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DIET, NUTRITION & GUT MICROBIOTA

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EDITORIAL

Professor Philip Calder

Professor Philip Calder is Head of the School of Human Development and Health in the Faculty of Medicine at the University of Southampton (UK). He is President of the Nutrition Society and President-Elect of the Federation of European Nutrition Societies (FENS). Professor Calder is a former chair of the Science Committee of the European Society for Clinical Nutrition and Metabolism (ESPEN) and former Editor-in-Chief of the British Journal of Nutrition.

Over the past decade of studying the gut microbiome, we have learned that environmental factors related to diet and drugs are major determinants of gut microbiota composition and that their effects outweigh the influence of genetics (Rothschild D *et al.*, 2018; Falony G *et al.*, 2016; Zhernakova A *et al.*, 2016).

This "Best of diet, nutrition and gut microbiota" document describes the latest evidence regarding the influencing role of diet and probiotics on human health linked to their effects on the gut microbiota.

The first three years of life represent the most critical period for dietary interventions aimed at microbiota modulation to improve child growth and development. The document starts by covering preliminary evidence about the role of early-life gut microbiome as a predictor of obesity and type 1 diabetes later in life. Diet exerts a crucial role in providing fermentable substrates for appropriately establishing the gut microbiota during the first five years of life (Stanislawsi MA *et al.*, 2018; Stewart CJ *et al.*, 2018; Vatanen T *et al.*, 2018).

Different levels of scientific evidence—from animal models to human studies—support the contribution of diet as a major factor in modulating the gut microbiota. Specific foods, nutrients and dietary patterns can influence health outcomes mediated by their effect on the gut microbiome (Valdes AM *et al.*, 2018). Considering the role played by diet in managing gut-related conditions through the shaping of gut microbes, the World Gastroenterology Organisation released a practice guideline in 2018 that provides nutritional healthcare professionals with tools for helping patients address lower gastrointestinal symptoms.

> Prebiotic foods, dietary fiber and probiotics have been the most frequently studied interventions aimed at influencing the balance and diversity of our gut microbiota. This document updates current strategies for modulating the gut microbiota through diet and probiotics.

Each of the major macronutrients—dietary carbohydrates, fats and proteins—and numerous micronutrients have been shown to modify the gut microbiome (Gentile CL & Weir TL, 2018). The most clearly characterized effects on the gut microbiome are those of carbohydrates, and they include microbiota-accessible carbohydrates (or MACs) found in dietary fiber, which play a significant role in shaping the gut microbial ecosystem. However, MACs are notably reduced in the Western diet (high in fat and simple carbohydrates and low in fiber) compared with a more traditional diet (Sonnenburg *et al.*, 2016). Indeed, some scientists now prefer the term MAC rather than the prebiotic concept for defining non-digestible carbohydrates that are metabolically available to gut microbes (Deehan EC *et*

al., 2017). Dietary MACs include both soluble fibers and resistant starches, which are readily fermented by gut microbes to produce short chain fatty acids (such as butyrate, propionate and acetate). These are involved in multiple physiological processes in the human host, ranging from energy metabolism to regulating immunity, inflammation and cancer risk (Gentile CL & Weir TL, 2018).

Apart from carbohydrates, omega-3 polyunsaturated fatty acids can also affect the gut microbiota composition through modulating specific gut bacteria. A recent randomized clinical trial has found that a daily intake of 4g of eicosapentaenoic and docosahexaenoic acids may lead to reversible changes in specific gut bacteria (Watson H *et al.*, 2018). This is consistent with previous observational research that also identified an association between omega-3 circulating levels and gut microbiome diversity, particularly with the *Lachnospiraceae* family (Menni C *et al.*, 2017). These findings raise the possibility that increasing intake of omega-3 fatty acids may represent an important dietary approach to improve gut microbiome health.

Prebiotic foods, dietary fiber and probiotics have been the most frequently studied interventions aimed at influencing the balance and diversity of our gut microbiota. This document updates current strategies for modulating the gut microbiota through diet and probiotics.

Gut microbiome studies have helped us answer why fiber is good for us in a wide range of pathologies, from colon cancer (Gianfredi V *et al.*, 2018) to metabolic diseases (Cani PD, 2019). Furthermore, randomized clinical trials have shown the efficacy of probiotics—usually added to yogurt or taken as food supplements—for tackling acute diarrhea, antibiotic-associated diarrhea, *Clostridium difficile* infections, symptoms of lactose intolerance, infantile colic, eczema and ulcerative colitis (Sanders ME *et al.*, 2018). Additionally, some fermented foods—primarily yogurts and cultured milks—are sources of probiotics and have beneficial health effects beyond their nutritional value. For instance, the consumption of fermented dairy products has been associated with a healthier lifestyle and greater adherence to the Mediterranean diet (Mena-Sánchez G *et al.*, 2018).

Beyond the effects of isolated foods and nutrients on the abundance and diversity of bacteria in the gut, the gut microbiome can also be modified by dietary patterns or periods of fasting. The health effects of dietary patterns mediated by the gut microbiome have been explored for the ketogenic diet, the Paleolithic diet, vegan/vegetarian diets and the Mediterranean diet (Gentile CL & Weir TL, 2018). Further nutrition intervention studies are needed to examine these diets' long-term impact on the gut ecosystem and safety. Meanwhile, microbiota-targeted diets that have recently emerged include specific carbohydrate diets, such the low-FODMAPs diet for reducing symptoms of irritable bowel syndrome. The impact of this restrictive diet on gut health is mediated through changes in the gut microbiome, though use should be tailored to individual needs as the long-term effects are unknown (Whelan K *et al.*, 2018).

Looking toward the future

Future directions on strategies for modulating the gut microbiota through diet and probiotics include the personalization of diet according to individual gut microbiota. The future of nutrition is personalized and, based on a person's food preference and dietary habits, biochemical markers commonly used in clinical practice and gut microbiota composition will help tailor dietary advice for better health.

Those passionate about the nutrition-gut microbiota interaction have an appointment on October 15-18 2019 in Dublin where the 13th European Nutrition Conference led by the Federation of European Nutrition Science (FENS) "Malnutrition in an Obese World: European Perspectives" will take place. A specific scientific symposia organised by the European Society of Neurogastroenterology & Motility (ESNM) will be dedicated to diet-microbiota interactions in human health and disease.

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Early life gut microbiome as an obesity and type 1 diabetes predictor

Published on November, 8, 2018 by Andreu Prados.

Previous research has suggested the gut microbiota's role in the risk of developing metabolic and immune-related disorders later in life. However, no studies have characterized the early-life gut microbiome longitudinally in large populations. Three recent studies shed light on how early-life gut microbiota composition might help identify which children are at risk of developing obesity and type 1 diabetes later in childhood.

The first prospective cohort study, led by Dr. Merete Eggesbø from the Norwegian Institute of Public Health (Oslo, Norway), concludes that gut microbiome composition at 2 years of age can predict obesity at age 12, suggesting the gut microbiome may play an early role in promoting obesity.

The researchers examined the association between gut microbiota composition on six occasions during the first two years of life and body mass index (BMI) —using BMI z-scores as measures of relative weight adjusted for child age and sex—at age 12 in a birth cohort of 165 Norwegian children (from the NoMIC cohort) and their mothers.

Gut microbiota composition at days 10 and 2 years of age was associated with childhood BMI at age 12. Specifically, the gut microbiota taxa at 2 years of age explained 53% of the variation in childhood BMI. It was also found that BMI-associated taxa in children correlated with maternal taxa relating to excess maternal weight and obesity and excessive gestational weight gain.

The other two studies have explored whether the gut microbiome in early life could be a predictive trigger of type 1 diabetes (T1D). With this goal in mind, longitudinal stool samples were collected from the largest microbiome study in children to date, which is part of the The Environmental Determinants of Type 1 Diabetes in the Young (TEDDY) study. The children under study included seroconverters, those diagnosed with T1D and controls.

In the first study, the researchers analyzed 16S ribosomal ribonucleic acid sequencing information in 12,500 stool samples from 905 children between 3 and 46 months of age.

The researchers detected that temporal development of the gut microbiome followed three distinct phases: one of development, which ran from 3 to 14 months; another one of transition, from 15 to 30 months; and that of progressive stabilization, from 31 months onwards. However, it cannot be inferred that gut microbiota maturation ends at 2.5 years of age. Previous data has shown that the gut microbiota is not established at 5 years of age and its maturation process becomes apparent even up to 20 years of age, experiencing another shift at 70 years into the elderly type.

Regarding maternal and postnatal influences on the developing gut microbiome, it was observed that, in the first phase, breastfeeding was associated with higher levels of bifidobacteria and that microbiota diver-

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sity increased when children began to incorporate solid foods. They also observed that children who had been born vaginally had a temporary increase in Bacteroides, which in turn was associated with greater gut diversity and maturation.

In the second study, the researchers focused on metagenomic sequencing data from 783 children over the first five years of life.

The gut microbiome of children who did not develop T1D later in childhood contained more genes related to fermentation and short-chain fatty acid production, whose protective role in metabolic conditions have been shown previously. Apart from considering intra-individual specific functions, the researchers found that a range of 20 microbial metabolic enzymes changed consistently over the first year of life. The lactate dehydrogenase enzyme decreased, whereas the trans-ketolase enzyme, which is involved in the metabolism of fiber, increased.

> Gut microbiota composition at days 10 and 2 years of age was associated with childhood BMI at age 12.

In contrast, children who developed T1D had a gut microbiota rich in *Bacteroides* species with depleted levels of SCFA-producing bacteria.

On the whole, these findings provide preliminary evidence that the early-life gut microbiome may help identify children who are at risk of obesity and of developing islet autoimmunity or T1D later in life, which may subsequently facilitate early prevention efforts, especially through diet.

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Omega-3 polyunsaturated fatty acids may lead to a reversible increase in some gut bacteria in healthy adults

Published on November, 29, 2018 by Stéphane Schneider

Considering that diet is—together with medication—one of the major influencing factors with regards to gut microbiota composition, research is now focusing on how dietary nutrients may affect gut microbial communities. Specifically, an association was previously found between essential omega-3 fatty acid DHA (docosahexaenoic acid) and gut microbiome diversity in healthy elderly people. However, evidence from randomized trials assessing the effect of omega-3 polyunsaturated fatty acids (PUFA) on human gut microbiota is scarce.

A new randomized clinical trial, led by Dr. Mark Hull from the Institute of Biomedical and Clinical Sciences at the University of Leeds (United Kingdom), has found that a daily intake of 4g of eicosapentaenoic and docosahexaenoic acids may lead to reversible changes in specific gut bacteria.

The researchers analyzed the effects of oral high-dose omega-3 PUFA on the fecal microbiota of 22 healthy middle-aged volunteers (median age 57 years; median body mass index 27 kg/m^2). A combination of 2 g/day eicosapentaenoic acid (EPA) and 2 g/day DHA were administered in capsules or drinks over an 8-week period in a randomized cross-over design. After each intervention, there was a washout period of 12 weeks. Fecal samples for microbiome analysis were collected at five time-points and omega-3 fatty acid levels were measured in red blood cell (RBC) membranes.

By and large, the effect of interindividual variability overcame the effect of the short-term omega-3 PUFA intervention on the gut microbiome composition. This was reflected by the fact that omega-3 PUFA supplementation, in either capsule or drink form, did not drive any gut microbiota taxonomic shift or changes in a and b diversity at the end of the study compared with baseline.

However, omega-3 PUFA interventions led to specific changes at family and genus levels, which returned to baseline once the intervention was complete. At the family level, *Clostridiaceae*, *Sutterellaceae* and *Akkermansiaceae* increased at the end of both interventions. At the genus level, *Bifidobacterium*, *Lactobacillus*, *Oscillospira* and *Lachnospira* increased. In contrast, there was a drop in the abundance of *Coprococcus* and *Faecalibacterium*.

The functional consequences of the increase in short-chain fatty acid producers—*Bifidobacterium*, *Lactobacillus*, *Lachnospira* and *Roseburia*—*after* the 8 weeks of omega-3 PUFA supplementation deserves further research. Researchers hypothesize that these findings might explain the role of SCFA signaling in omega-3 PUFA chemopreventive activity, whereas mechanistic studies are needed to resolve the matter.

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The type of omega-3 PUFA administration (capsules vs. drinks) also had a different effect on the abundance of genera at the end of the study. For example, the increase in both *Roseburia* and *Lachnospira* was only observed during the drink intervention.

On the other hand, microbiome changes did not correlate with omega-3 PUFA exposure quantified with RBC omega-3 fatty acid incorporation or development of omega-3 PUFA-induced diarrhea.

Furthermore, incorporation of omega-3 PUFA within RBC did not vary depending on the type of formulation (capsules vs. drinks). However, EPA and DHA administered in drinks led to a larger decrease in omega-6 PUFA arachidonic acid (AA) compared with capsules. This larger drop in AA content explained the increase in the omega-3:omega-6 ratio—a commonly used biomarker for assessing omega-3 PUFA bioactivity—after consumption of drinks compared with capsules.

As for adverse reactions from the intervention, some patients experienced minor and moderate dyspeptic symptoms and diarrhea.

In conclusion, these findings show that even short-term interventions driven by omega-3 PUFA may lead to reversible changes in the gut microbiota, which can only be appreciated at the family and genus level. On the other hand, the fact that the food matrix drives differential changes in the gut microbiota opens the avenue for taking them into account as a confounder in human nutrition microbiome studies.

“The type of omega-3 PUFA administration (capsules vs drinks) also had a different effect on the abundance of genera at the end of the study. For example, the increase in both Roseburia and Lachnospira was only observed during the drink intervention.

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A new review explores the latest knowledge about resistant starch in nutrition and as a modulator of the gut microbiota

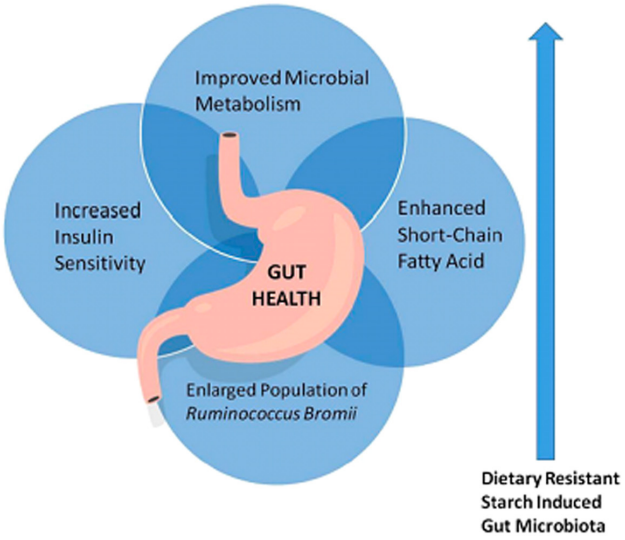
Published on November, 20, 2017 by Andreu Prados

When it comes to studying the effects of complex dietary carbohydrates on the gut microbiota, resistant starch (RS) is a type of dietary fiber that is receiving increasing attention as a dietary intervention that can benefit the host through mechanisms that include altering the gut microbiota. Although starch is a major energy source in human and animal diets, little is known about the biochemistry, mechanism(s), pathway(s) and cell signalling by which RS affects host nutrition and health.

A recent review, led by Dr. Yulong Yin from the College of Life Sciences at Hunan Normal University and the Chinese Academy of Sciences at the Institute of Subtropical Agriculture from the Ministry of Agriculture in Changsha (China), explores current knowledge about resistant starch's impact on nutrition through its effects on the gut microbiota.

Three kinds of starch are classified according to the rate and extent of digestion and absorption of starch in the small intestine: rapidly digestible starch (RDS)—the starch fraction that is digested to glucose within 20 min after ingestion and causes a rapid increase in blood glucose levels; slowly digestible starch (SDS)—a starch fraction that is digested to glucose within 20-120 min; and resistant starch (RS)—the starch portion that is digested after 120 min, is not absorbed in the small intestine and is fermented by the gut microbiota within the colon. As has been explained in a previous post, there are 5 types of RS that can be found naturally in vegetable foods (mainly grains, legumes, seeds, tubers and green banana) or can be produced industrially and incorporated afterwards into food products. All these types of starch can act at several sites including the oesophagus, liver, stomach, small intestine and large intestine.

The amylose (starch's lineal fraction) content varies depending on the different forms of starch, and when its content is high this will imply lower digestible activity of starch by host enzymes and, as a result, a major fraction of undigestible starch reaches the colon and is accessible to the commensal gut microbiota. RS has the highest content of amylose followed by SDS and finally RDS.



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Food processing has significant effects on starch nutritional fractions. For instance, cooking increases RDS and RS content, whereas it decreases SDS content. Besides this, food storage increases both RDS and SDS, but has no effect on RS levels. For instance, cooking and cooling in the fridge (to 4ºC) tubers, grains and legumes increase their content of RS. Besides this, RS content varies also depending on the food variety within a specific category. For instance, RS content of rice varies with rice variety and cooking method. Among different rice varieties and cooking techniques,

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refrigerated long-grain rice cooked in a conventional rice cooker had the highest RS content and refrigerated short-grain rice cooked in a pressure cooker had the lowest RS content.

The review emphasizes that several experimental and clinical studies have found that RS has positive effects on inflammatory status and it may have a protective role against type 2 diabetes mellitus, cardiovascular health, gastric health, colonic colitis, and chronic kidney disease progression. Underlying mechanisms that could explain the beneficial impact of RS for treating those conditions include improvement of cardiovascular disease morbidity (via multiple mechanisms, such as decreasing serum triacylglycerols), attenuating inflammatory markers and reducing oxidative stress. Further human studies with bigger samples and longer follow-up periods are needed to explore the impact of RS in those conditions.

In addition, RS has specific beneficial effects on the gut environment including increased populations of *Ruminococcus bromii*—a dominant member of the phylum *Firmicutes* that plays a primary role in releasing energy from dietary starches that escape digestion by host enzymes through its exceptional activity against particulate resistant starches. Besides this, ingestion of food products rich in RS has been shown to increase luminal short-chain fatty acid levels, modulate microbial metabolism and improve markers of glucose homeostasis and insulin sensitivity. Interestingly, the increased butyric acid after administration of RS is a variable response that depends on each person's individual gut microbiome. These effects of RS on the gut environment suggest that RS can have a positive impact on the physiological functions of the gut microbiota and on the host: metabolic activities, trophic effects on intestinal epithelia and on immune structure and function, and protection of the colonised host against invasion by pathogens.

> RS has positive effects on inflammatory status and it may have a protective role against type 2 diabetes mellitus, cardiovascular health, gastric health, colonic colitis, and chronic kidney disease progression.

Regarding cell signalling pathways that can explain physiological effects of RS, using animal models it has been well documented that RS has strong anti-inflammatory properties, possibly through the induction of a regulatory T cell response, and direct and indirect effects related to increased peptide YY (PYY)—a hormone made in the small intestine in response to a meal, that helps to reduce appetite and limit food intake—and glucagon-like peptide (GLP)-1 levels and reduced protein levels of free fatty acids and interleukin (IL)-6 via either the inflammatory IL-10 pathway or GLP-1 receptor hormone pathways. These effects suggest that RS may have a role in weight gain not only by targeting gut microbiota, but also by inducing alterations in appetite regulating hormones. Supplementation of RS has also represented an approach for treating acute diarrhoea in children via increasing production of short-chain fatty acids, which are absorbed by colonic epithelial cells and enhance Na-dependent fluid absorption, therefore resulting in conservation of fluid and electrolytes. Distal effects of RS beyond the gut include, among others, attenuation of disruption in vitamin D homeostasis in type 1 diabetic rats.

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However, some undesirable effects have been reported with a RS-supplemented diet in mice, including lack of weight gain and increased anxiety-related behaviours. These data suggest further research is needed in order to elucidate the role of diets rich in RS in humans and animal models.

In conclusion, when studying the role of complex carbohydrates in nutrition RS should be included based on the increasing amount of evidence that supports its effects on host health via modulating the gut microbiota. Although current research in this area is at an early stage, further studies will depict a clearer picture on specific recommendations for including RS as a part of the daily diet.

> These effects suggest that RS may have a role in weight gain not only by targeting gut microbiota, but also by inducing alterations in appetite regulating hormones.

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Consuming fermented dairy products is associated with a healthier life-style and greater adherence to the Mediterranean diet

Published on November, 12, 2018 by Researchers from the Human Nutrition Unit (URV)

Fermented foods have been used for thousands of years and they come about through extensive microbial growth. These foods are known for improving shelf life, safety and organoleptic and nutritional properties when compared with the original food substrates. Furthermore, fermented foods that retain living cultures (e.g. yogurt and some cheeses) may reduce the risk of some diseases. Although the impact of fermented foods on human health enjoys a positive perception, well designed studies that objectively evaluate their health benefits remain scarce.

A new cross-sectional study, led by researchers from CIBEROBN centre at the Universitat Rovira i Virgili in Tarragona (Spain) in collaboration with another 23 research groups from the PREDIMED-Plus clinical trial, has found that consuming fermented dairy products is associated with a healthier life-style and greater adherence to the Mediterranean diet.

This observational study evaluated the associations between consuming fermented dairy products, diet quality and the prevalence of metabolic syndrome (MetS) components in 6,572 Mediterranean men and women (mean age 65 years) who were overweight or obese and suffered from MetS.

Participants who consumed higher amounts of fermented dairy products and especially yogurt showed greater adherence to the Mediterranean diet. Likewise, they reported higher levels of consumption of healthy foods including fruit, vegetables, fish, nuts and wholemeal bread, while consuming lower levels of white bread, alcohol and cookies. These participants also smoked less, which suggests that consuming fermented dairy products is a possible marker of a healthy lifestyle.

In line with these findings, another previous study by our research group found that yogurt consumption is inversely associated with a lower risk of metabolic syndrome (MetS) incidence, which supports yogurt consumption as a diet quality indicator. These data also add to previous studies supporting the beneficial effect of yogurt on risk factors for type 2 diabetes.

Meanwhile, high levels of cheese consumption were associated with a low risk of hypertriglyceridemia and low HDL-cholesterol plasma levels. These results were observed when comparing participants located in the highest quartile of cheese consumption (350 grams/day) with those who consumed smaller amounts of cheese. In the case of yogurt consumption, total, low and whole-fat yogurt intake was not associated with any of the MetS components.

The results obtained in this observational study can be explained by the intrinsic components of fermented dairy products. Yogurt and cheese are actually nutritionally dense foods, with a matrix of nutrients that make them unique. These fermented dairy products, and especially cheese, typically have a high content of good quality protein and calcium bioavailability. Fermented dairy products also typically contain other sources of minerals, vitamins and bacteria with potential benefits for human health. Furthermore, the increased bioavailability of insulinotropic amino acids

Consuming fermented dairy products is associated with a healthier life-style and greater adherence to the Mediterranean diet

and peptides, as well as the bacterial biosynthesis of vitamin K2, have been proposed as potential mechanisms that explain the results of this observational study.

As we did not analyze participants' gut microbiota in the study, we are not familiar with the role played by cheese and yogurt bacterial strains in modulating the gut microbiota as a mechanism of action. However, adherence to the Mediterranean diet was recently associated with higher bifidobacterial counts and higher levels of total short-chain fatty acids, which might explain the gut microbiota's partial role in mediating the Mediterranean diet's health benefits.

The different ways the studies looking at fermented dairy products have been designed means we cannot elucidate how fermented foods contribute to human health. Clinical trials and large prospective epidemiological studies are required to confirm our findings, along with studies specifically designed to address the impact of food fermentation on health outcomes.

> Participants who consumed higher amounts of fermented dairy products and especially yogurt showed greater adherence to the Mediterranean diet. Likewise, they reported higher levels of consumption of healthy foods including fruit, vegetables, fish, nuts and wholemeal bread [...].

Researchers from the Human Nutrition Unit (URV). Human Nutrition Unit, University Hospital of Sant Joan de Reus, Department of Biochemistry and Biotechnology, Pere Virgili Institute for Health Research, Rovira i Virgili University, Reus, Spain: http://www.nutricio.urv.cat/

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Different diets, different effects on the microbiota, similar short-term symptom improvement but different sustained effects in IBS

Published on October, 29, 2018 by Andrea Hardy

Traditionally, the diet low in fermentable oligo-, di-, and monosaccharide and polyol (FODMAP)—best as a 2-phased intervention, with strict reduction of all slowly absorbed or indigestible carbohydrates (i.e., FODMAPs) followed by reintroduction of some of them according to tolerance—has been widely used for overall gastrointestinal symptom relief in patients with irritable bowel syndrome (IBS). However, decreasing intake of fermentable carbohydrates reduces available fuel for the gut microbiota, subsequently altering bacterial composition in the colon.

Although it has been shown that incorporating fermentable carbohydrates may increase the severity of IBS symptoms (pain, bloating) due to gas production from fermentation, they may also help manage other symptoms of IBS (constipation, diarrhea) through impact on the gut microbiota. While these prebiotic fibers have varying effects on IBS symptoms, little is known about the impact specific types and doses of prebiotics have in IBS management. Dr. Fernando Azpiroz and his team from the Vall d'Hebron Research Institute in Barcelona (Spain) set out to clarify whether certain prebiotics help or hinder IBS symptoms and evaluate their utility in maintaining the gut microbiota, when compared to the low-FODMAP diet.

The researchers compared the effects of a low-FODMAP diet plus a placebo supplement (low-FODMAP group, n=21) versus a prebiotic supplement (galacto-oligosaccharides) plus a Mediterranean-type (prebiotic group, n=19) diet for 4 weeks on the gut microbiota composition and gas production. The gut microbiota was analyzed prior to and at the end of intervention, as well as 2 weeks following discontinuation of the intervention.

As expected, the low-FODMAP diet improved IBS symptoms (such as pain, distension, bloating, and flatulence), but decreased bifidobacteria, in line with previous studies. Bifidobacteria increased 2 weeks following discontinuation of the low FODMAP diet, showing this change was transient. The participants on the low-FODMAP diet had an increase in *Bilophila wadsworthia*, a bacterium implicated in excess gas and intestinal inflammation. This increase persisted for 2 weeks following discontinuation of the low-FODMAP diet and was correlated with an increase in bloating frequency after intervention.

These findings show that changes in the gut microbiota composition driven by a low-FODMAP diet may persist after 2 weeks of stopping the diet and may perpetuate IBS symptoms, such as bloating. Interestingly, the prebiotic group had a similar reduction in symptoms of pain, distension, and bloating by the end of the 4-week intervention, but with an increase in *Bifidobacterium* as well as a decrease in *Bilophila wadsworthia*, that persisted 2 weeks after discontinuation of the prebiotic.

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Initially, the prebiotic group reported an increase in flatulence, which resolved as the gut microbiota adapted to the substrate. This returned to baseline after 7-10 days of adjusting to the supplement—however it was not improved as was with the low-FODMAP diet. Remarkably, 2 weeks following discontinuation of the intervention, symptom improvement was maintained in the prebiotic group, but not in the low-FODMAP group. This suggests that positive symptom changes were likely attributable to changes in the gut microbiota.

This study highlights the role of prebiotic fibers in ameliorating IBS symptoms through changes in the gut microbiota composition. Future research looking at how long microbial changes are sustained post-treatment for IBS would help in understanding how to best use prebiotic fibers in functional gastrointestinal disorders.

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Registered Dietitian, Andrea Hardy from Calgary, Canada specializes in gastrointestinal disorders and the gut microbiome. She is recognized as Canada's gut health dietitian—educating health care professionals and the public on the pivotal role nutrition plays in gut health. You can find her at Ignite Nutrition, or on Twitter (@AndreaHardyRD).

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Baseline gut microbiota composition and habitual dietary intakes are implicated in individual microbiota responses to diet

Published on February, 12, 2018 by Andreu Prados

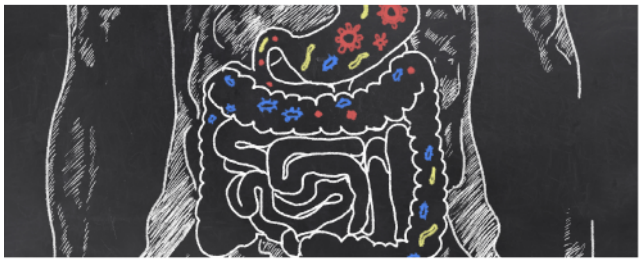
Although previous research has shown that both diet and medications are the primary factors involved in the modulation of both structural and functional capacity of the human gut microbiota, dietary intervention studies often do not show reliable changes in the gut microbiota from an intervention.

A review, led by Dr. Genelle Healey from the Massey Institute of Food Science and Technology at School of Food and Nutrition at the Massey University (Palmerston North, New Zealand), has concluded that interindividual variability in the gut microbiota and host responsiveness make it difficult to identify reliable gut microbiota responses to a given dietary intervention.

The review first explores the current scientific evidence supporting the relationship between the gut microbiota and human diseases. Secondly, the contribution of both baseline gut microbiota composition and habitual dietary intake on how host responds to diet is covered in further detail.

The review broadly explains the role of gut microbiota dysbiosis in human disease and what is known about gut microbiota modulation strategies for enhancing human health.

The article mentions several murine and human studies that have supported the link between dysbiotic gut microbiota and the promotion or aggravation of certain chronic diseases-such as obesity, type 2 diabetes mellitus, inflammatory bowel disease, and colorectal cancer. However, the authors emphasized that uncertainty remains around whether dysbiosis is a cause or consequence of these diseases. Furthermore, a dysbiotic gut microbiota may be the result of people's dietary patterns and commonly-prescribed medications. Even if the gut microbiota is involved in their pathogenesis, to what extent novel microbiota-based therapeutic strategies have the potential to reduce disease incidence and severity remains unknown.



Despite these limitations, it is noted that the gut microbiota is involved in human disease and diet is considered one of the main contributors to the composition, diversity, and metabolic activity of commensal microbes that reside within the gastrointestinal tract. Based on the fact that habitual dietary intakes have a relevant impact on the composition of the gut microbiota, the review then shows several human observational and dietary intervention studies that have been conducted to explore to what extent diet—focusing on dietary fiber-associated changes in the functional capacity of the gut microbiota—could be used to modulate the gut microbiota to decrease disease risk.

Few human studies have demonstrated what influence diet can have on the entire microbial community. However, those studies that have demonstrated a beneficial role of plant-based dietary substrates in the structure and functional capacity of the gut microbiota have also shown that gut microbiota modifications are also related to improvements in host health outcomes such as immune and inflammatory markers and post-oral glucose tolerance test glycemia.

Finally, the review focuses on response of gut microbiota and host to dietary interventions. Some human intervention studies in healthy subjects, overweight or

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obese individuals or patients with irritable bowel syndrome have demonstrated that baseline gut microbiota composition and habitual dietary intakes are factors involved in gut microbiota responses to the diet. However, a limited number of studies have found no link between responsiveness and baseline gut microbiota composition or dietary pattern. The relevance of baseline microbiota may be related to heterogeneity in participant characteristics—different external factors including age, sex, antibiotics, and disease—and the differing dietary assessment methods and gut microbial analysis methods used. Besides this, it has been suggested that individualized gut microbiota resilience may play a more important role in gut microbiota response than dietary change itself. Further studies that determine what factors are involved in individualized responsiveness are needed in order to better design personalized gut microbiota-targeted interventions.

In an interview with GMFH editors, Dr. Genelle Healey explained how baseline gut microbiota may depend on habitual dietary patterns: "(...) if people have very distinctive diets their baseline gut microbiota composition will be quite distinctive as well. And some studies have shown maybe it's not the makeup of the gut microbiota that's distinctive but it's how they function. So whether they can actually utilize the substrates that you make available to them or not, might depend on the substrates that you're giving them on a day to day basis".

On the whole, these results show that high inter-individual variability in gut microbiota and host responsiveness makes it hard to predict the impact of specific dietary interventions on both gut microbiota and host response. Both individualized gut microbiota and host responsiveness have the potential to influence study results and affect reproducibility among studies. Therefore, taking into account both baseline gut microbiota composition and habitual dietary intake could better establish successful gut microbiota modulation strategies.

According to Dr. Healey: "There's some preliminary evidence to suggest that things like baseline gut microbiota composition and habitual diet actually should be considered by researchers when recruiting their participants, and/or when they're analysing the data that they generate from dietary intervention studies. This might help ensure that the true effectiveness or efficacy of a dietary intervention is determined".

Andreu Prados holds a Bachelor of Science Degree in Pharmacy & Human Nutrition and Dietetics. Science writer specialised in gut microbiota and probiotics, working also as lecturer and consultant in nutrition and healthcare. Follow Andreu on Twitter @andreuprados

Reference:
Healey GR, Murphy R, Brough L, Butts CA, Coad J. Interindividual variability in gut microbiota and host response to dietary interventions. Nutr Rev. 2017; 75(12):1059-80. doi: 10.1093/nutrit/nux062.

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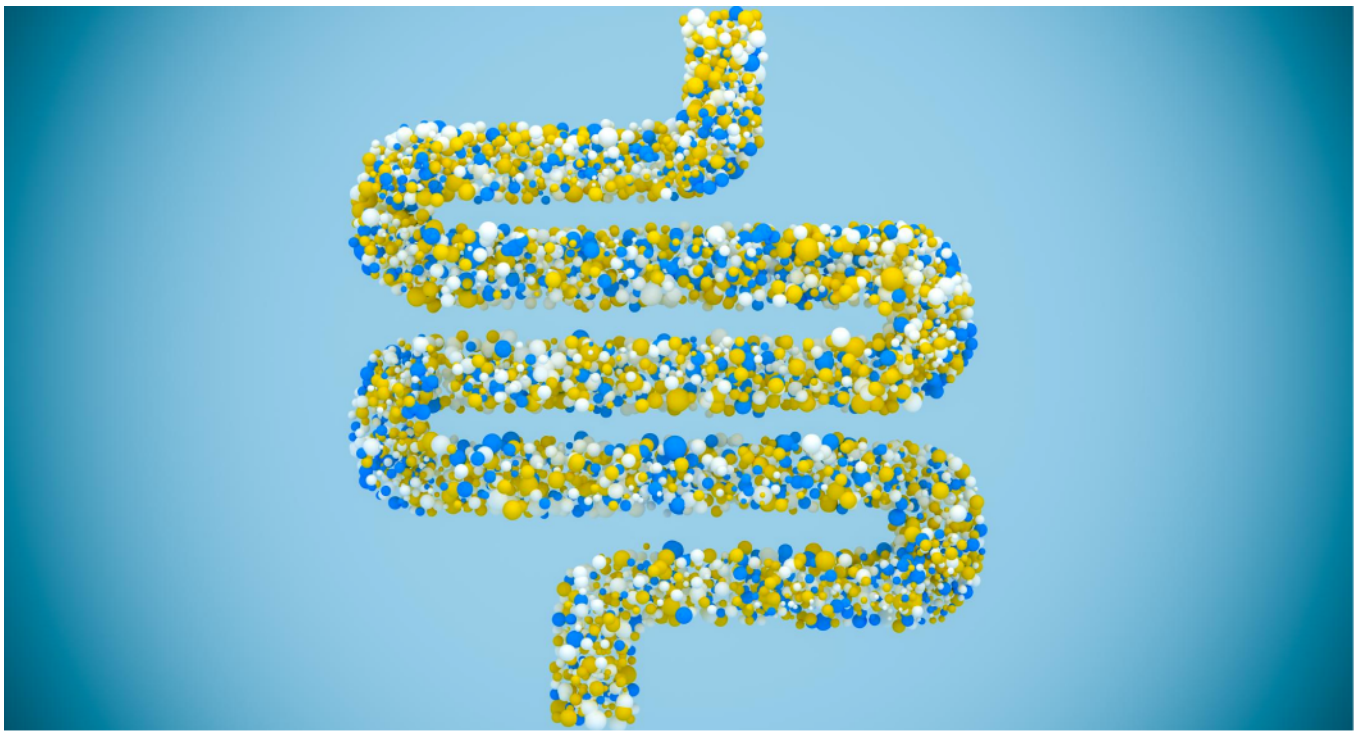
New ISAPP Paper: Probiotics for Human Use

Published on September, 17, 2018 by Mary Ellen Sanders

Looking for a review that covers all the bases of probiotic health effects? A new, open access paper may serve that purpose. "Probiotics for human use" is a peer-reviewed paper published by the Nutrition Bulletin. This was a collaborative effort by experts in clinical effects (Prof. Dan Merenstein MD from Georgetown University, Claire Merrifield PhD from Imperial College London), fermented foods (Prof. Bob Hutkins PhD, University of Nebraska) and probiotic microbiology and regulatory matters (Mary Ellen Sanders PhD from ISAPP). Although many modern reviews of probiotics provide in-depth coverage of a specific health benefit, this paper covers all benefits with robust evidence.



The paper opens with a general overview of probiotics, detailing the importance of adhering to the accepted definition (see ISAPP consensus paper, Hill *et al.* 2014), strain-specificity of effects and the need to identify probiotics using current nomenclature. This last point is especially relevant today, considering that many probiotic lactobacilli are being renamed and no longer will be considered part of the *Lactobacillus* genus. The paper also discusses the concept that core benefits may be expressed by many strains of a probiotic species and, as such, some general effect may be considered to be associated with a given, well-studied species, and not be limited to specific strains. The importance of high quality probiotics that are safe for their intended use—in some cases in vulnerable populations—was also emphasized.

The paper reviews the strength of evidence for probiotic health effects in humans, focusing on infantile colic, eczema, inflammatory bowel diseases, antibiotic-

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associated diarrhea, *Clostridium* infections, and necrotizing enterocolitis. Probiotic applications for healthy people are also discussed, with Table 1 providing a list of benefits and effect sizes as determined from meta-analyses.

A section on fermented foods provides clarity about the difference between probiotics and fermented foods. Fermented foods are made by live microbes, but live microbes might not survive in the final food product due to heat treatments or other processing steps. Furthermore, fermented foods may not have been tested for benefits beyond the basic nutritional value of the food, which means fermented foods are not necessarily probiotic foods. However, it should also be remembered that some fermented foods—primarily yogurts and cultured milks—are sources of probiotics and have been subjected to controlled human studies documenting health effects.

Finally, the paper explores marketplace issues, including how to read a probiotic product label and understanding the complexities of regulatory issues regarding making health benefit claims for probiotics. The article also features the ISAPP infographic on Deciphering a Probiotic Label from an EU perspective.

The paper includes a box of frequently asked questions about probiotics.

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Mary Ellen Sanders is a consultant in the area of probiotic microbiology, with special expertise on paths to scientific substantiation of probiotic product label claims. Dr. Sanders served as the founding president of the International Scientific Association for Probiotics and Prebiotics (www.isappscience.org) and is currently the organization's Director of Scientific Affairs/ Executive Officer.

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