Dietary modulation of gut functional ecology studied by fecal metabonomics.

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Abstract

A major source of intestinal metabolites results from both host and microbial processing of dietary nutrients. (1)H NMR-based metabolic profiling of mouse feces was carried out over time in different microbiome mouse models, including conventional (n = 9), conventionalized (n = 10), and "humanized" gnotobiotic mice inoculated with a model of human baby microbiota (HBM, n = 17). HBM mice were supplemented with Lactobacillus paracasei with (n = 10) and without (n = 7) prebiotics. Animals not supplemented with prebiotics received a diet enriched in glucose and lactose as placebo. In conventionalized animals, microbial populations and activities converged in term of multivariate mapping toward conventional mice. Both groups decreased bacterial processing of dietary proteins when switching to a diet enriched in glucose and lactose, as described with low levels of 5-aminovalerate, acetate, and propionate and high levels of lysine and arginine. The HBM model differs from conventional and conventionalized microbiota in terms of type, proportion, and metabolic activity of gut bacteria (lower short chain fatty acids (SCFAs), lactate, 5-aminovalerate, and oligosaccharides, higher bile acids and choline). The probiotics supplementation of HBM mice was associated with a specific amino acid pattern that can be linked to L. paracasei proteolytic activities. The combination of L. paracasei with the galactosyl-oligosaccharide prebiotics was related to the enhanced growth of bifidobacteria and lactobacilli, and a specific metabolism of carbohydrates, proteins, and SCFAs. The present study describes how the assessment of metabolic changes in feces may provide information for studying nutrient-microbiota relationships in different microbiome mouse models.

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Supplemental Content

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Potential role of the intestinal microbiota of the mother in neonatal immune education.
Abstract

Mucosal dendritic cells are at the heart of decision-making processes that dictate immune reactivity to intestinal microbes. They ensure tolerance to commensal bacteria and a vigorous immune response to pathogens. It has recently been demonstrated that the former involves a limited migration of bacterially loaded dendritic cells from the Peyer's patches to the mesenteric lymph nodes. During lactation, cells from gut-associated lymphoid tissue travel to the breast via the lymphatics and peripheral blood. Here, we show that human peripheral blood mononuclear cells and breast milk cells contain bacteria and their genetic material during lactation. Furthermore, we show an increased bacterial translocation from the mouse gut during pregnancy and lactation and the presence of bacterially loaded dendritic cells in lactating breast tissue. Our observations show bacterial translocation as a unique physiological event, which is increased during pregnancy and lactation. They suggest endogenous transport of intestinally derived bacterial components within dendritic cells destined for the lactating mammary gland. They also suggest neonatal immune imprinting by milk cells containing commensal-associated molecular patterns.

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Supplemental Content


Application of probiotics in food products--challenges and new approaches.

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Abstract

The probiotic research conducted over the past 20 years has resulted in a valuable source of data related to health beneficial effects of probiotics. Nevertheless, documentation of probiotic benefits remains challenging, especially in functional foods that are designed for the generally healthy population that, however, regularly experiences episodes of 'suboptimal' health. In addition, in view of today's application of probiotics in an increasing variety of food matrixes, process optimization and product design need to take into account cell viability and
probiotic function altogether. To meet this challenge, medium to high-throughput bioassays - based on the identification of active compounds and their mechanism of action - have to be developed and their predictive value established. Together with validated biomarkers for health and disease, this should help rationalize probiotic product development and associated health claim substantiation in human studies.

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Supplemental Content

HspR mutations are naturally selected in Bifidobacterium longum when successive heat shock treatments are applied.

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Abstract

The development of molecular tools allowed light to be shed on several widespread genetic mechanisms aiming at limiting the effect of molecular damage on bacterial survival. For some bacterial taxa, there are limited tools in the genetic toolbox, which restricts the possibilities to investigate the molecular basis of their stress response. In that case, an alternative strategy is to study genetic variants of a strain under stress conditions. The comparative study of the genetic determinants responsible for their phenotypes, e.g., an improved tolerance to stress, offers precious clues on the molecular mechanisms effective in this bacterial taxon. We applied this approach and isolated two heat shock-tolerant strains derived from Bifidobacterium longum NCC2705. A global analysis of their transcriptomes revealed that the dnaK operon and the clpB gene were overexpressed in both heat shock-tolerant strains. We sequenced the hspR gene coding for the negative regulator of dnaK and clpB and found point mutations affecting protein domains likely responsible for the binding of the regulators to the promoter DNA. Complementation of the mutant strains by the wild-type regulator hspR restored its heat sensitivity and thus demonstrated that these mutations were responsible for the observed heat tolerance phenotype.

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The effect of Bifidobacterium lactis on the growth of infants: a pooled analysis of randomized controlled studies.

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Abstract

BACKGROUND/AIMS: Breast milk is the best source of nutrition for the growth of the newborn infant. It is therefore essential that mothers who cannot breastfeed or choose not to are provided with alternatives that closely match the composition and functionality of breast milk. This study aimed to investigate the growth effects of probiotic-supplemented formulas on both healthy and vulnerable populations of infants.

METHODS: A meta-analysis of data from 5 randomized controlled clinical trials that included infants fed formulas containing a probiotic Bifidobacterium lactis CNCM I-3446 was performed (n = 525). A sub-analysis was performed among infants of HIV-positive mothers (n = 120). Growth measurements (gain in weight and body mass index, BMI, from enrollment to 120 days) were compared between infants fed a formula containing B. lactis and those fed a control formula. Changes in length and Z-scores were also compared.

RESULTS: Formula with B.lactis was demonstrated to be at least as good as formula without B. lactis in the meta-analysis of 5 studies. The lower boundary of the 95% confidence interval (CI) of the differences in mean weight gain (95% CI 0.09-2.93 g/day) was above the predefined non-inferiority margin of -3.0 g/day. Moreover, among infants with HIV-positive mothers, weight gain of those taking B. lactis was significantly higher than of those not taking B. lactis, by 3.1 g/day (95% CI 0.4-5.8 g/day, p = 0.0226) and the BMI gains were significantly higher, by 6.4 g/m(2)/day (95% CI 0.3-12.5 g/m(2)/day, p = 0.0400). The corresponding weight for age and BMI Z-scores were also significantly higher, by 0.37 (95% CI 0.03-0.71, p = 0.0308) and by 0.42 (95% CI 0.02-0.83, p = 0.0377), respectively, whereas differences in length gain or length-for-age Z-score were not significant. Among infants in the non-HIV mothers group, there were no significant differences between infants fed formulas with or without B. lactis, for any of the growth parameters.

CONCLUSIONS: The analysis suggests that B. lactis may have a positive effect on growth in vulnerable populations, specifically in infants born to mothers with HIV.
Probiotic yogurt in the elderly with intestinal bacterial overgrowth: endotoxaemia and innate immune functions.

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Abstract

A study was conducted in healthy elderly living independently in senior housing to assess the impact of a probiotic yoghurt supplement on small intestinal bacterial overgrowth. Twenty-three participants with positive and thirteen participants with negative hydrogen breath test were studied before and after a period of 4 weeks of probiotic yoghurt administration. Intestinal permeability, plasma endotoxin levels, phagocytic activity of leucocytes, cytokine production by monocytes and free radical response of neutrophils were determined. Intestinal permeability was similar for the two groups and was unaffected by probiotic treatment. Both plasma endotoxin levels and the basal phagocytic activity of leucocytes decreased after yoghurt intake in the two groups. Exposure of monocytes and neutrophils ex vivo led to an increased cytokine response and free radical response, respectively. The normalisation of the various cytokine responses was more apparent in the group with positive breath test. In addition, the plasma levels of lipopolysaccharide binding protein and soluble CD14, lipopolysaccharide pattern recognition receptors and surrogate markers of lipopolysaccharide permeability were diminished by the end of the study. In conclusion, probiotic administration in the elderly normalises the response to endotoxin, and modulates activation markers in blood phagocytes, and therefore may help reduce low-grade chronic inflammation.

Panorganismal gut microbiome-host metabolic crosstalk.
Coevolution shapes interorganismal crosstalk leading to profound and diverse cellular and metabolic changes as observed in gut dysbiosis in human diseases. Here, we modulated a simplified gut microbiota using pro-, pre-, and synbiotics to assess the depth of systemic metabolic exchanges in mice, using a multicompartmental modeling approach with metabolic signatures from 10 tissue/fluid compartments. The nutritionally induced microbial changes modulated host lipid, carbohydrate, and amino acid metabolism at a panorganismal scale. Galactosyl-oligosaccharides reduced lipogenesis, triacylglycerol incorporation into lipoproteins and triglyceride concentration in the liver and the kidney. Those changes were not correlated with decreased plasma lipoproteins that were specifically induced by L. rhamnosus supplementation. Additional alteration of transmethylation metabolic pathways (homocysteine-betaine) was observed in the liver and the pancreas following pre- and synbiotic microbial modulation, which may be of interest for control of glucose metabolism and insulin sensitivity. Probiotics also reduced hepatic glycogen and glutamine and adrenal ascorbate with inferred effects on energy homeostasis, antioxidation, and steroidogenesis. These studies show the breadth and the depth of gut microbiome modulations of host biochemistry and reveal that major mammalian metabolic processes are under symbiotic homeostatic control.

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Supplemental Content


**Gut decontamination with norfloxacin and ampicillin enhances insulin sensitivity in mice.**

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Abstract
Recent data suggest that gut microbiota plays a significant role in fat accumulation. However, it is not clear whether gut microbiota is involved in the pathophysiology of type-2 diabetes. To address this issue, we modulated gut microbiota with two combinations of antibiotics in two different mouse models with insulin resistance. Treatment with norfloxacin and ampicillin for 2 weeks reduced the cecal bacterial DNA below the level of detection in ob/ob, diet-induced obese and insulin resistance (DIO) mice, and significantly improved fasting glycemia and oral glucose tolerance of the treated animals. The enhanced insulin sensitivity was independent of food intake or adiposity because pair-fed ob/ob mice were as glucose intolerant as the untreated ob/ob mice. The reduced liver triglycerides, increased liver glycogen and improved glucose tolerance in the treated mice indicate broad impacts on metabolism by gut decontamination. The treatment with non-absorbable antibiotics polymyxin B and neomycin significantly modified cecal microbiota profile in the DIO mice, and the modified intestinal microbiota was associated with a gradual reduction in glycemia during a washout period. In summary, modulation of gut microbiota ameliorated glucose intolerance in mice and altered the hormonal, inflammatory and metabolic status of the host.

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Supplemental Content


Effect of dietary modulation of intestinal microbiota on reproduction and early growth.

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Abstract

An optimal balance of intestinal microbiota is necessary for digestive and immune health. Poor performance, susceptibility to infections, and decreased growth rate can be signs of an imbalanced microbiome. Dietary strategies to establish and maintain an optimal balance of microbiota include prebiotics (food for indigenous microbiota in the gastrointestinal tract) and probiotics (beneficial microbiota consumed by the animal). Recent research regarding use of probiotics and prebiotics in reproducing and growing livestock and companion animals is summarized. Documented benefits include prevention of diarrhea, decreased mortality, establishment of a healthy microbiota balance, and improved immune function.

PMID: 18533245 [PubMed - indexed for MEDLINE]
Gut microbiota modulation with norfloxacin and ampicillin enhances glucose tolerance in mice.

Membrez M, Blancher F, Jaquet M, Bibiloni R, Cani PD, Burcelin RG, Corthesy I, Macé K, Chou CJ.

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Abstract

Recent data suggest that the gut microbiota plays a significant role in fat accumulation. However, it is not clear whether gut microbiota is involved in the pathophysiology of type 2 diabetes. To assess this issue, we modulated gut microbiota via antibiotics administration in two different mouse models with insulin resistance. Results from dose-determination studies showed that a combination of norfloxacin and ampicillin, at a dose of 1 g/L, maximally suppressed the numbers of cecal aerobic and anaerobic bacteria in ob/ob mice. After a 2-wk intervention with the antibiotic combination, both ob/ob and diet-induced obese and insulin-resistant mice showed a significant improvement in fasting glycemia and oral glucose tolerance. The improved glycemic control was independent of food intake or adiposity because pair-fed ob/ob mice were as glucose intolerant as the control ob/ob mice. Reduced liver triglycerides and increased liver glycogen correlated with improved glucose tolerance in the treated mice. Concomitant reduction of plasma lipopolysaccharides and increase of adiponectin further supported the antidiabetic effects of the antibiotic treatment in ob/ob mice. In summary, modulation of gut microbiota ameliorated glucose tolerance of mice by altering the expression of hepatic and intestinal genes involved in inflammation and metabolism, and by changing the hormonal, inflammatory, and metabolic status of the host.

Systemic inflammatory markers in older persons: the effect of oral nutritional supplementation with prebiotics.

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Abstract

OBJECTIVE: To evaluate the effect of oral nutritional supplementation with and without oligosaccharides on gut bacteriology, in particular the bifidogenic flora, and on immunology and inflammatory parameters in older persons at risk of malnutrition.

DESIGN: Prospective, randomized, double-blind, controlled study.

SETTING: Division of Geriatric Medicine, St. Louis University, Missouri, United States. Participants: Seventy-four community dwelling elderly and/or nursing home subjects (age superior 70 y; 84 +/- 7 years) either undernourished or at risk of undernutrition. Intervention: Daily liquid supplements, with (1.3 g/250 ml) and without oligosaccharides (OS) for 12 weeks.

MEASUREMENTS: Nutritional evaluation, serum immunoglobulins, lymphocyte subsets, various cytokines and the endotoxin soluble receptor CD14 (sCD14) in serum, and cytokines specific mRNA in peripheral blood mononuclear cells at baseline and 12 weeks, and fecal bacteriologicy.

RESULTS: Specific mRNA extracted from blood leucocytes showed a different level of pro-inflammatory gene activation: TNF-alpha mRNA and IL-6 mRNA diminished in the OS group after 12 weeks, while no changes were detected in the control group (P=0.05 and P=0.04 respectively). Serum levels of sCD14, a product shed by activated macrophages, decreased only in the OS group without reaching statistical significance (P=0.08). No significant differences were detected in the fecal gut flora or in the nutritional parameters.

CONCLUSIONS: This study shows that the administration of supplements in older persons at risk of malnutrition may benefit from the addition of prebiotics that can improve the low noise inflammatory process frequently observed in this population.


A serpin from the gut bacterium Bifidobacterium longum inhibits eukaryotic elastase-like serine proteases.
Abstract

Serpins form a large class of protease inhibitors involved in regulation of a wide spectrum of physiological processes. Recently identified prokaryotic members of this protein family may provide a key to the evolutionary origins of the unique serpin fold and the associated inhibitory mechanism. We performed a biochemical characterization of a serpin from Bifidobacterium longum, an anaerobic Gram-positive bacterium that naturally colonizes human gastrointestinal tract. The B. longum serpin was shown to efficiently inhibit eukaryotic elastase-like proteases with a stoichiometry of inhibition close to 1. Porcine pancreatic elastase and human neutrophil elastase were inhibited with the second order association constants of 4.7 x 10^4 m(-1) s(-1) and 2.1 x 10^4 m(-1) s(-1), respectively. The B. longum serpin is expected to be active in the gastrointestinal tract, because incubation of the purified recombinant serpin with mouse feces produces a stable covalent serpin-protease adduct readily detectable by SDS-PAGE. Bifidobacteria may encounter both pancreatic elastase and neutrophil elastase in their natural habitat and protection against exogenous proteolysis may play an important role in the interaction between these commensal bacteria and their host.


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