Recent Studies on Immunity & Probiotics

STUDIES (2017-2020)

1. Immunization With Mycobacterium Vaccae Induces An Anti-Inflammatory Milieu In The CNS: Attenuation Of Stress-Induced Microglial Priming, Alarmins And Anxiety

A new probiotic-based immunization treatment to protect against post-traumatic stress disorder (PTSD), anxiety, and depression may be on the horizon. According to researchers, immunization with beneficial bacteria can have long-lasting anti-inflammatory effects on the brain, making it more resilient to the physical and behavioral effects of stress. Researchers have found that in rodents this particular bacterium, Mycobacterium vaccae, actually shifts the environment in the brain towards an anti-inflammatory state.

Source: Matthew G Frank, Department of Psychology and Neuroscience and Center for Neuroscience, University of Colorado Boulder, USA. Immunization with mycobacterium vaccae induces an anti-inflammatory milieu in the cns: attenuation of stress-induced microglial priming, alarmins and anxiety-like behavior. Brain, Behavior, and Immunity, Volume 73, October 2018, Pages 352-363. https://doi.org/10.1016/j.bbi.2018.05.020

2. Yogurt And Other Fermented Foods As Sources Of Health-Promoting Bacteria

Epidemiological studies have shown that the consumption of fermented foods is associated with reduced risks of type 2 diabetes, metabolic syndrome, and heart disease, along with improved weight management. The microorganisms present in these foods are suggested to contribute to these health benefits. Among these are the yogurt starter culture organisms ***Streptococcus thermophilus*** and ***Lactobacillus delbrueckii subsp bulgaricus*** as well as ***Bifidobacterium*** and ***Lactobacillus*** strains that are added for their probiotic properties. In contrast, for other fermented foods, such as sauerkraut, kimchi, and miso, fermentation is initiated by autochthonous microbes present in the raw material***. Several studies have shown that consumption of yogurt and other fermented foods may improve intestinal and extra-intestinal health and might be useful in improving lactose mal-absorption, treating infectious diarrhea, reducing the duration and incidence of respiratory infections, and enhancing immune and anti-inflammatory responses.***

Source: Robert Hutkins, Department of Food Science and Technology, University of Nebraska, USA. Yogurt and other fermented foods as sources of health-promoting bacteria. Nutrition Reviews, Volume 76, Issue Supplement_1, December 2018, Pages 4–15, https://doi.org/10.1093/nutrit/nuy056

3. A Systematic Evaluation Of The Immunomodulatory And Functional Properties Of Probiotic Bifidobacterium Breve BR03 (DSM 16604) Lactobacillus Plantarum LP01 (LMG P-21021)

This study was conducted to evaluate the capability of the bacterial strains Bifidobacterium breve BR03 (DSM 16604) and Lactobacillus plantarum LP01 (LMG P-21021) which induce an in vitro immune response in the peripheral blood mononuclear cells (PBMCs) of healthy adult volunteers and to modify the state of oxidative stress and intestinal permeability of in vitro cell models. It was found that the species Bifidobacterium breve could be fruitfully employed in both IBS and chronic gut dysbiosis associated with impaired mucosal permeability like in coeliac disease and thus potentially contrasting the progression of irritable bowel diseases in predisposed patients.

Source: Luca Mogna, Research and Development, Probiotical Research Ltd, Italy. A systematic evaluation of the immunomodulatory and functional properties of probiotic Bifidobacterium breve BR03 (DSM 16604) Lactobacillus plantarum LP01 (LMG P-21021). J Prob Health. 7:214. DOI: 10.35248/2329-8901.19.7.214

4. Probiotic Lactobacillus Johnsonii BS15 Promotes Growth Performance, Intestinal Immunity And Gut Microbiota

The present study was conducted to understand the growth-promoting effects of Lactobacillus Johnsonii on piglets. It also determined the effects of *L. johnsonii* BS15 and a commercial probiotic strain, *Bacillus subtilis* JS01.

Seventy-two suckling piglets (1 ± 2-day-old) were divided into three groups and fed with diets supplemented with 1×10^6 colony-forming units (cfu) L. johnsonii per gram of feed (BS15 group); 1×10^6 cfu Bacillus subtilis per gram of feed (JS01 group); or de Man, Rogosa, and Sharpe liquid medium (control group) 35 days. Compared with Bacillus subtilis, L. johnsonii significantly improved the daily weight gain and diarrhea index of the piglets. The *L. johnsonii* group had higher fecal sIgA levels, whereas the Bacillus subtilis group had high fecal sIgA levels only after 35 days of treatment. Additionally, ***L. johnsonii altered T cell subsets in peripheral blood by significantly increasing the $CD3^+CD4^+$ T cell percentage and $CD3^+CD4^+/CD3^+CD8^+$ ratio and decreasing the $CD3^+CD8^+$ T cell percentage.*** Moreover, L. johnsonii exerted better beneficial effects on fecal microbiota than Bacillus subtilis. Specifically, the L. johnsonii group had markedly increased ***Clostridium, Peptococcus, and Lactobacillus*** populations on days 7 and 21 of treatment and reduced *Escherichia coli* populations on day 35 of treatment. These findings indicate that L. johnsonii can be applied as a probiotic that promotes growth performance and controls diarrhea in piglets.

Source: Xueqin Ni, College of Veterinary Medicine, Sichuan Agricultural University, Chengdu, Sichuan, China. Probiotic Lactobacillus Johnsonii BS15 Promotes Growth Performance, Intestinal Immunity, And Gut Microbiota In Piglets. Probiotics & Antimicro. Prot. 12, 184–193 (2020). https://doi.org/10.1007/s12602-018-9511-y

5. Growth Promotion And Immune Stimulation In Nile Tilapia, Oreochromis Niloticus, Fingerlings Following Dietary Administration Of A Novel Marine Probiotic, Psychrobacter Maritimus

A 50-day feeding trial was conducted to evaluate the effects of dietary supplementation of a novel marine psychrotrophic bacterium, ***Psychrobacter maritimus S***, on growth performance and immune responses of Nile tilapia (*Oreochromis niloticus*) fingerlings.

Triplicate groups of Nile tilapia (10 fish each) were fed for 50 days with three different diets: T_0 (without probiotic, negative control), $T_{0.5}$ (supplemented with 3.3×10^8 CFU g^{-1} *P. maritimus* S), and T_1 (supplemented with 6.6×10^8 CFU g^{-1} *P. maritimus* S). The test diets were fed to fish at a daily rate of 3% of their live weights, three times per day. On the 50th day, fish were weighed and blood samples were collected to determine the main nonspecific humoral and cellular immune responses and digestive enzymes (protease, amylase, and lipase). Fish performance (weight gain, specific growth rate, feed conversion ratio, protein efficiency ratio, and protein productive value) was also calculated.

Growth rates and digestive enzyme activity were significantly increased with increasing dietary P. maritimus S up to 0.5%, and levelled off with further increase in bacterial concentrations. Phagocytic activity, lysozyme activity, alternative complement hemolysis, and hematological parameters were also significantly increased ($P < 0.05$) with increasing P. maritimus S concentration to 0.5%, followed by a slight decrease ($P > 0.05$) at 1% level. ***The expression of interleukin-4 and interleukin-12 genes was significantly upregulated, while heat shock protein gene was downregulated, with dietary supplementation of P. maritimus S up to 0.5% level. These results suggest that 0.5% of dietary Psychrobacter maritimus S supplementation could be considered as a novel probiont for optimum growth performance and immune response of Nile tilapia fingerlings.***

Source: Sarah O. Makled, Oceanography Department, Faculty of Science, Alexandria University, Moharem Bek, Alexandria, Egypt. Growth Promotion And Immune Stimulation In Nile Tilapia, Oreochromis Niloticus, Fingerlings Following Dietary Administration Of A Novel Marine Probiotic, Psychrobacter Maritimus S. Probiotics & Antimicro. Prot. 12, 365–374 (2020). https://doi.org/10.1007/s12602-019-09575-0

6. Effects Of Bacillus Cereus PAS38 On Immune-Related Differentially Expressed Genes Of Spleen

This study mainly explored the immunomodulatory mechanisms of the ***probiotic Bacillus cereus PAS38 (PB)*** on broiler spleen.

A total of 120 avian white feather broilers were randomly divided into 4 groups (N = 30), as follows: control (CNTL, fed with basal diet), PB (fed with diet supplemented with probiotic B. cereus PAS38), vaccine (VAC, fed with basal diet and injected with Newcastle disease virus vaccine), and vaccine + PB group (PBVAC, fed with basal diet supplemented with B. cereus PAS38 and injected with NDV vaccine). The experiment was conducted for 42 days. Twelve spleens were collected from four different groups, weighed, and cut into histological sections, and transcriptome analysis was performed using RNA-seq.

Results of the spleen and histological section relative weights showed that feeding with probiotic B. cereus PAS38 and vaccination had a similar tendency to promote spleen development. ***Compared with the CNTL group, 21 immune-related genes were significantly downregulated in the PB and PBVAC groups. These genes were mainly involved in attenuating inflammatory response. The upregulated antimicrobial peptide NK-lysin and guanylate-binding protein 1 expression levels indicated that this strain enhanced the body's antimicrobial capacity. B. cereus PAS38 also amplified the broilers' immune response to the vaccine, which mainly reflected on nonspecific immunity. Hence, the researchers observe that, probiotic B. cereus PAS38 can regulate and promote the immune function of broilers.***

Source: Kangcheng Pan, College Of Veterinary Medicine, Sichuan Agricultural University, Huimin Road, Wengjiang District, Chengdu, Sichuan, People's Republic Of China. Effects Of Bacillus Cereus PAS38 On Immune-Related Differentially Expressed Genes Of Spleen In Broilers. Probiotics & Antimicro. Prot. 12, 425–438 (2020). https://doi.org/10.1007/s12602-019-09567-0

7. Effect Of Encapsulated Lactobacillus Bulgaricus On Innate Immune System And Hematological Parameters In Rainbow Trout (Oncorhynchus Mykiss), Post-Administration Of Probiotic

The present study was conducted to investigate the effects of probiotic (Pb) and encapsulated Lactobacillus bulgaricus on hematological and immunological factors after lead toxicity in rainbow trout (Oncorhynchus mykiss).

Two hundred and forty fish weighing about 16 ± 3.8 g were divided randomly in to four groups including two groups which were fed by a diet containing ~ 10^8 CFU g^{-1}*Lactobacillus bulgaricus* and encapsulated *Lactobacillus bulgaricus* bacteria and also the third group diet without *Lactobacillus bulgaricus*. After 45 days, in addition to probiotic (~ 10^8 CFU g^{-1}), 500 µg kg of lead nitrate was added to the food of the three groups for 21 days. The fourth group (control) was first fed to the normal diet for 45 days then exposed to Pb. Blood samples were collected at days 45, 52, 59, and 66, and hematological and some immunological parameters were assessed.

Results showed that Hemogolbin, red blood cells, white blood cells, and lysozyme activity in the two probiotics groups were increased significantly up to 45 day, but followed by a decreasing trend by adding Pb. Complement and bactericidal activities were enhanced significantly in the bulgaricus group. Respiratory burst activity at day 45 in group bulgaricus had significant increase and decreased in all groups particularly after Pb exposure. ***The achieved data shows that microencapsulation of probiotics with alginate-chitosan may be a suitable method to improve the fish condition against heavy metal.***

Source: Takavar Mohammadian, Department of Clinical Sciences, Faculty of Veterinary Medicine, Shahid Chamran University of Ahvaz, Iran. Effect Of Encapsulated Lactobacillus Bulgaricus On Innate Immune System And Hematological Parameters In Rainbow Trout (Oncorhynchus Mykiss), Post-Administration Of Pb. Probiotics & Antimicro. Prot. 12, 375–388 (2020). https://doi.org/10.1007/s12602-019-09544-7

8. Boosted Growth Performance, Mucosal And Serum Immunity, And Disease Resistance Nile Tilapia (Oreochromis Niloticus) Fingerlings Using Corncob Derived Xylooligosaccharide And Lactobacillus Plantarum

The present work studied the effects of corncob-derived ***xylooligosaccharides (CDXOS)*** and **Lactobacillus plantarum CR1T5 (LP)** integrated into fish diets (diet 1 (0—control), diet 2 (10 g kg^{-1} CDXOS), diet 3 (10^8 CFU g^{-1}*L. plantarum* CR1T5), diet 4 (10 g kg^{-1} CDXOS +10^8 CFU g^{-1}*L. plantarum* CR1T5)) on growth performance, innate immune parameters, and disease resistance of ***Nile tilapia (Oreochromis niloticus)***.

The results indicated that fish fed CDXOS and LP had significantly improved final weight (FW), weight gain (WG), specific growth rate (SGR), and feed conversion ratio (FCR). However, no significant difference in survival rate was observed between specimens fed the supplemented diets and the control. Regarding skin mucus, the dietary inclusion of CDXOS and LP significantly increased lysozyme and peroxidase activities compared with the control. ***Similarly, significant increases in serum lysozyme, peroxidase, alternative complement, phagocytosis, and respiratory burst activities were observed in the fish fed the supplemented diets.*** However, no significant differences were found in these parameters between fish fed CDXOS and LP diets. For the challenge test, diet 4 produced a higher relative percentage of survival (RPS) and resistance to *S. agalactiae* than fish from the other experimental groups. The results suggest that CDXOS and *L. plantarum* CR1T5 are viable considerations for potential feed-additive sources.

Source: Maria Ángeles Esteban, Fish Innate Immune System Group, Department of Cell Biology & Histology, Faculty of Biology, Regional Campus of International Excellence "Campus Mare Nostrum", University of Murcia, Murcia, Spain. Boosted Growth Performance, Mucosal And Serum Immunity, And Disease Resistance Nile Tilapia (Oreochromis Niloticus) Fingerlings Using Corncob-Derived Xylooligosaccharide And Lactobacillus Plantarum CR1T5. Probiotics & Antimicro. Prot. 12, 400–411 (2020). https://doi.org/10.1007/s12602-019-09554-5

9. Lactobacillus Acidophilus And L. Plantarum Improve Health Status, Modulate Gut Microbiota And Innate Immune Response

This study investigated the combined effects of two most potent probiotic bacteria ***Lactobacillus acidophilus*** and ***Lactobacillus plantarum*** on overall health and immune status of freshwater crayfish, marron under laboratory conditions.

Study results show that there are no significant differences in weight gain, however, probiotic feed significantly enhanced some hemolymph parameters and biochemical composition of tail muscle. Histology data revealed better hepatopancreas health and higher microvilli counts in the marron gut fed probiotic diet. The probiotic bacteria triggered significant shift of microbial communities at different taxa level, mostly those reported as beneficial for crayfish. ***The probiotic diet also enriched the metabolic functions and genes associated with innate immune response of crayfish. Further correlation analysis revealed significant association of some taxa with increased activity for hemolymph and immune genes. Therefore, dietary Lactobacillus supplementation can modulate the overall health and immunity as well as gut microbial composition and interaction network between gut microbiota and immune system in crayfish.***

Source: Md Javed Foysal, School of Molecular and Life Sciences, Curtin University, Australia. Lactobacillus Acidophilus And L. Plantarum Improve Health Status, Modulate Gut Microbiota And Innate Immune Response Of Marron (Cherax Cainii). Sci Rep 10, 5916 (2020). https://doi.org/10.1038/s41598-020-62655-y

10. Effect Of A Potential Probiotic Candidate Enterococcus Faecalis-1 On Growth Performance, Intestinal Microbiota, And Immune Response Of Commercial Broiler

The probiotic effect of ***Enterococcus faecalis-1*** (isolated from healthy chickens) on growth performance, immune response, and modulation of the intestinal microbiota of broilers was assessed with a total of 100-day-old commercial Cobb chicks.

The chicks were randomly divided into two equal groups. The control group received a basal diet, while the test group received a basal diet and was orally supplied with *E. faecalis* at a dose of 10^8 CFU/bird/day.

Results showed that *E. faecalis*-1 supplement significantly improved the body weight and feed conversion ratio of treated broilers compared with the control ones. The mortality percentage was reduced in *E. faecalis*-1-supplemented group. ***The total IgY serum level was significantly increased in broilers receiving E. faecalis-1 supplement (7.1 ± 0.39) compared with the control group (5.8 ± 0.3), while the serum avidin level was significantly decreased in E. faecalis-1-supplemented broilers (76 ± 11.1).*** There was no significant change in the immune response towards avian influenza and Newcastle vaccines in both groups. The total Lactobacillus and Enterococcus counts were significantly higher in the cecal contents of broilers given E. faecalis-1 than those that received the control treatment. E. faecalis-1 supplement enhanced the enzyme activities, antioxidant system, and liver functions of treated broilers compared with those in the control group. ***Collectively, these results showed that E. faecalis-1 could promote growth performance and immunological status and convey beneficial modulation of the cecal microbiota in broilers.***

Source: A. A. Shehata, Avian And Rabbit Diseases Department, Faculty Of Veterinary Medicine, University Of Sadat City, Sadat City, Egypt. Effect Of A Potential Probiotic Candidate Enterococcus Faecalis-1 On Growth Performance, Intestinal Microbiota, And Immune Response Of Commercial Broiler Chickens. Probiotics & Antimicro. Prot. 12, 451–460 (2020). https://doi.org/10.1007/s12602-019-09557-2

11. Nasal Priming With Lactobacillus Rhamnosus CRL1505 Stimulates Mononuclear Phagocytes Of Immunocompromised Malnourished Mice: Improvement Of Respiratory Immune Response

The effect of **Lactobacillus rhamnosus CRL1505 (Lr)** on ***macrophages (Ma)*** and ***dendritic cells (DC)*** in the orchestration of anti-pneumococcal immunity was studied using malnutrition and pneumococcal infection mouse models. ***Monocytes (Mo)***, Ma, and DC in two groups of malnourished mice fed with ***balanced diet (BCD)*** were studied through flow cytometry; one group was nasally administered with Lr (BCD+Lr group), and the other group was not (BCD group). ***Well-nourished (WNC)*** and ***malnourished (MNC)*** mice were used as controls.

Malnutrition affected the number of respiratory and splenic mononuclear phagocytes. The BCD+Lr treatment, unlike BCD, was able to increase and normalize lung Mo and Ma. The BCD+Lr mice were also able to upregulate the expression of the activation marker MHC II in lung DC and to improve this population showing a more significant effect on $CD11b^+$ DC subpopulation. At post-infection, lung Mo values were higher in BCD+Lr mice than in BCD mice and similar to those obtained in WNC group. Although both repletion treatments showed similar values of lung Ma post-infection, the Ma activation state in BCD+Lr mice was higher than that in BCD mice. Furthermore, BCD+Lr treatment was able to normalize the number and activation of splenic Ma and DC after the challenge.

Lr administration stimulates respiratory and systemic mononuclear phagocytes. Stimulation of Ma and DC populations would increase the microbicide activity and improve the adaptive immunity through its antigen-presenting capacity. Thus, Lr contributes to improved outcomes of pneumococcal infection in immunocompromised hosts.

Source: Susana Alvarez, Laboratorio De Inmunobiotecnología, Centro De Referencia Para Lactobacilos (CERELA-CONICET), Chacabuco, San Miguel Detucumán And Instituto De Bioquímica Aplicada, Facultad De Bioquímica, Química Y Farmacia, Universidad Nacional De Tucumán, Balcarce, San Miguel Detucumán, Tucumán, Argentina. Nasal Priming With Lactobacillus Rhamnosus CRL1505 Stimulates Mononuclear Phagocytes Of Immunocompromised Malnourished Mice: Improvement Of Respiratory Immune Response. Probiotics & Antimicro. Prot. 12, 494–504 (2020). https://doi.org/10.1007/s12602-019-09551-8

12. In Vivo Implications Of Potential Probiotic Lactobacillus Reuteri LR6 On The Gut And Immunological Parameters As An Adjuvant Against Protein Energy Malnutrition

The present study investigated the impact of *probiotic Lactobacillus reuteri LR6* on the gut and systemic immunity using protein energy malnourished (PEM) murine model.

Thirty male Swiss albino mice were divided into five groups: control (C), malnourished (M), probiotic fermented milk (PFM), skim milk (SM), and bacterial suspension (BS) with six mice per group. Group C was fed with conventional diet throughout the study while the other groups were fed with protein calorie restricted diet until the development of malnutrition. After development of malnutrition, group M was continued with the restricted diet while other groups were fed with re-nourished diet supplemented with PFM, SM, and BS for 1 week, respectively. Thereafter, mice were sacrificed and different histological, microbiological, and immunological parameters were studied.

Probiotics feeding in PEM model as fermented product or bacterial suspension improved the intestinal health in terms of intact morphology of colonic crypts, normal goblet cells, and intact lamina propria with no inflammation in large intestine, absence of fibrosis, and no inflammation in spleen. ***The number of secretory IgA$^+$ cells was significantly higher in group PFM and BS. Also, increase in the phagocytic percentage of the macrophages and bone marrow derived dendritic cells (DCs) were observed in the PFM and BS group in comparison to the group M. In comparison to the group M and SM, lactobacilli, bifidobacteria, and Firmicutes counts were significantly higher in the group PFM and BS.*** This study concludes that probiotic supplementation to re-nutrition diet could emerge as wonder therapeutics against PEM.

Source: Sheenam Garg, Dairy Microbiology Division, National Dairy Research Institute, Karnal, India. In Vivo Implications Of Potential Probiotic Lactobacillus Reuteri LR6 On The Gut And Immunological Parameters As An Adjuvant Against Protein Energy Malnutrition. Probiotics & Antimicro. Prot. 12, 517–534 (2020). https://doi.org/10.1007/s12602-019-09563-4