM: 8659893

ABSTRACT: Numerous studies have focused on the beneficial effects of probiotics in animals. Even so, additional information should be obtained about the mechanisms by which a useful probiotic strain successfully exerts such beneficial effects. In this study, we evaluated the effect of the dietary supplementation of both live and disrupted Lactobacillus johnsonii (LJ) strain BS15 in broilers at different ages. Specifically, growth performance, lipid metabolism, gut microbiota, intestinal development, and digestive ability of the broilers were assessed. A total of 180 1-day-old Cobb 500 chicks were randomly distributed into three groups. These chicks were fed diets supplemented with 1 x 106 colony-forming units (cfu) LJ per gram of feed (LJ group); 1 x 106 cfu disrupted LJ per gram of feed (D-LJ group); and de Man, Rogosa, and Sharpe liquid medium (control group), respectively, throughout a 42-day experimental period. The results demonstrated that LJ supplementation of feed had a positive effect on the average daily gain and starter feed conversion ratio. In addition, LJ supplementation of feed decreased serum triglyceride and low-density lipid cholesterol levels, as well as abdominal fat deposition. LJ also reduced the mRNA levels of lipoprotein lipase in adipose tissue and stearoyl-CoA desaturase-1 in the liver. LJ diminished the mRNA quantities of the sterol regulatory element binding protein-1c and fatty acid synthase, as well as increased the level of serum high-density lipid cholesterol. LJ increased the mRNA quantities of peroxisome proliferator-activated receptor alpha, acyl-CoA oxidase in the liver, and carnitine palmitoyltransferase-1. LJ also improved the intestinal development and digestive ability mainly by increasing the villus height/crypt depth ratio in the ileum. The probiotic increased the levels of epidermal growth factor and insulin-like growth factor-1, as well as the activities of trypsin and lipase in the jejunum and ileum. LJ exerted beneficial effects on the intestinal flora. Specifically, LJ markedly enhanced the population of Bacteroidetes and Lactobacillus spp. Moreover, the probiotic reduced the population of Enterobacteriaceae and the Firmicutes/Bacteroidetes ratio. Slight changes caused by disrupted LJ were detected. These findings indicated that live LJ supplementation may promote growth performance and lower fat deposition in broilers.

Wang, W., Li, Y., Qin, W., Sun, C., Tan, H., and Cao, L. Using Illumina-Based Sequence Analysis to Guide Probiotic Candidate Selection and Isolation. Probiotics.Antimicrob.Proteins. 6-22-2017; PM: 28643225

ABSTRACT: Selection for probiotic candidates by in vivo experimental trials is time and labor consuming; more informed strategy is needed to select successful probiotic candidates. The aim of the study was to elucidate the microbial taxa transmitted from maize seeds to seedlings during the germination process of maize and their probiotic effects. The bacterial and fungal taxa in kernel germs and sprouts were analyzed by Illumina-based sequencing. The sprouts contained more diverse fungi than those in germs. The bacterial species (OTUs) declined with the germination from germs to the sprouts. However, the endophytic fungal diversity increased during the germination

process. Seed-borne dominant bacterial genera Bacillus, Halomonas, and Shewanella and dominant fungal genera Aspergillus were also detected in sprouts. The spore-forming bacteria BS3 isolated directly from sprouts could promote growth of maize seedling and resistance to F. verticillioides under F. verticillioides-infested soils. The results suggested that maize contained core bacterial and fungal taxa during the development from seeds to sprouts, and the core endophytes showed more intimate correlation with host plants than did other microbial taxa. Illumina-based sequence analysis is feasible to guide probiotic candidate selection and isolation.

Wang, X., Juan, Q. F., He, Y. W., Zhuang, L., Fang, Y. Y., and Wang, Y. H. Multiple effects of probiotics on different types of diabetes: a systematic review and meta-analysis of randomized, placebo-controlled trials. J.Pediatr.Endocrinol.Metab. 5-24-2017; 30(6):611-622; PM: 28599375

ABSTRACT: ***BACKGROUND***: A systematic review and meta-analysis was designed to evaluate the effect of probiotics on diabetes and its associated risk factors. ***METHODS***: We systematically searched the Cochrane Library, PubMed, EMBASE and Web of Science to June 2016. We also hand-searched the citation lists of included studies and previously identified systematic reviews to identify further relevant trials. Our primary outcome variables included glucose, glycated hemoglobin (HbA1c) and insulin. The pooled standardized mean difference was used to compare the effect between the probiotics and controlled groups, and the pooled standardized mean difference effect size with a 95% confidence interval (CI) was estimated using a random-effect model. Heterogeneity was assessed with Cochran's Q and Higgins I2 tests. Two reviewers assessed trial quality and extracted data independently. The analysis and bias for each included study was performed and assessed using Review Manager 5.2. ***RESULTS***: Eighteen randomized, placebo-controlled studies (n=1056 participants, 527 consuming probiotics, 529 not consuming probiotics) were included for analysis. Comparing the probiotics groups with the control groups, there were statistically significant pooled standardized mean differences on the reduction of glucose (-0.61, 95% CI -0.98, -0.24; p=0.001), insulin (-0.49, 95% CI -0.93, -0.04; p=0.03) and HbA1c (-0.39, 95% CI -0.60, -0.19%; p=0.0001). Subgroup analysis also indicated statistical significance on the reduction of low-density lipoprotein cholesterol (LDL-C) in non-type 2 diabetes (non-T2DM) mellitus patients with diabetes, for the pooled standardized mean difference was -0.29 (95% CI -0.54, -0.04; p=0.02). ***CONCLUSIONS***: Probiotics may have beneficial effects on the reduction of glucose, insulin and HbA1c for diabetes, especially for T2DM mellitus patients.

Wang, Y., Sun, J., Zhong, H., Li, N., Xu, H., Zhu, Q., and Liu, Y. Effect of probiotics on the meat flavour and gut microbiota of chicken. Sci.Rep. 7-25-2017; 7(1):6400; PM: 28743928

ABSTRACT: To date, no report has demonstrated the use of beneficial microbes for contributing to the flavour characteristics and gut microbiota diversity of chicken. Here, we selected six probiotics obtained from our laboratory and supplemented them in six different combinations to 420 newborn male Qingjiaoma chickens under the same controlled living environment (60 birds, no probiotic supplements). The results showed that chicken supplemented with Bacillus species showed beneficial effects in body weight. Acetate is the major fermentation production in the chicken caecum, and chicken supplemented with Pediococcus pentosaceus had the average higher short chain fatty acids (SCFAs) contents. In chicken caecal microflora, the abundance of

Bacteroidetes bacteria was positively correlated with the content of propionate, butyrate, and isobutyrate, whereas an increase in acetate content was positively correlated to the abundance of Firmicutes. Compared to chickens without probiotic supplement, chickens supplemented with P. pentosaceus had more characteristic flavour compounds in the sampled breast meat, especially higher concentrations of (E)-2-heptenal, (E,E)-2,4-nonadienal, and certain C6-C9 unsaturated fatty acids. This resulted in a stronger chicken-fatty or fatty odour which directly improved the flavour. These findings suggest that probiotics can improve chicken meat flavour and increase gut microbiota diversity.

Wang, Y., Wu, Y., Wang, Y., Xu, H., Mei, X., Yu, D., Wang, Y., and Li, W. Antioxidant Properties of Probiotic Bacteria. Nutrients. 5-19-2017; 9(5); PM: 28534820

ABSTRACT: Oxidative stress defines a condition in which the prooxidant-antioxidant balance in the cell is disturbed, resulting in DNA hydroxylation, protein denaturation, lipid peroxidation, and apoptosis, ultimately compromising cells' viability. Probiotics have been known for many beneficial health effects, and the consumption of probiotics alone or in food shows that strain-specific probiotics can present antioxidant activity and reduce damages caused by oxidation. However, the oxidation-resistant ability of probiotics, especially the underling mechanisms, is not properly understood. In this view, there is interest to figure out the antioxidant property of probiotics and summarize the mode of action of probiotic bacteria in antioxidation. Therefore, in the present paper, the antioxidant mechanisms of probiotics have been reviewed in terms of their ability to improve the antioxidant system and their ability to decrease radical generation. Since in recent years, oxidative stress has been associated with an altered gut microbiota, the effects of probiotics on intestinal flora composition are also elaborated.

Wang, Z., Xue, K., Bai, M., Deng, Z., Gan, J., Zhou, G., Qian, H., Bao, N., and Zhao, J. Probiotics protect mice from CoCrMo particles-induced osteolysis. Int.J.Nanomedicine. 2017; 12:5387-5397; PM: 28794630

ABSTRACT: Wear particle-induced inflammatory osteolysis is the primary cause of aseptic loosening, which is the most common reason for total hip arthroplasty (THA) failure in the med- and long term. Recent studies have suggested an important role of gut microbiota (GM) in modulating the host metabolism and immune system, leading to alterations in bone mass. Probiotic bacteria administered in adequate amounts can alter the composition of GM and confer health benefits to the host. Given the inflammatory osteolysis that occurs in wear debris-induced prosthesis loosening, we examined whether the probiotic Lactobacillus casei could reduce osteolysis in a mouse calvarial resorption model. In this study, L. casei markedly protected mice from CoCrMo particles (CoPs)-induced osteolysis. Osteoclast gene markers and the number of osteoclasts were significantly decreased in L. casei-treated mice. Probiotic treatment decreased the M1-like macrophage phenotype indicated by downregulation of tumor necrosis factor alpha (TNF-alpha), interleukin (IL)-6 and inducible nitric oxide synthase (iNOS) and increased the M2-like macrophage phenotype indicated by upregulation of IL-4, IL-10 and arginase. Collectively, these results indicated that the L. casei treatment modulated the immune status and suppressed wear particle-induced osteolysis in vivo. Thus, probiotic treatment may represent a potential preventive and therapeutic approach to reduced wear debris-induced osteolysis.

Wang, Z. J., Chen, X. F., Zhang, Z. X., Li, Y. C., Deng, J., Tu, J., Song, Z. Q., and Zou, Q. H. Effects of anti-Helicobacter pylori concomitant therapy and probiotic supplementation on the throat and gut microbiota in humans. Microb.Pathog. 2017; 109:156-161; PM: 28552806

ABSTRACT: The microbiota within humans maintains homeostasis and plays important roles in human health. However, some situations such as the use of antibiotics may disrupt the microbiota balance and result in a series of adverse effects. This study aimed to investigate the effects of a commonly used anti-Helicobacter pylori concomitant therapy on the composition of the gut and throat microbiota and any antibiotic resistance that may develop. In addition to the standard regimen, two different supplementary probiotic regimens that both used Saccharomyces boulardii were included. Microbiological culture-based techniques were used to analyse the microbiota composition and antibiotic resistance. Our results showed marked quantitative and qualitative alterations in both the gut and throat microbiota after treatment with not only the standard concomitant therapy but also with either supplementary probiotic regimen. Nevertheless, most of the changes in the gut microbiota (except for yeast and Bacteroides spp. counts) reverted by Day 71, whereas the alterations in the throat microbiota appeared to persist. Patients treated with the eradication therapy in the absence of probiotic supplementation experienced the most pronounced disturbances in the throat microbiota, whereas changes in the throat microbiota appeared to stabilize in the groups that received probiotic supplementation. We also detected higher antibiotic resistance rates for Enterobacteriaceae, Enterococcus spp. and Bacteroides spp. after treatment with the eradication therapy. Co-administration of probiotics is likely to be more effective than post-antibiotic supplementation, and although some beneficial effects were observed, the probiotic combination did not exert significant effects on the unbalanced commensal gut and throat microbiota composition.

Watts, J. E. M., Schreier, H. J., Lanska, L., and Hale, M. S. The Rising Tide of Antimicrobial Resistance in Aquaculture: Sources, Sinks and Solutions. Mar.Drugs. 6-1-2017; 15(6); PM: 28587172

ABSTRACT: As the human population increases there is an increasing reliance on aquaculture to supply a safe, reliable, and economic supply of food. Although food production is essential for a healthy population, an increasing threat to global human health is antimicrobial resistance. Extensive antibiotic resistant strains are now being detected; the spread of these strains could greatly reduce medical treatment options available and increase deaths from previously curable infections. Antibiotic resistance is widespread due in part to clinical overuse and misuse; however, the natural processes of horizontal gene transfer and mutation events that allow genetic exchange within microbial populations have been ongoing since ancient times. By their nature, aquaculture systems contain high numbers of diverse bacteria, which exist in combination with the current and past use of antibiotics, probiotics, prebiotics, and other treatment regimens-singularly or in combination. These systems have been designated as "genetic hotspots" for gene transfer. As our reliance on aquaculture grows, it is essential that we identify the sources and sinks of antimicrobial resistance, and monitor and analyse the transfer of antimicrobial resistance between the microbial community, the environment, and the farmed product, in order to better understand the implications to human and environmental health.

Wen, C., Zheng, Z., Shao, T., Liu, L., Xie, Z., Le, Chatelier E., He, Z., Zhong, W., Fan, Y., Zhang, L., Li, H., Wu, C., Hu, C., Xu, Q., Zhou, J., Cai, S., Wang, D., Huang, Y., Breban, M., Qin, N., and Ehrlich, S. D. Quantitative metagenomics reveals unique gut microbiome biomarkers in ankylosing spondylitis. Genome Biol. 7-27-2017; 18(1):142; PM: 28750650

ABSTRACT: ***BACKGROUND***: The assessment and characterization of the gut microbiome has become a focus of research in the area of human autoimmune diseases. Ankylosing spondylitis is an inflammatory autoimmune disease and evidence showed that ankylosing spondylitis may be a microbiome-driven disease. ***RESULTS***: To investigate the relationship between the gut microbiome and ankylosing spondylitis, a quantitative metagenomics study based on deep shotgun sequencing was performed, using gut microbial DNA from 211 Chinese individuals. A total of 23,709 genes and 12 metagenomic species were shown to be differentially abundant between ankylosing spondylitis patients and healthy controls. Patients were characterized by a form of gut microbial dysbiosis that is more prominent than previously reported cases with inflammatory bowel disease. Specifically, the ankylosing spondylitis patients demonstrated increases in the abundance of Prevotella melaninogenica, Prevotella copri, and Prevotella sp. C561 and decreases in Bacteroides spp. It is noteworthy that the Bifidobacterium genus, which is commonly used in probiotics, accumulated in the ankylosing spondylitis patients. Diagnostic algorithms were established using a subset of these gut microbial biomarkers. ***CONCLUSIONS***: Alterations of the gut microbiome are associated with development of ankylosing spondylitis. Our data suggest biomarkers identified in this study might participate in the pathogenesis or development process of ankylosing spondylitis, providing new leads for the development of new diagnostic tools and potential treatments.

West, C. E., Dzidic, M., Prescott, S. L., and Jenmalm, M. C. Bugging allergy; role of pre-, pro- and synbiotics in allergy prevention. Allergol.Int. 8-30-2017; PM: 28865967

ABSTRACT: Large-scale biodiversity loss and complex changes in social behaviors are altering human microbial ecology. This is increasingly implicated in the global rise in inflammatory diseases, most notably the "allergy epidemic" in very early life. Colonization of human ecological niches, particularly the gastrointestinal tract, is critical for normal local and systemic immune development and regulation. Disturbances in composition, diversity and timing of microbial colonization have been associated with increased allergy risk, indicating the importance of strategies to restore a dysbiotic gut microbiota in the primary prevention of allergic diseases, including the administration of probiotics, prebiotics and synbiotics. Here, we summarize and discuss findings of randomized clinical trials that have examined the effects of these microbiome-related strategies on short and long-term allergy preventative effects - including new guidelines from the World Allergy Organization which now recommend probiotics and prebiotics for allergy prevention under certain conditions. The relatively low quality evidence, limited comparative studies and large heterogeneity between studies, have collectively hampered recommendations on specific probiotic strains, specific timing and specific conditions for the most effective preventive management. At the same time the risk of using available products is low. While further research is needed before specific practice guidelines on supplement probiotics and prebiotics, it is equally important that the underlying dietary and lifestyle factors of dysbiosis are addressed at both the individual and societal levels.

Westfall, S., Lomis, N., Kahouli, I., Dia, S. Y., Singh, S. P., and Prakash, S. Microbiome, probiotics and neurodegenerative diseases: deciphering the gut brain axis. Cell Mol.Life Sci. 6-22-2017; PM: 28643167

ABSTRACT: The gut microbiota is essential to health and has recently become a target for live bacterial cell biotherapies for various chronic diseases including metabolic syndrome, diabetes, obesity and neurodegenerative disease. Probiotic biotherapies are known to create a healthy gut environment by balancing bacterial populations and promoting their favorable metabolic action. The microbiota and its respective metabolites communicate to the host through a series of biochemical and functional links thereby affecting host homeostasis and health. In particular, the gastrointestinal tract communicates with the central nervous system through the gut-brain axis to support neuronal development and maintenance while gut dysbiosis manifests in neurological disease. There are three basic mechanisms that mediate the communication between the gut and the brain: direct neuronal communication, endocrine signaling mediators and the immune system. Together, these systems create a highly integrated molecular communication network that link systemic imbalances with the development of neurodegeneration including insulin regulation, fat metabolism, oxidative markers and immune signaling. Age is a common factor in the development of neurodegenerative disease and probiotics prevent many harmful effects of aging such as decreased neurotransmitter levels, chronic inflammation, oxidative stress and apoptosis-all factors that are proven aggravators of neurodegenerative disease. Indeed patients with Parkinson's and Alzheimer's diseases have a high rate of gastrointestinal comorbidities and it has be proposed by some the management of the gut microbiota may prevent or alleviate the symptoms of these chronic diseases.

White, R., Atherly, T., Guard, B., Rossi, G., Wang, C., Mosher, C., Webb, C., Hill, S., Ackermann, M., Sciabarra, P., Allenspach, K., Suchodolski, J., and Jergens, A. E. Randomized, controlled trial evaluating the effect of multi-strain probiotic on the mucosal microbiota in canine idiopathic inflammatory bowel disease. Gut Microbes. 7-5-2017; 1-16; PM: 28678609

ABSTRACT: The intestinal microbiota is increasingly linked to the pathogenesis of idiopathic inflammatory bowel disease (IBD) in dogs. While studies have reported alterations in fecal (luminal) microbial populations, only limited information is available about the mucosal microbiota of IBD dogs at diagnosis and following medical therapy. Our aim was to characterize the mucosal microbiota and determine the clinical, microbiological, and mucosal homeostatic effects of probiotic treatment in dogs with IBD. Thirty four IBD dogs were randomized to receive standard therapy (ST = diet + prednisone) with or without probiotic. Tissue sections from endoscopic biopsies were evaluated by fluorescence in situ hybridization (FISH) on a quantifiable basis. Disease activity and changes in mucosal microbiota and tight junction protein (TJP) expression were assessed before and after 8 weeks of IBD therapy. ST and ST/probiotic therapy modulated the number of mucosal bacteria of IBD dogs in a similar fashion. Both treatments increased the numbers of total bacteria and individual species residing within adherent mucus, with ST therapy increasing Bifidobacterium spp. and ST/probiotic therapy increasing Lactobacillus spp ($P < 0.05$ for both), respectively. Both treatments were associated with rapid clinical remission but not improvement in histopathologic inflammation. Probiotic therapy was associated with upregulated ($P < 0.05$) expression of TJPs E-cadherin, occludin, and zonulin versus ST. The probiotic effect on mucosal bacteria is similar to that of IBD dogs receiving ST. IBD dogs fed probiotic had increased TJP

expression suggesting that probiotic may have beneficial effects on mucosal homeostasis.

Wilkins, T. and Sequoia, J. Probiotics for Gastrointestinal Conditions: A Summary of the Evidence. Am.Fam.Physician. 8-1-2017; 96(3):170-178; PM: 28762696

ABSTRACT: Probiotics contain microorganisms, most of which are bacteria similar to the beneficial bacteria that occur naturally in the human gut. Probiotics have been widely studied in a variety of gastrointestinal diseases. The most-studied species include Lactobacillus, Bifidobacterium, and Saccharomyces. However, a lack of clear guidelines on when to use probiotics and the most effective probiotic for different gastrointestinal conditions may be confusing for family physicians and their patients. Probiotics have an important role in the maintenance of immunologic equilibrium in the gastrointestinal tract through the direct interaction with immune cells. Probiotic effectiveness can be species-, dose-, and disease-specific, and the duration of therapy depends on the clinical indication. There is high-quality evidence that probiotics are effective for acute infectious diarrhea, antibiotic-associated diarrhea, Clostridium difficile- associated diarrhea, hepatic encephalopathy, ulcerative colitis, irritable bowel syndrome, functional gastrointestinal disorders, and necrotizing enterocolitis. Conversely, there is evidence that probiotics are not effective for acute pancreatitis and Crohn disease. Probiotics are safe for infants, children, adults, and older patients, but caution is advised in immunologically vulnerable populations.

Witte, T., Pieper, D. H., and Heidrich, B. [Intestinal microbiota in individualized therapies]. Internist (Berl). 2017; 58(7):682-686; PM: 28540475

ABSTRACT: During recent years, the analysis of the human microbiota has been receiving more and more scientific focus. Deep sequencing analysis enables characterization of microbial communities in different environments without the need of culture-based methods. Hereby, information about microbial communities is increasing enormously. Numerous studies in humans and animal models revealed the important role of the microbiome in emergence and natural course of diseases such as autoimmune diseases and metabolic disorders, e. g., the metabolic syndrome. The identification of causalities between the intestinal microbiota composition and function, and diseases in humans and animal models can help to develop individualized therapies targeting the microbiome and its modification. Nowadays, it is established that several factors influence the composition of the microbiota. Diet it is one of the major factors shaping the microbiota and the use of pro- and prebiotica may induce changes in the microbial community. Fecal microbiome transfer is the first approach targeting the intestinal microbiota which is implemented in the clinical routine for patients with therapy-refractory infections with Clostridium difficile. Herewith, the recipient's microbiota can be changed permanently and the patient can be cured from the infection.

Wojtyniak, K. and Szajewska, H. Systematic review: probiotics for functional constipation in children. Eur.J.Pediatr. 8-1-2017; PM: 28762070

ABSTRACT: We updated our 2010 systematic review on the efficacy of probiotics in the treatment of constipation in children. The MEDLINE, EMBASE, and Cochrane Library databases; clinical trial registries; and reference lists of included studies were searched to February 2017 for randomized controlled trials (RCTs) performed in children, with no

language restriction. The primary outcome measure was treatment success, as defined by the investigators. We included seven RCTs with a total of 515 participants. Included trials were heterogeneous with respect to study population, probiotic strains, dosages, study duration, and follow-up. Pooled results of two RCTs showed no significant difference between the Lactobacillus rhamnosus casei Lcr35 and placebo groups with respect to treatment success. Other probiotics were studied in single trials only. There was no significant difference between the probiotic and control groups with respect to treatment success. While some probiotic strains showed some effects on defecation frequency, none of the probiotics had beneficial effects on frequency of fecal incontinence or frequency of abdominal pain. Adverse events were rare and not serious. ***CONCLUSION***: Limited evidence does not support the use of any of currently evaluated probiotics in the treatment of functional constipation in children. What is Known: * Conventional treatment for functional constipation in children does not always provide satisfying improvement. * Probiotics have been suggested as potential treatment modalities for this condition. What is New: * Probiotics are ineffective for the management of functional constipation in children in terms of treatment success, frequency of fecal incontinence, and frequency of abdominal pain.

Wu, X. D., Chen, Y., and Huang, W. A Perspective on the Application of Pro-/Synbiotics in Clinical Practice. Front Microbiol. 2017; 8:866; PM: 28588559

No Abstract Available.

Wuyts, S., Wittouck, S., De, Boeck, I, Allonsius, C. N., Pasolli, E., Segata, N., and Lebeer, S. Large-Scale Phylogenomics of the Lactobacillus casei Group Highlights Taxonomic Inconsistencies and Reveals Novel Clade-Associated Features. mSystems. 2017; 2(4); PM: 28845461

ABSTRACT: Although the genotypic and phenotypic properties of the Lactobacillus casei group have been studied extensively, the taxonomic structure has been the subject of debate for a long time. Here, we performed a large-scale comparative analysis by using 183 publicly available genomes supplemented with a Lactobacillus strain isolated from the human upper respiratory tract. On the basis of this analysis, we identified inconsistencies in the taxonomy and reclassified all of the genomes according to their most closely related type strains. This led to the identification of a catalase-encoding gene in all 10 L. casei sensu stricto strains, making it the first described catalase-positive species in the Lactobacillus genus. Moreover, we found that 6 of 10 L. casei genomes contained a SecA2/SecY2 gene cluster with two putative glycosylated surface adhesin proteins. Altogether, our results highlight current inconsistencies in the taxonomy of the L. casei group and reveal new clade-associated functional features. ***IMPORTANCE***: The closely related species of the Lactobacillus casei group are extensively studied because of their applications in food fermentations and as probiotics. Our results show that many strains in this group are incorrectly classified and that reclassifying them to their most closely related species type strain improves the functional predictive power of their taxonomy. In addition, our findings may spark increased interest in the L. casei species. We find that after reclassification, only 10 genomes remain classified as L. casei. These strains show some interesting properties. First, they all appear to be catalase positive. This suggests that they have increased oxidative stress resistance. Second, we isolated an L. casei strain from the human upper respiratory tract and discovered that it and multiple other L. casei strains harbor one or even two large, glycosylated putative surface

adhesins. This might inspire further exploration of this species as a potential probiotic organism.

Xinias, I., Analitis, A., Mavroudi, A., Roilides, I., Lykogeorgou, M., Delivoria, V., Milingos, V., Mylonopoulou, M., and Vandenplas, Y. Innovative Dietary Intervention Answers to Baby Colic. Pediatr.Gastroenterol.Hepatol.Nutr. 2017; 20(2):100-106; PM: 28730134

ABSTRACT: ***PURPOSE***: The purpose of this paper is to evaluate the efficacy of a lactose-reduced synbiotic partial whey hydrolysate in formula fed infants presenting with colic and the impact of this dietary intervention in mean crying time and quality of life. ***METHODS***: Forty infants with infantile colic were treated during one month with parental reassurance and the intervention formula (partial whey hydrolysate, reduced lactose, Bifidobacterium lactis BB12 and galacto-oligosaccharides) and were compared to a control group of 20 infants with infantile colic treated with parental reassurance and a standard infant formula. Parents completed a quality of life (QoL) questionnaire assessing the burden of infantile colic. Wilcoxon test, t-test and Mann-Whitney test were used to compare QoL scores before and after intervention as well as between the intervention and control group. ***RESULTS***: At inclusion, duration of crying did not differ between both groups. Crying duration decreased with 2.7 hours (from 3.2 to 0.5 hours) in the intervention group while duration of crying decreased only with 1.2 hours in the control group ($p<0.001$). Stool composition became looser in the intervention group, but defecation frequency did not change. The median scores of the QoL questionnaire improved significantly in the intervention group for all parameters. In the control group, parameters improved significantly also but not for the parent-child and social interaction. The score changes were significantly greater in the intervention than in the control group. ***CONCLUSION***: The intervention formula (partial whey hydrolysate, synbiotic, reduced lactose) significantly reduced the duration of crying and improved QoL of the parents and infants.

Yadav, R. and Shukla, P. An overview of advanced technologies for selection of probiotics and their expediency: A review. Crit Rev.Food Sci.Nutr. 10-13-2017; 57(15):3233-3242; PM: 26505073

ABSTRACT: It has become easy to identify and select an appropriate microorganism with the advancement in various molecular biology and analytical techniques. The majority of the novel techniques are being implemented for the identification and characterization of microorganisms used for probiotic application. Standard microbial techniques such as biochemical testing and culture techniques routinely used for probiotic microbes screening, identification and selection. However, these standard techniques may not give complete information on the microbes that can be used for probiotic production. Furthermore, alternative molecular and analytical techniques such as 16S and 23S ribosomal DNA sequencing, RNA analysis by reverse transcriptase (RT-PCR), fluorescent in situ hybridization (FISH), quantitative analysis by real time PCR (RT-PCR or qPCR) and fluorescent activated cell sorting (FACS) are potentially used to confirm and select all types of lactic acid microorganism. All these approaches can be employed in the screening and selection of appropriate lactic acid bacteria which can be potentially used for the production of human use probiotics in large scale fermentation. This review mainly focuses on various tools and techniques used for effective screening and selection of a better candidate bacterium for probiotic applications.

Yan, J. and Charles, J. F. Gut Microbiome and Bone: to Build, Destroy, or Both? Curr.Osteoporos.Rep. 2017; 15(4):376-384; PM: 28620867

ABSTRACT: ***PURPOSE OF REVIEW***: The gut microbiota can be considered a hidden organ that plays essential roles in host homeostasis. Exploration of the effects of microbiota on bone has just begun. Complimentary studies using germ-free mice, antibiotic, and probiotic treatments reveal a complicated relationship between microbiota and bone. Here, we review recent reports addressing the effect of gut microbiota on bone health, discuss potential reasons for discrepant findings, and explore potential mechanisms for these effects. ***RECENT FINDINGS***: Manipulation of microbiota by colonization of germ-free mice, antibiotics, or probiotic supplementation significantly alters bone remodeling, bone development and growth, as well as bone mechanical strength. Different experimental models reveal context-dependent effects of gut microbiota on bone. By examining phenotypic effects, experimental context, and proposed mechanisms, revealed by recent reports, we hope to provide comprehensive and fresh insights into the many facets of microbiota and bone interactions.

Yang, G., Peng, M., Tian, X., and Dong, S. Molecular ecological network analysis reveals the effects of probiotics and florfenicol on intestinal microbiota homeostasis: An example of sea cucumber. Sci.Rep. 7-6-2017; 7(1):4778; PM: 28684750

ABSTRACT: Animal gut harbors diverse microbes that play crucial roles in the nutrition uptake, metabolism, and the regulation of host immune responses. The intestinal microbiota homeostasis is critical for health but poorly understood. Probiotics Paracoccus marcusii DB11 and Bacillus cereus G19, and antibiotics florfenicol did not significantly impact species richness and the diversity of intestinal microbiota of sea cucumber, in comparison with those in the control group by high-throughput sequencing. Molecular ecological network analysis indicated that P. marcusii DB11 supplementation may lead to sub-module integration and the formation of a large, new sub-module, and enhance species-species interactions and connecter and module hub numbers. B. cereus G19 supplementation decreased sub-module numbers, and increased the number of species-species interactions and module hubs. Sea cucumber treated with florfenicol were shown to have only one connecter and the lowest number of operational taxonomic units (OTUs) and species-species interactions within the ecological network. These results suggested that P. marcusii DB11 or B. cereus G19 may promote intestinal microbiota homeostasis by improving modularity, enhancing species-species interactions and increasing the number of connecters and/or module hubs within the network. In contrast, the use of florfenicol can lead to homeostatic collapse through the deterioration of the ecological network.

Yang, J., Tamura, R. N., Uusitalo, U. M., Aronsson, C. A., Silvis, K., Riikonen, A., Frank, N., Joslowski, G., Winkler, C., Norris, J. M., and Virtanen, S. M. Vitamin D and probiotics supplement use in young children with genetic risk for type 1 diabetes. Eur.J.Clin.Nutr. 9-13-2017; PM: 28901336

ABSTRACT: ***BACKGROUND/OBJECTIVES***: Vitamin D and probiotics are nutrients of interest in the context of type 1 diabetes (T1D). We assessed the prevalence of and factors associated with vitamin D and probiotic supplementations among young children with genetic risk of T1D. ***SUBJECTS/METHODS***: Use of supplements during the first 2 years of life

was collected prospectively from 8674 children in The Environmental Determinants of Diabetes in the Young (TEDDY) study. ***RESULTS***: Single and/or multivitamin/mineral (MVM) supplements were reported by 81% of the children. The majority of participants in Finland, Germany and Sweden (97-99%) and 50% in the United States received vitamin D supplements that were mostly MVMs. Probiotics use varied from 6% in the United States to 60% in Finland and was primarily from probiotics-only preparations. More than 80% of the vitamin D and probiotics supplementation was initiated during infancy, and more than half of the uses lasted longer than a year. Being the first child, longer duration of breastfeeding, born in a later year, older maternal age and higher maternal education level were associated with both vitamin D and probiotics use. Shorter gestational age and mother not smoking during pregnancy were associated with a higher likelihood of probiotics supplementation only. ***CONCLUSIONS***: Vitamin D and probiotics supplementations are popular in children 0-2 years old and are associated with common factors. Data documented here will allow evaluation of the relationship between early childhood dietary intake and the development of islet autoimmunity and progression to T1D.European Journal of Clinical Nutrition advance online publication, 13 September 2017; doi:10.1038/ejcn.2017.140.

Yao, K., Zeng, L., He, Q., Wang, W., Lei, J., and Zou, X. Effect of Probiotics on Glucose and Lipid Metabolism in Type 2 Diabetes Mellitus: A Meta-Analysis of 12 Randomized Controlled Trials. Med.Sci.Monit. 6-22-2017; 23:3044-3053; PM: 28638006

ABSTRACT: ***BACKGROUND***: It has been unclear whether supplemental probiotics therapy improves clinical outcomes in type 2 diabetic patients. This meta-analysis aimed to summarize the effect of probiotics on glucose and lipid metabolism and C-reactive protein (CRP) from 12 randomized controlled trials (RCTs). ***MATERIAL AND METHODS***: An up-to-date search was performed for all relevant RCTs up to April 2016 from PubMed, Embase, and Cochrane Library. Standardized mean difference (SMD) and weighted mean difference (WMD) were calculated for a fixed-effect and random-effect meta-analysis to assess the impact of supplemental probiotics on fasting plasma glucose (FPG), glycated hemoglobin (HbA1c), fasting insulin, homeostasis model assessment of insulin resistance (HOMA-IR), lipid profile, and CRP level. ***RESULTS***: A total of 12 studies (684 patients) were entered into the final analysis. The effect of probiotics was significant on reducing HbA1c level (standardized mean difference [SMD], -0.38; confidence interval [CI], -0.62 to -0.14, P=0.002; I(2)=0%, P=0.72 for heterogeneity), fasting insulin level (SMD, -0.38; CI -0.59 to -0.18, P=0.0003; I(2)=0%, P=0.81 for heterogeneity), and HOMA-IR (SMD, -0.99; CI -1.52 to -0.47, P=0.0002; I(2)=86%, P<0.00001 for heterogeneity). Pooled results on effects of probiotics on FPG, CRP, or lipid profile were either non-significant or highly heterogeneous. ***CONCLUSIONS***: This meta-analysis demonstrated that probiotics supplementation was associated with significant improvement in HbA1c and fasting insulin in type 2 diabetes patients. More randomized placebo-controlled trials with large sample sizes are warranted to confirm our conclusions.

Yaqoob, P. Ageing alters the impact of nutrition on immune function. Proc.Nutr.Soc. 2017; 76(3):347-351; PM: 27821203

ABSTRACT: Immunosenescence during ageing is a major challenge which weakens the ability of older individuals to respond to infection or vaccination. There has been much interest in dietary strategies to improve immunity in older people, but there is an assumption that modulation of the immune response in older people will be based on the same principles as for younger adults. Recent evidence suggests that ageing

fundamentally alters the impact of nutrition on immune function. As a result, interpretation of data from studies investigating the impact of diet on immune function is highly dependent on subject age. Study design is critically important when investigating the efficacy of dietary components, and most studies involving older people include rigorous inclusion/exclusion criteria based on medical history, laboratory tests, general health status and often nutritional status. However, immunological status is rarely accounted for, but can vary significantly, even amongst healthy older people. There are several clear examples of age-related changes in immune cell composition, phenotype and/or function, which can directly alter the outcome of an intervention. This review uses two case studies to illustrate how the effects of n-3 PUFA and probiotics differ markedly in young v. older subjects. Evidence from both suggests that baseline differences in immunosenescence influence the outcome of an intervention, highlighting the need for detailed immunological characterisation of subjects prior to interventions. Finally, future work elucidating alterations in metabolic regulation within cells of the immune system as a result of ageing may be important in understanding the impact of diet on immune function in older people.

Yoshioka, K., Kakihana, K., Doki, N., and Ohashi, K. Gut microbiota and acute graft-versus-host disease. Pharmacol.Res. 2017; 122:90-95; PM: 28576475

ABSTRACT: Although allogeneic stem cell transplantation (allo-SCT) is a potentially curative treatment for various hematological diseases, acute graft-versus-host disease (GVHD) is a major cause of morbidity and mortality, and its management is clinically important. Advances in biological techniques have led to great progress in understanding the complex interactions between the host and the gut microbiota. The gut microbiota clearly modulates the immune response and is associated with the pathogenesis of various disorders. Also in allo-SCT, both preclinical and clinical results indicate that the gut microbiota is closely associated with the development of acute GVHD and transplant outcomes. These results led to the idea that improvement in quantitative and/or qualitative abnormalities of microbiota (dysbiosis) may be a new treatment strategy for acute GVHD. Evaluations of therapies targeting the gut microbiota such as probiotics or fecal microbiota transplantation have just begun. Furthermore, intervention in the gut microbiota with a nutritional approach including prebiotics, postbiotics, and antibiotics selection may also be another promising treatment option for acute GVHD.

Younes, J. A., Lievens, E., Hummelen, R., van der, Westen R., Reid, G., and Petrova, M. I. Women and Their Microbes: The Unexpected Friendship. Trends Microbiol. 8-22-2017; PM: 28844447

ABSTRACT: Communities of microbiota have been associated with numerous health outcomes, and while much emphasis has been placed on the gastrointestinal niche, there is growing interest in the microbiome specific for female reproductive health and the health of their offspring. The vaginal microbiome plays an essential role not only in health and dysbiosis, but also potentially in successful fertilization and healthy pregnancies. In addition, microbial communities have been isolated from formerly forbidden sterile niches such as the placenta, breast, uterus, and Fallopian tubes, strongly suggesting an additional microbial role in women's health. A combination of maternally linked prenatal, birth, and postnatal factors, together with environmental and medical interventions, influence early and later life through the microbiome. Here, we review the

role of microbes in female health focusing on the vaginal tract and discuss how male and female reproductive microbiomes are intertwined with conception and how mother-child microbial transfer is a key determinant in infant health, and thus the next generation.

Young, G. R., Smith, D. L., Embleton, N. D., Berrington, J. E., Schwalbe, E. C., Cummings, S. P., van der Gast, C. J., and Lanyon, C. Reducing Viability Bias in Analysis of Gut Microbiota in Preterm Infants at Risk of NEC and Sepsis. Front Cell Infect.Microbiol. 2017; 7:237; PM: 28634574

ABSTRACT: Necrotising enterocolitis (NEC) and sepsis are serious diseases of preterm infants that can result in feeding intolerance, the need for bowel resection, impaired physiological and neurological development, and high mortality rates. Neonatal healthcare improvements have allowed greater survival rates in preterm infants leading to increased numbers at risk of developing NEC and sepsis. Gut bacteria play a role in protection from or propensity to these conditions and have therefore, been studied extensively using targeted 16S rRNA gene sequencing methods. However, exact epidemiology of these conditions remain unknown and the role of the gut microbiota in NEC remains enigmatic. Many studies have confounding variables such as differing clinical intervention strategies or major methodological issues such as the inability of 16S rRNA gene sequencing methods to determine viable from non-viable taxa. Identification of viable community members is important to identify links between the microbiota and disease in the highly unstable preterm infant gut. This is especially important as remnant DNA is robust and persists in the sampling environment following cell death. Chelation of such DNA prevents downstream amplification and inclusion in microbiota characterisation. This study validates use of propidium monoazide (PMA), a DNA chelating agent that is excluded by an undamaged bacterial membrane, to reduce bias associated with 16S rRNA gene analysis of clinical stool samples. We aim to improve identification of the viable microbiota in order to increase the accuracy of clinical inferences made regarding the impact of the preterm gut microbiota on health and disease. Gut microbiota analysis was completed on stools from matched twins (n = 16) that received probiotics. Samples were treated with PMA, prior to bacterial DNA extraction. Meta-analysis highlighted a significant reduction in bacterial diversity in 68.8% of PMA treated samples as well as significantly reduced overall rare taxa abundance. Importantly, overall abundances of genera associated with protection from and propensity to NEC and sepsis such as: Bifidobacterium; Clostridium, and Staphylococcus sp. were significantly different following PMA-treatment. These results suggest non-viable cell exclusion by PMA-treatment reduces bias in gut microbiota analysis from which clinical inferences regarding patient susceptibility to NEC and sepsis are made.

Yousuf, A., Sidiq, M., Ganta, S., Nagaraj, A., Vishnani, P., and Jan, I. Effect of Freeze Dried Powdered Probiotics on Gingival Status and Plaque Inhibition: A Randomized, Double-blind, Parallel Study. Contemp.Clin.Dent. 2017; 8(1):116-121; PM: 28566862

ABSTRACT: ***OBJECTIVE***: The study aimed to evaluate the effectiveness of freeze dried powdered probiotics on gingival status and plaque inhibition among 12-15-year-old schoolchildren. ***MATERIALS AND METHODS***: This randomized controlled trial was conducted among 12-15-year-old schoolchildren in Jaipur. Commercially available freeze dried probiotics containing Lactobacillus acidophilus, Bifidobacterium longum, Bifidobacterium bifidum and Bifidobacterium lactis (Prowel, Alkem Laboratories), lactic

acid bacillus only (Sporolac, Sangyo), and a placebo powder calcium carbonate 250 g (Calcium Sandoz, Novartis) were assigned to two intervention groups and a placebo group each comprising 11 schoolchildren. All subjects were instructed to mix the powder in 30 ml of water and swish once daily for 3 min, for 3 weeks. Periodontal clinical parameters were assessed by examining the subjects for Turesky-Gilmore-Glickman plaque index (PI) (Modification of Quigley-Hein PI) and gingival index at baseline, 7th day, 14th day, and 21st day. ***RESULTS***: For both the probiotic groups, a statistically significant reduction ($P < 0.05$) in gingival status and plaque inhibition was recorded up to 2nd week of probiotic ingestion. However, no significant difference was observed in the placebo group. ***CONCLUSION***: The use of probiotic mouth rinses improves the oral health in children by significantly reducing the plaque and gingival scores. Further studies are warranted to prove or refute the long-term effects, means of administering probiotics and the dosages needed to achieve different preventive or therapeutic purposes.

Yu, B., Zhu, Q., Meng, G., Gu, Y., Zhang, Q., Liu, L., Wu, H., Xia, Y., Bao, X., Shi, H., Su, Q., Fang, L., Yu, F., Yang, H., Sun, S., Wang, X., Zhou, M., Jia, Q., Guo, Q., Song, K., Steptoe, A., and Niu, K. Habitual yoghurt consumption and depressive symptoms in a general population study of 19,596 adults. Eur.J.Nutr. 8-30-2017; PM: 28856430

ABSTRACT: ***PURPOSE***: Epidemiological studies directly examining the association between habitual yoghurt consumption and mental health remain scarce. The aim of this study is to investigate the association of yoghurt consumption with depressive symptoms in adults. ***METHODS***: This is a cross-sectional study of 19,596 Chinese adults (mean age 41.2, standard deviation 11.8 years; males, 54.3%). Depressive symptoms were assessed using the Self-Rating Depression Scale (SDS). Dietary intake was obtained through a valid food frequency questionnaire. Multiple logistic regression analysis was conducted to assess the association between yoghurt consumption and depressive symptoms. A number of potential confounders were adjusted in the model. ***RESULTS***: The prevalence of elevated depressive symptoms was 17.1% (SDS >/=45). The multivariable adjusted odds ratios (95% CI) of having elevated depressive symptoms by increasing levels of yoghurt consumption (1-3 times/week, 4-7 times/week, and >/=twice/day) were 1.05 (0.96, 1.15), 1.02 (0.91, 1.15), and 2.10 (1.61, 2.73) in comparison with lowest consumption group (<once/week or hardly ever). ***CONCLUSIONS***: These findings suggest no significant association between habitual yoghurt consumption and self-reported depressive symptoms, while the relatively high frequency of yoghurt consumption (>/=twice/day), which was seen in a small subset of subjects, was associated with increased depressive symptoms. These results need to be interpreted with caution because of the cross-sectional nature of the data.

Yu, J., Ahn, S., Kim, K., Caetano-Anolles, K., Lee, C., Kang, J., Cho, K., Yoon, S. H., Kang, D. K., and Kim, H. Comparative Genomic Analysis of Lactobacillus plantarum GB-LP1 Isolated from Traditional Korean Fermented Food. J.Microbiol.Biotechnol. 8-28-2017; 27(8):1419-1427; PM: 28621109

ABSTRACT: As probiotics play an important role in maintaining a healthy gut flora environment through antitoxin activity and inhibition of pathogen colonization, they have been of interest to the medical research community for quite some time now. Probiotic bacteria such as Lactobacillus plantarum, which can be found in fermented food, are of particular interest given their easy accessibility. We performed whole-genome sequencing and genomic analysis on a GB-LP1 strain of L. plantarum isolated

from Korean traditional fermented food; this strain is well known for its functions in immune response, suppression of pathogen growth, and antitoxin effects. The complete genome sequence of GB-LP1 is a single chromosome of 3,040,388 bp with 2,899 predicted open reading frames. Genomic analysis of GB-LP1 revealed two CRISPR regions and genes showing accelerated evolution, which may have antibiotic and antitoxin functions. The aim of the present study was to predict strain specific-genomic characteristics and assess the potential of this new strain as lactic acid bacteria at the genomic level using in silico analysis. These results provide insight into the L. plantarum species as well as confirm the possibility of its utility as a candidate probiotic.

Yu, W., Sui, W., Mu, L., Yi, W., Li, H., Wei, L., and Yin, W. Preventing necrotizing enterocolitis by food additives in neonates: A network meta-analysis revealing the efficacy and safety. Medicine (Baltimore). 2017; 96(21):e6652; PM: 28538366

ABSTRACT: ***BACKGROUND***: Necrotizing enterocolitis (NEC) is a serious multifactorial gastrointestinal disease which is often discovered in premature infants. Various additives have been used to prevent NEC; yet, their relative efficacy and safety remain disputed. This study aims to compare the efficacy and safety of 5 food additives, namely, probiotics, probiotics + fructo-oligosaccharides, pentoxifylline, arginine, and lactoferrin in preventing NEC in neonates. ***METHODS***: Embase, PubMed, and Cochrane Library had been searched for all eligible randomized control trials. Odds ratios (ORs) were estimated for dichotomous data and mean differences with 95% credible intervals (CrIs) were estimated for continuous data. Surface under the cumulative ranking curve was used to rank efficacy and safety of the prevention methods on each endpoint. ***RESULTS***: A total of 27 eligible studies with 4649 preterm infants were included in this network meta-analysis (NMA), and the efficacy and safety of 5 food additives were evaluated. Probiotic and arginine exhibited better preventive efficacy compared with placebo (OR = 0.50, 95% CrIs: 0.32-0.73; OR = 0.30, 95% CrIs: 0.12-0.73, respectively). Only probiotic achieved a considerable decrease in the risk of mortality compared to placebo (OR = 0.68, 95% CrIs: 0.46-0.98). NEC patients with lactoferrin appeared to have lower incidence of sepsis than those of placebo (OR = 0.13, 95% CrIs: 0.03-0.61) or probiotic (OR = 0.18, 95% CrIs: 0.03-0.83). ***CONCLUSION***: Based on this NMA, probiotics had the potential to be the most preferable additive, since it exhibited a significant superiority for NEC and mortality as well as a relatively balanced performance in safety.

Yucel, Falco C., Falkman, P., Risbo, J., Cardenas, M., and Medronho, B. Chitosan-dextran sulfate hydrogels as a potential carrier for probiotics. Carbohydr.Polym. 9-15-2017; 172:175-183; PM: 28606523

ABSTRACT: Physical and chemical (crosslinked with genipin) hydrogels based on chitosan and dextran sulfate were developed and characterized as novel bio-materials suitable for probiotic encapsulation. The swelling of the hydrogels was dependent on the composition and weakly influenced by the pH of the media. The morphology analysis supports the swelling data showing distinct changes in microstructure depending on the composition. The viability and culturability tests showed approx. 3.6 log CFU/mL decrease of cells (L. acidophilus as model) incorporated into chemical hydrogels when compared to the number of viable native cells. However, the live/dead viability assay evidenced that a considerable amount of viable cells were still entrapped in the hydrogel network and therefore the viability is most likely underestimated. Overall, the developed systems

are robust and their structure, rheology and swelling properties can be tuned by changing the blend ratio, thus constituting appealing bio-matrices for cell encapsulation.

Yun, B., Song, M., Park, D. J., and Oh, S. Beneficial Effect of Bifidobacterium longum ATCC 15707 on Survival Rate of Clostridium difficile Infection in Mice. Korean J.Food Sci.Anim Resour. 2017; 37(3):368-375; PM: 28747822

ABSTRACT: Clostridium difficile infection (CDI) is the main cause of hospital-acquired diarrhea that can cause colitis or even death. The medical-treatment cost and deaths caused by CDI are increasing annually worldwide. New approaches for prevention and treatment of these infections are needed, such as the use of probiotics. Probiotics, including Bifidobacterium spp. and Lactobacillus, are microorganisms that confer a health benefit to the host when administered in adequate amounts. The effect of Bifidobacterium longum ATCC 15707 on infectious disease caused by C. difficile 027 was investigated in a mouse model. The survival rates for mice given the pathogen alone, and with live cells, or dead cells of B. longum were 40, 70, and 60%, respectively. In addition, the intestinal tissues of the B. longum-treated group maintained structural integrity with some degree of damage. These findings suggested that B. longum ATCC 15707 has a function in repressing the infectious disease caused by C. difficile 027.

Zago, M., Scaltriti, E., Bonvini, B., Fornasari, M. E., Penna, G., Massimiliano, L., Carminati, D., Rescigno, M., and Giraffa, G. Genomic diversity and immunomodulatory activity of Lactobacillus plantarum isolated from dairy products. Benef.Microbes. 8-24-2017; 8(4):597-604; PM: 28555501

ABSTRACT: In this study, we aimed to investigate some functional characteristics and the immunomodulatory properties of three strains of Lactobacillus plantarum of dairy origin which, in a previous screening, showed to be candidate probiotics. Genome sequencing and comparative genomics, which confirmed the presence of genes involved in folate and riboflavin production and in the immune response of dendritic cells (DCs), prompted us to investigate the ability of the three strains to accumulate the two vitamins and their immunomodulation properties. The ability of the three strains to release antioxidant components in milk was also investigated. Small amounts of folate and riboflavin were produced by the three strains, while they showed a good antioxidant capacity in milk with FRAP method. The immune response experiments well correlated with the presence of candidate genes influencing in DCs cytokine response to L. plantarum. Specifically, the amounts of secreted cytokins by DCs after stimulation with cells of Lp790, Lp813 and Lp998 resulted pro-inflammatory whereas stimulation with culture supernatants (postbiotics) inhibited the release of interleukin (IL)-12p70 and increased the release of the anti-inflammatory IL-10 cytokine. This study adds further evidence on the importance of L. plantarum in human health. Understanding how probiotics (or postbiotics) work in preclinical models can allow a rational choice of the different strains for clinical and/or commercial use.

Zahumensky, J., Hederlingova, J., and Psenkova, P. [The importance of maternal microbiome in pregnancy]. Ceska.Gynekol. 2017; 82(3):211-217; PM: 28593775

ABSTRACT: ***OBJECTIVE***: To bring the most actual published findings of the influence of maternal microbiome on the development of pregnancy and possibilities of its adjusting.

DESIGN: Review. ***SETTING***: 2nd Department of Gyneacology and Obstetrics of the Faculty of Medicine and the University Hospital, Bratislava. ***METHODS***: Review of the literature. ***CONCLUSIONS***: The appearance of microbes on various body surface areas determines the overall health status of the individual in significant manner. The change in composition of microbioma in pregnant woman is well known. It was believed that the placenta and the body of the newborn is sterile environment. Modern diagnostic methods proved the presence of microorganisms inside the fetoplacentar unit without the signs of inflammation. Mutual interaction between the immune system of the mother, microbioma and immune system of the newborn can decrease the risk of serious obstetrical syndromes as well as define the lifelong health status of the newborn. The risk can be decreased by the administration of probiotics during the pregnancy.

Zeng, Y., Zeng, D., Zhang, Y., Ni, X. Q., Wang, J., Jian, P., Zhou, Y., Li, Y., Yin, Z. Q., Pan, K. C., and Jing, B. Lactobacillus plantarum BS22 promotes gut microbial homeostasis in broiler chickens exposed to aflatoxin B1. J.Anim Physiol Anim Nutr.(Berl). 8-3-2017; PM: 28771826

ABSTRACT: Probiotics promote the health of the host by maintaining intestinal microbial homeostasis. This study aimed to investigate the benefits of Lactobacillus plantarum BS22 (LP) in the gastrointestinal tract (GIT) microbial homeostasis of broiler chickens exposed to aflatoxin B1 using the PCR-DGGE, viable count and real-time PCR. The toxin adsorption experiment demonstrated that treatment R5 (1.0 x 108 CFU/g LP) exhibited good absorptive effect in adsorbing the aflatoxin B1 (AFB1) in vitro. DGGE showed that the composition and structure of gut microbiota were more similar in the mucosa than in the content of all the samples. In addition, higher diversity of the microbiota was observed in the caecum and glandular stomach than in other segments. Lactobacillus, Enterococcus and Enterobacteriaceae were more abundant in the ileum than in the other segments. Enterobacteriaceae in groups I (basal diet) and II (basal diet+50 mug/kg AFB1) showed a significant difference in group III (basal diet + 50 mug/kg AFB1 + 1 x 108 CFU/g LP) in the crop content and duodenum mucosa ($p < .05$). This investigation indicates that the L. plantarum BS22 promotes GIT microbial homeostasis in broiler chickens exposed to AFB1 , particularly for the intestine mucosa microbiota. Thus, L. plantarum BS22 is a possible candidate for degrading AFB1.

Zhang, A. M., Sun, Z. Q., and Zhang, L. M. Mosapride combined with probiotics on gastrointestinal function and growth in premature infants. Exp.Ther.Med. 2017; 13(6):2675-2680; PM: 28587329

ABSTRACT: The aim of this study was to investigate the effects of mosapride combined with probiotics on gastrointestinal function and growth and development in premature infants. A total of 240 premature infants treated at Weifang People's Hospital between June 2012 and May 2015 who matched our criteria were randomly divided into three groups of 80 cases each. Group A received routine treatment, group B received routine treatment combined with live B. subtilis and E. faecium granules with multivitamins (Medilac-Vita), and group C received routine treatment and Saccharomyces boulardii sachets (Bioflor). Mosapride was administered to patients in groups B and C to promote intestinal peristalsis. Gastrin and bilirubin levels, as well as jaundice fade time, were recorded. Growth and development condition (i.e., head circumference and weight), duration and incidence of feeding intolerance (FI), as well as other symptoms were also analyzed. By day 14, gastrin concentrations in groups B and C were significantly higher than those in group A ($P<0.05$). Serum bilirubin levels in groups B and C showed a

progressive decline from day 7 to day 14, and jaundice duration in group A was significantly longer (P<0.05). Furthermore, at 2 weeks, the average weight growth rate and head circumference were significantly greater in groups B and C, weight loss recovery time was shorter, and EUGR incidence was lower (P<0.05). The incidence rate of gastric retention and FI were lower in groups B and C than group A (P<0.05), and neonatal hyperbilirubinemia, parenteral nutrition-associated cholestasis, necrotizing enterocolitis, and neonatal sepsis incidence was significantly lower in groups B and C (P<0.05). Mosapride combined with probiotics can effectively reduce FI incidence in premature infants, shorten enteral feeding time, promote the absorption of required nutrients, and promote the development and recovery of early physiological weight loss in preterm infants.

Zhang, H., Zhang, Z., Song, G., Tang, X., Song, H., Deng, A., Wang, W., Wu, L., and Qin, H. Development of an XBP1 agonist, HLJ2, as a potential therapeutic agent for ulcerative colitis. Eur.J.Pharm.Sci. 7-28-2017; 109:56-64; PM: 28757346

ABSTRACT: There is a severe lack of effective treatments for ulcerative colitis (UC), a recurrent and intractable inflammatory bowel disease. The identification of valid targets and new drugs is an urgent need. In this study, we identified the XBP-1 agonist HLJ2 as a promising treatment candidate. In an in vivo mouse model of DSS-induced colitis, HLJ2 decreased weight loss, colon contracture, disease activity index (DAI), colon mucosa damage index (CMDI) and histopathological index (HI). HLJ2 also decreased myeloperoxidase (MPO) activity and reduced production of the inflammatory cytokines TNF-alpha, IL-1beta, and IL-6. HLJ2 improved intestinal mucosa damage induced by dextran sodium sulfate (DSS) and increased the expression of ZO-1 and claudin-1. Fecal 16s rRNA high-throughput sequencing demonstrated a significant improvement in UC intestinal dysbacteriosis in mice treated with HLJ2, including increased abundance of probiotics such as Lachnospiraceae, Prevotellaceae, and Lactobacillaceae. At the same time there was a reduction in the abundance of pathogenic or conditional pathogenic microorganisms such as Bacteroidaceae, Porphyromonadaceae, Deferribacteraceae, and Pseudomonadaceae in HLJ2-treated mice compared with untreated mice. Our results demonstrated that the XBP1 agonist HLJ2 inhibits inflammation, regulates the intestinal flora, and protects the intestinal mucosa. It is thus a potential therapeutic agent for ulcerative colitis.

Zhang, J., Zhao, X., Jiang, Y., Zhao, W., Guo, T., Cao, Y., Teng, J., Hao, X., Zhao, J., and Yang, Z. Antioxidant status and gut microbiota change in an aging mouse model as influenced by exopolysaccharide produced by Lactobacillus plantarum YW11 isolated from Tibetan kefir. J.Dairy Sci. 2017; 100(8):6025-6041; PM: 28551178

ABSTRACT: This study investigated the effect of exopolysaccharide (EPS) produced by Lactobacillus plantarum YW11 on the oxidative status and gut microbiota in an aging mouse model induced with d-galactose. The in vitro assay of the antioxidant activity of the EPS showed concentration-dependent (0.25-3.0 mg/mL) activities. At 3.0 mg/mL, the EPS reached the highest scavenging activities with half maximal inhibitory concentration values against hydroxyl radicals at 75.10% and 1.22 mg/mL, superoxide anion at 62.71% and 1.54 mg/mL, 2, 2-diphenyl-1-picrylhydrazyl at 35.11% and 0.63 mg/mL, and the maximal chelating rate on ferrous ion and the half-maximal chelating concentration of the EPS at 41.09% and 1.07 mg/mL, respectively. High doses of EPS (50 mg/kg per day) effectively relieved the oxidative stress in the aging mice with increased levels of

glutathione peroxidase, superoxide dismutase, catalase, and total antioxidant capacity in mice serum by 21.55, 33.14, 61.09, and 38.18%, respectively, and decreased malondialdehyde level from 11.69 to 5.89 mmol/mL compared with those in the untreated aging mice model. The analysis of pyrosequencing sequence data from the gut microbiota revealed that the EPS could recover the microbiota diversity and phylotypes decreased or eliminated by the d-galactose treatment. The EPS could selectively decrease the abundance of Flexispira (37.5 fold), and increase the abundance of Blautia (36.5 fold) and Butyricicoccus (9.5 fold), which correspondingly decreased the content of nitrogen oxides to 9.87% and increased the content of short-chain fatty acids by 2.23 fold, thereby improving the oxidative and health conditions of the host intestinal tract. Further correlation analysis of core-microbiota variation induced by different treatments showed a strong correlation with oxidative phenotypes [catalase, goodness of prediction (Q2) = 0.49; total antioxidant capacity, Q2 = 0.45; nitrogen oxides, Q2 = 0.67; short-chain fatty acids, Q2 = 0.55]. The fermented milk with L. plantarum YW11 containing EPS also showed favorable antioxidant and gut microbiota regulating activities. The present finding provided new insights into the functional mechanism of probiotics bioactivity.

Zhao, L., Zhao, Y., Liu, R., Zheng, X., Zhang, M., Guo, H., Zhang, H., and Ren, F. The Transcription Factor DAF-16 is Essential for Increased Longevity in C. elegans Exposed to Bifidobacterium longum BB68. Sci.Rep. 8-7-2017; 7(1):7408; PM: 28785042

ABSTRACT: The longevity-promoting benefits of lactobacilli were hypothesized as early as 1907. Although the anti-aging effects of lactic acid bacteria (LAB) have been observed in nematodes, rodents and humans for over a century, the mechanisms underlying the effects of probiotics on aging have rarely been assessed. Using the Caenorhabditis elegans (C. elegans) model, various studies have elucidated the role of different signaling cascades, especially the DAF-16 cascade, on lifespan extension by LAB. In this study, the mechanisms through which Bifidobacterium longum strain BB68 affects the longevity of C. elegans were assessed. The lifespan of nematodes increased by 28% after worms were fed BB68, and this extension of lifespan was completely lost in backgrounds containing a mutated DAF-16 gene. High levels of DAF-16 (in the daf-16 (mu86); muIs61 strain) nuclear accumulation and high expression of the SOD-3 gene (a DAF-16-specific target gene) were observed as a result of BB68 treatment. Immunofluorescence microscopy revealed that TIR-1 and JNK-1 are involved in the phosphorylation and activation of DAF-16. Thus, BB68 increased the longevity of nematodes by activating the TIR-1 - JNK-1 - DAF-16 signaling pathway, and the cell wall component of BB68 contributed to longevity.

Zhao, X., Chen, Z., Yin, Y., and Li, X. Effects of polysaccharide from Physalis alkekengi var. francheti on liver injury and intestinal microflora in type-2 diabetic mice. Pharm.Biol. 2017; 55(1):2020-2025; PM: 28832229

ABSTRACT: ***CONTEXT***: Diabetic liver injury is a serious diabetic complication. The alterations of intestinal microbiota play an important role in induction and promotion of liver injury progression. Physalis alkekengi L. var. francheti (Mast.) Makino (Solanaceae) has been used as a water decoction for treating diabetes. ***OBJECTIVE***: To study the effects of a polysaccharide (PPSB) from Physalis alkekengi var. francheti on liver injury and intestinal microflora in type-2 diabetic mice. ***MATERIALS AND METHODS***: Streptozotocin (160 mg/kg) was injected i.p. for 3 days to build model. The diabetic mice

were randomly divided into four groups together with control group (10 mice in each group). The doses of PPSB were 50 and 100 mg/kg, respectively. After 5 weeks administration, level of blood glucose, ALT and AST were measured. Alterations of intestinal microflora, and protein expression of TGF-beta1, TNF-alpha and DCN were detected. ***RESULTS***: Level of blood glucose decreased from (25.38 +/- 2.21) mmol/L to (18.01 +/- 2.53) mmol/L, ALT and AST decreased to (24.67 +/- 4.86) U/L and (30.84 +/- 7.50) U/L in PPSB-H group. Lactobacillus, Clostridium butyricum, and Bacteroides increased remarkably with increasing concentration of PPSB, but Enterobacter was inhibited. The relative expression of TGF-beta1 and TNF-alpha decreased to (0.70 +/- 0.17) and (0.39 +/- 0.06), and the expression of DCN increased to (0.65 +/- 0.13). ***DISCUSSION AND CONCLUSIONS***: Probiotics have been promoted by PPSB, and protein expressions have been modulated in the progression of liver injury. PPSB could be used as a natural agent for treating diabetic liver injury and intestinal microflora imbalance.

Zheng, M., Zhang, R., Tian, X., Zhou, X., Pan, X., and Wong, A. Assessing the Risk of Probiotic Dietary Supplements in the Context of Antibiotic Resistance. Front Microbiol. 2017; 8:908; PM: 28579981

ABSTRACT: Probiotic bacteria are known to harbor intrinsic and mobile genetic elements that confer resistance to a wide variety of antibiotics. Their high amounts in dietary supplements can establish a reservoir of antibiotic resistant genes in the human gut. These resistant genes can be transferred to pathogens that share the same intestinal habitat thus resulting in serious clinical ramifications. While antibiotic resistance of probiotic bacteria from food, human and animal sources have been well-documented, the resistant profiles of probiotics from dietary supplements have only been recently studied. These products are consumed with increasing regularity due to their health claims that include the improvement of intestinal health and immune response as well as prevention of acute and antibiotic-associated diarrhea and cancer; but, a comprehensive risk assessment on the spread of resistant genes to human health is lacking. Here, we highlight recent reports of antibiotic resistance of probiotic bacteria isolated from dietary supplements, and propose complementary strategies that can shed light on the risks of consuming such products in the context of a global widespread of antibiotic resistance. In concomitant with a broader screening of antibiotic resistance in probiotic supplements is the use of computational simulations, live imaging and functional genomics to harvest knowledge on the evolutionary behavior, adaptations and dynamics of probiotics studied in conditions that best represent the human gut including in the presence of antibiotics. The underlying goal is to enable the health benefits of probiotics to be exploited in a responsible manner and with minimal risk to human health.

Zheng, X., Duan, Y., Dong, H., and Zhang, J. Effects of Dietary Lactobacillus plantarum on Growth Performance, Digestive Enzymes and Gut Morphology of Litopenaeus vannamei. Probiotics.Antimicrob.Proteins. 7-15-2017; PM: 28712022

ABSTRACT: A 15-day feeding trial was conducted to investigate the effect of dietary Lactobacillus plantarum on growth performance, digestive enzyme activities and gut morphology of juvenile Pacific white shrimp, Litopenaeus vannamei (initial body weight = 7.96 +/- 0.59 g). Four microbound diets were formulated to contain fermentation supernatant (FS), live bacteria (LB), dead bacteria (DB), and cell-free extract (CE) of L. plantarum. Results indicated that final weight was significantly higher in FS, DB, and CE

group in comparison to the control group (P < 0.05). The maximum weight gain rate (WGR) and specific growth rate (SGR) of the CE diet group were significantly higher than that of other groups (P < 0.05). The FCR of CE diet group was lower than that of the control, LB, DB, and FS diets groups (P < 0.05). The highest digestive enzyme activities (amylase, lipase, and pepsin activity) in the hepatopancreas and gut of shrimp were observed in the CE diet group. Histological study revealed that dietary CE diet could significantly increase the enterocytes height of shrimp. The administration of cell-free extract of L. plantarum could effectively improve the growth performance of L. vannamei via the improvement of digestive enzyme activities and the enterocytes height of shrimp. The results of this study will be essential to promote application of probiotics in shrimp aquaculture.

Zhou, H. B., Chen, J., Li, S., Zhang, J., Zhu, C. E., Ran, H., Luo, M., Pan, X., Hu, H., and Wu, C. Preparation of Acid-Resistant Microcapsules with Shell-Matrix Structure to Enhance Stability of Streptococcus Thermophilus IFFI 6038. J.Food Sci. 2017; 82(8):1978-1984; PM: 28696506

ABSTRACT: Microencapsulation is an effective technology used to protect probiotics against harsh conditions. Extrusion is a commonly used microencapsulation method utilized to prepare probiotics microcapsules that is regarded as economical and simple to operate. This research aims to prepare acid-resistant probiotic microcapsules with high viability after freeze-drying and optimized storage stability. Streptococcus thermophilus IFFI 6038 (IFFI 6038) cells were mixed with trehalose and alginate to fabricate microcapsules using extrusion. These capsules were subsequently coated with chitosan to obtain chitosan-trehalose-alginate microcapsules with shell-matrix structure. Chitosan-alginate microcapsules (without trehalose) were also prepared using the same method. The characteristics of the microcapsules were observed by measuring the freeze-dried viability, acid resistance, and long-term storage stability of the cells. The viable count of IFFI 6038 in the chitosan-trehalose-alginate microcapsules was 8.34 +/- 0.30 log CFU g-1 after freeze-drying (lyophilization), which was nearly 1 log units g-1 greater than the chitosan-alginate microcapsules. The viability of IFFI 6038 in the chitosan-trehalose-alginate microcapsules was 6.45 +/- 0.09 log CFU g-1 after 120 min of treatment in simulated gastric juices, while the chitosan-alginate microcapsules only measured 4.82 +/- 0.22 log CFU g-1 . The results of the long-term storage stability assay indicated that the viability of IFFI 6038 in chitosan-trehalose-alginate microcapsules was higher than in chitosan-alginate microcapsules after storage at 25 degrees C. Trehalose played an important role in the stability of IFFI 6038 during storage. The novel shell-matrix chitosan-trehalose-alginate microcapsules showed optimal stability and acid resistance, demonstrating their potential as a delivery vehicle to transport probiotics.

Zhu, J. J., Cheng, M. L., Zhou, M. Y., and Zhao, X. K. [The Effect of p-JAK1/p-STAT3 Signaling Way in Intervening NAFLD by Blueberry Probiotic Serum]. Sichuan.Da.Xue.Xue.Bao.Yi.Xue.Ban. 2017; 48(2):203-209; PM: 28612527

ABSTRACT: ***OBJECTIVES***: To explore the mechanism of interlukin-22 (IL-22)-mediated phosphor-Janus kinase-1(p-JAK1)/phosphor-signal transducer and activator of transcription 3 (p-STAT3) signaling way in the experiment of improving non-alcholic fatty liver disease (NAFLD) by blueberry probiotic serum. ***METHODS***: The rat serums with low-, medium-, and high-dose of 10% blueberry probiotics, as well as saline were prepared. NAFLD model was built by inducing normal liver cell line L-02 with free fatty acid

(FFA).NAFLD model cells were cultured with saline serum (model group), low-, medium-, and high-dose blueberry probiotics serums (low-, medium-, and high-dose serum groups) , respectively .Normal liver cell group (normal group) was cultured with saline serum . Oil Red O staining was used to detect the lipid deposition in the cells; the intracellular level of triglyceride (TG) was quantitatively determined; the gene and protein expressions of IL-22, p-JAK1, p-STAT3, sterol-regulatory element binding protein-1c (SREBP-1c) were detected by RT-PCR, Western blot and immunofluorescence methods. ***RESULTS***: Twenty-four hours after modeling, a large amount of lipid deposition could be observed in model group. Compared with normal group, model group showed lower gene and protein expression levels of IL-22, p-JAK1 and p-STAT3 (P <0.01), and higher SREBP-1c and TG levels (P <0.01).Compared with model group, TG level and the lipid deposition in low-, medium-, and high-dose blueberry probiotics serum groups were gradually reduced. High-dose serum group showed higher gene and protein expression levels of IL-22, p-JAK1, p-STAT3 and lower SREBP-1c compared with the model, low-, and medium-dose serum groups (P <0.01). No significant [CM(155.3mm]differences in gene and protein levels between low- andmedium-doseserum groups were found (P >0.05). ***CONCLUSION***: The blueberry probiotics could antagonize the NAFLD via p-JAK1/p-STAT3 signaling way.

Zhu, X. Y., Du, J., Wu, J., Zhao, L. W., Meng, X., and Liu, G. F. [Influence of Saccharomyces boulardii Sachets combined with bismuth quadruple therapy for initial Helicobacter pylori eradication]. Zhonghua Yi.Xue.Za Zhi. 8-8-2017; 97(30):2353-2356; PM: 28822453

ABSTRACT: ***Objective***: To evaluate the efficacy and safety of Saccharomyces boulardii Sachets combined with bismuth quadruple therapy for initial Helicobacter pylori(H.pylori) eradication. Methods: From March 2014 to March 2015, 240 participants from the third hospital of Hebei medical university with H. pylori infection were recruited and randomized into three groups: Quadruple therapy group received bismuth potassium citrate 220 mg bid + Rabeprazole 10 mg bid + amoxicillin 1 000 mg bid+ furazolidone 100 mg bid for 10 days. Short-term group and long-term group received the same quadruple therapy for 10 days as above, as well as Saccharomyces boulardii Sachets 500 mg bid for 14 days and 28 days, respectively. H. pylori eradication was confirmed by (13)C/(14)C-UBT at least 4 weeks after completion of therapy. And side effects were investigated during the therapy. ***Results***: The H. pylori eradication rates in quadruple therapy, short-term and long-term group were 80%, 87.5% and 87.5% by ITT analysis (P=0.321) and 92.8%, 94.6% and 95.9% by PP analysis (P=0.717), respectively. The overall side effect rate and occurrence of diarrhea and abdominal distension were significantly lower in short-term or long-term group as compared with quadruple therapy group(P=0.007, 0.003, 0.004), but there was no significant difference between the two probiotics groups. ***Conclusions***: Both short and long-term Saccharomyces boulardii Sachets reduced the overall side effect rate and occurrence of diarrhea or abdominal distension when combined with bismuth quadruple therapy for initial H. pylori eradication and no difference was observed in efficacy or safety between the two groups.

Zimmerman, T., Gyawali, R., and Ibrahim, S. Autolyse the cell in order to save it? Inducing, then blocking, autolysis as a strategy for delaying cell death in the probiotic Lactobacillus reuteri. Biotechnol.Lett. 6-16-2017; PM: 28623443

ABSTRACT: ***OBJECTIVE***: To examine whether choline and its derivatives can be used to preserve viable cells of Lactobacillus reuteri in autolytic models. ***RESULTS***: A phosphate-induced autolytic model in de Man, Rogosa and Sharpe medium (MRS) was used. Viable

cell counts were determined by plated on MRS-agar. Choline and hemicholinium-3 (HC-3) significantly blocked autolysis of L. reuteri at 360 mM and 4 mM, respectively. Viable cell counts corroborated these observations. Importantly, autolytically induced cells treated with choline and hemicholinium-3 were significantly more viable then even non-induced cells. Over-production of a known autolytic protein, spirosin, was not attenuated in the presence of choline and hemicholinium-3. ***CONCLUSION***: Inducing autolysis and then blocking it with choline and its analogs is a promising approach for retaining the viability of L. reuteri cells.

Zommiti, M., Connil, N., Hamida, J. B., and Ferchichi, M. Probiotic Characteristics of Lactobacillus curvatus DN317, a Strain Isolated from Chicken Ceca. Probiotics.Antimicrob.Proteins. 7-24-2017; PM: 28741151

ABSTRACT: The probiotic characteristics of Lactobacillus curvatus DN317, a strain isolated from chicken ceca, were evaluated. This strain was selected for study from the isolated Lactobacillus strains because it has specific anti-microbial activity against Campylobacter jejuni ATCC 33560, Camp. jejuni NCTC 11168, Listeria monocytogenes ATCC 7644, and Bacillus subtilis ATCC 8633. Lact. curvatus DN317 showed an auto-aggregation percentage of 72% and presented the highest co-aggregation with Lact. monocytogenes ATCC 7644 (68%) compared to B. subtilis ATCC 8633 (45%), Camp. jejuni ATCC 33560 (36%), and Camp. jejuni NCTC 11168 (35%). The data revealed that Lact. curvatus DN317 could survive at 0.25% bile, maintain viability at pH 2.5 for 30 min, produce biosurfactants, and adhere to Caco-2 cells. Quantification of IL-6, IL-8, IL-10, and beta-defensin 2 levels shows that Lact. curvatus DN317 induces an increase in IL-8 and beta-defensin 2 secretion, while the levels of IL-6 and IL-10 do not change. Lact. curvatus DN317 showed high levels of esterase and cysteine arylamidase activities (5); moderate levels of esterase lipase, beta-galactosidase, and alpha-galactosidase activities (4, 3); and weak levels of leucine arylamidase, valine arylamidase, and acid phosphatase activity (1). Various activities were obtained of alpha-chymotrypsin, beta-glucuronidase, beta-glucosidase, and N-acetyl-beta-glucosaminidase, which have been associated with intestinal diseases. Lact. curvatus DN317 lowered the cholesterol level in MRS with and without bile. Antibiotic susceptibility tests indicated that DN317 was sensitive to ampicillin, gentamicin, kanamycin, streptomycin, tetracycline, clindamycin, erythromycin, and vancomycin but was resistant to chloramphenicol and ciprofloxacin. These results suggest that Lact. curvatus DN317 could potentially function as a probiotic.

Zorzela, L., Ardestani, S. K., McFarland, L. V., and Vohra, S. Is there a role for modified probiotics as beneficial microbes: a systematic review of the literature. Benef.Microbes. 9-8-2017; 1-16; PM: 28884589

ABSTRACT: Our objective was to conduct a systematic review and meta-analysis for the use of modified (heat-killed or sonicated) probiotics for the efficacy and safety to prevent and treat various diseases. Recent clinical research has focused on living strains of probiotics, but use in high-risk patients and potential adverse reactions including bacteremia has focused interest on alternatives to the use of live probiotics. We searched MEDLINE/PubMed, Embase, Cochrane Central Register of Controlled Trials, CINAHL, Alt Health Watch, Web of Science, Scopus, PubMed, from inception to February 14, 2017 for randomised controlled trials involving modified probiotic strains. The primary outcome was efficacy to prevent or treat disease and the secondary outcome was incidence of adverse events. A total of 40 trials were included (n=3,913): 14 trials (15 arms

with modified probiotics and 20 control arms) for the prevention of diseases and 26 trials (29 arms with modified probiotics and 32 control arms) for treatment of various diseases. Modified microbes were compared to either placebo (44%), or the same living probiotic strain (39%) or to only standard therapies (17%). Modified microbes were not significantly more or less effective than the living probiotic in 86% of the preventive trials and 69% of the treatment trials. Modified probiotic strains were significantly more effective in 15% of the treatment trials. Incidence rates of adverse events were similar for modified and living probiotics and other control groups, but many trials did not collect adequate safety data. Although several types of modified probiotics showed significant efficacy over living strains of probiotics, firm conclusions could not be reached due to the limited number of trials using the same type of modified microbe (strain, daily dose and duration) for a specific disease indication. Further research may illuminate other strains of modified probiotics that may have potential as clinical biotherapeutics.

Zununi, Vahed S., Barzegari, A., Rahbar, Saadat Y., Goreyshi, A., and Omidi, Y. Leuconostoc mesenteroides-derived anticancer pharmaceuticals hinder inflammation and cell survival in colon cancer cells by modulating NF-kappaB/AKT/PTEN/MAPK pathways. Biomed.Pharmacother. 8-14-2017; 94:1094-1100; PM: 28821160

ABSTRACT: Promising results from different studies on the effect of probiotics in cancer prevention and therapy have so far been reported. However, the molecular mechanism of the interaction of probiotics with cancer cells is yet to be fully understood. In the present study, Leuconostoc mesenteroides was isolated from traditional dairy products, and its probiotic characteristics were determined. HT-29 cells were treated with conditioned-medium of designated bacteria and the cell apoptosis was studied at cellular and molecular level using DAPI staining, flow cytometry, DNA ladder assays, and real-time quantitative-PCR (q-PCR). Based on our findings, L. mesenteroides promoted apoptosis in colon cancer cell line by upregulation of MAPK1, Bax, and caspase 3, and downregulation of AKT, NF-kappaB, Bcl-XL expressions and some key oncomicroRNAs such as miRNA-21 and miRNA-200b significantly (p</=0.03). The results indicated the likelihood of the examined probiotic as an alternative or complementary treatment modality in signaling-targeted cancer therapy.



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