GUT MICROBIOTA
RESEARCH & PRACTICE
edited by ESNM

YEAR AT A GLANCE

A selection of content from the
Gut Microbiota for Health 2017

January 2018

www.gutmicrobiotaforhealth.com

TABLE OF CONTENT

EDITORIAL

Dr. Azpiroz

Dr. Azpiroz is currently Chief of the Department of Digestive Diseases at the University Hospital Vall d'Hebron, Autonomous University of Barcelona, Spain, since the year 2009, and Professor of Medicine. At present he also serves as Chairman of the Microbiota & Health Section, European Society of Neurogastroenterology and Motility and he is a member of the Board of Directors, Rome Foundation for the Study of Functional Gastrointestinal Disorders.

2017 was an important year in the field of microbiome research: ten years ago marked the launch of the European Metagenomics of the Human Intestinal Tract (MetaHIT) project, US National Institutes of Health Human Microbiome Project (HMP) as well as the beginning of the Chinese metagenomics projects. Looking back, it is clear that the past decade has brought us into a new era of understanding the relevance of the gut microbiota in health and disease. Today, microbiome science—and in particular the gut microbiome—is a leading scientific topic, with a PubMed search on "gut microbiota" since 1977, yielding more than 15,000 publications, which increases year by year.

Increased awareness of the importance of the microbiota and its role on health has developed in parallel with this surge in research. And, for the past five years, the Gut Microbiota for Health initiative has been instrumental in raising awareness about the gut microbiota—not only through its website and digital ecosystem, but also through its yearly Gut Summit event, the leading event on gut microbiota and health addressed to clinical researchers and healthcare practitioners. The initiative was born after the creation of the Gut Microbiota & Health section within the European Society of Neurogastroenterology & Motility (ESNM), with the involvement of European and international experts.

Today, the digital community of Gut Microbiota for Health (GMFH) numbers over 50,000, including scientists, healthcare professionals, and the general public. In 2017 the website had more than 950,000 visits and was, for the second year in a row, selected as one of the best gut health blogs by Healthline—a consumer health information website with over 65 million readers per month.

GMFH also makes it easier for health professionals to understand the clinical applications of gut microbiota science— and, for this reason, an e-learning course was developed by members of the Gut Microbiota & Health Section of the ESNM, and was approved by the Board of Directors of the Section and by the Steering Committee of the ESNM. This online course, accessed on the website of United European Gastroenterology (UEG), was updated this year and re-accredited by EACCME.

In 2017 the website had more than 950,000 visits and was, for the second year in a row, selected as one of the best gut health blogs by Healthline

EDITORIAL

With the aim of helping professionals grasp the main themes of this emerging science, GMFH arranged sessions on gut microbiota and nutrition at two international dietetics conferences this year: the 10th European Federation of the Associations of Dietitians (EFAD) conference in Rotterdam (the Netherlands) and the 21st International Congress of Nutrition (ICN) in Buenos Aires (Argentina).

The 2017 GMFH Gut Summit, held in Paris, was a top international event that drew over 400 professionals from more than 30 countries. The topics included:

- An overview of major projects in the past ten years of microbiome research, from Dr. James Versalovic (Human Microbiome Project), Dusko Ehrlich (MetaHIT), and Liping Zhao (Chinese metagenomics Project).

- A special session for dietitians, called "Nutrition and the Human Gut Microbiome: What should health professionals know for their daily practice?". This workshop covered dietary tools for shaping the gut microbiota and managing functional gastrointestinal disorders and food sensitivities.

The 2018 Gut Summit, to be held in Rome, promises an equally illuminating overview of gut microbiota science, with topics ranging from immune mechanisms to cancer-targeting drugs.

Gut microbiota science is a dynamic field—and as we move beyond association studies to discussions of gut microbiota manipulation for prevention or treatment of disease, it is more important than ever to stay up-to-date on clinical applications. Stay in touch with GMFH to learn about the latest studies and connect with the experts who are pushing this field forward.

A decade studying the human microbiome

Published on June, 26, 2017 by GMFH Editing Team.

After the Human Genome Project success, at the beginning of 21st century, the scientific community agreed the human microbiome was a major challenge in medical research. As many of the bacteria integrating it could not be cultivated in a petri dish in a lab, little was known about this huge community of microorganisms inhabiting our body. It began to be suspected they played a key role in health but also in disease. At that time, 10 years ago, the United States Institutes of Health decided to launch the Human Microbiome Project, in which took part several biomedical research institutes.

Almost at the same time, in Europe, MetaHit was conceived, although unlike the American project, it focused on the link between microbiota and two more and more common diseases, obesity and type 2 diabetes. And finally, and fruit of the collaboration between Chinese and French scientists, the Chinese Microbiome Project was set up; its main goal was to understand the obesity and type 2 diabetes epidemics in the Asian country.

The main researchers behind those successful and ambitious projects attended the Gut Microbiota for Health World Summit held in Paris, in March 2017, where we could interview them.

Read the original post online at:
http://www.gutmicrobiotaforhealth.com/en/decade-studying-human-microbiome/

New hypothesis: 'All healthy microbiomes are similar; each dysbiotic microbiome is dysbiotic in its own way'

Published on November, 13, 2017 by Kristina Campbell.

Science writer Kristina Campbell (M.Sc.), from British Columbia (Canada), specializes in communicating about the gut microbiota, digestive health, and nutrition. Author of the best selling Well-Fed Microbiome Cookbook, her freelance work has appeared in publications around the world. Kristina joined the Gut Microbiota for Health publishing team in 2014.

When Leo Tolstoy wrote the first line of his classic novel Anna Karenina—"All happy families are like one another; each unhappy family is unhappy in its own way"—he probably never thought it would apply to gut microbiomes.

But researchers from University of Washington (USA) and Oregon State University (USA) recently put forward the "Anna Karenina principle" as a way of explaining what might happen when microbial communities in many different environments are subject to perturbation: random variation may occur in microbiota community composition—and compared to baseline, the microbiota may become more varied and unstable.

"Anna Karenina effects", as the authors call them, could be commonly observed when a host is confronted with a stressor that reduces its ability to regulate microbiota composition; furthermore, these effects are often associated with a decline in host health. So while microbiomes of healthy hosts may all look similar, microbiomes of unhealthy hosts may end up looking very different from one another.

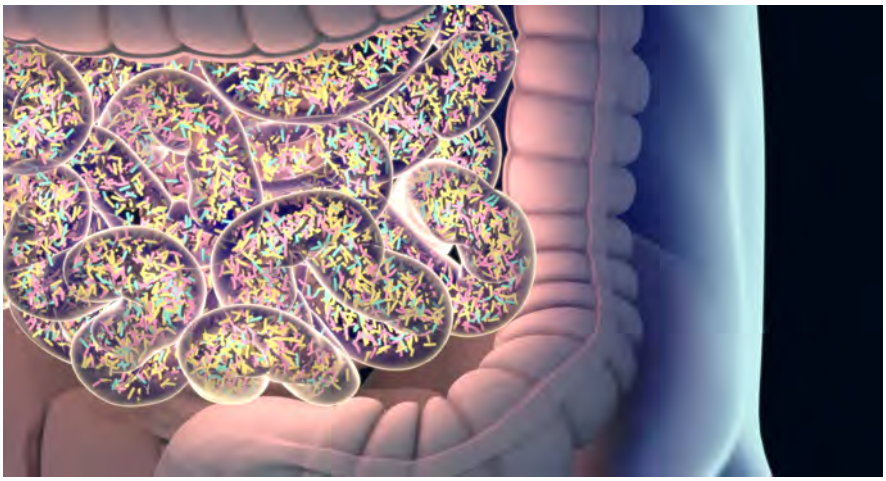
In a Perspective published in Nature Microbiology, Jesse Zaneveld, Ryan McMinds, and Rebecca Vega Thurber cite evidence for Anna Karenina effects in diverse systems, from the microbiome of corals to that of the human upper respiratory tract. When it comes to the authors' own work on corals, they found stressors including overfishing and nutrient pollution may allow random changes to occur in the coral surface microbiome, allowing algal competitors to flourish and ultimately reducing the growth of corals or killing them altogether.

Zaneveld, *et al*. write: "Rather than shift the microbiome to a new discrete configuration, producing clusters, these stressors allow the microbiomes of stressed individuals to take on a wider range of possible configurations than healthy controls, producing a constrained 'core' of control microbiomes surrounded by a large 'halo' or 'smear' of stressed or diseased microbiomes."

Applied to the gut microbiota, the principle may lend unique interpretations to previous studies and provide a useful framework for interpreting future studies. To wit: what would it mean for research on gut microbiota if every dysbiosis were slightly different?

SELECTED CONTENT

New hypothesis: 'All healthy microbiomes are similar; each dysbiotic microbiome is dysbiotic in its own way'



Numerous studies have linked ulcerative colitis with gut microbiota composition, for example, with identification of species that are depleted or enriched in the disease state; however, so far a specific biomarker has not been identified. If the Anna Karenina principle indeed applies in this disease state, scientists may never find a stable dysbiosis associated with ulcerative colitis. Random gut microbiota changes in response to disease-related factors could mean many different configurations are associated with the disease state, and therefore, identification of a highly sensitive and specific gut microbial biomarker of disease may prove difficult. Also, interventions aimed at modulating the gut microbiome in ulcerative colitis in a specific way would be met with varying success.

Many more possible examples of the Anna Karenina principle exist in the body of literature linking gut microbiota dysbiosis to disease. And in the authors' discussion of examples related to the human gut microbiota, they emphasize the importance of immunity—evidence suggests disruption of normal immune function in a host can destabilize the gut microbiome and possibly induce random variation.

The article details the greater microbiome variability seen in individuals positive for human immunodeficiency virus (HIV), who have severely disrupted immunity.

"Predicting when and how normal regulation of microbiomes breaks down is at the heart of many important problems in microbial ecology," the authors write. More specifically, predicting this is essential in knowing how to modulate the gut microbial ecosystem for better health. On the path toward personalized medicine, the Anna Karenina principle could give scientists new direction for finding biologically meaningful effects of gut microbiota alterations.

References:
Zaneveld JR, McMinds R, & Thurber RV. Stress and stability: applying the Anna Karenina principle to animal microbiomes. Nature Microbiology. 2017; 2. doi:10.1038/nmicrobiol.2017.121

Read the original post online at:
http://www.gutmicrobiotaforhealth.com/en/new-hypothesis-healthy-microbiomes-similar-dysbiotic-microbiome-dysbiotic-way/

Gut Microbiota Clinical Minute: Do fermented foods contribute to health?

Published on March, 30, 2017 by Kristina Campbell.

Science writer Kristina Campbell (M.Sc.), from British Columbia (Canada), specializes in communicating about the gut microbiota, digestive health, and nutrition. Author of the best selling Well-Fed Microbiome Cookbook, her freelance work has appeared in publications around the world. Kristina joined the Gut Microbiota for Health publishing team in 2014.

In the new Gut Microbiota for Health "Clinical Minute" series, we get a scientific expert's take on one or more gut-microbiota-related questions that patients frequently ask their healthcare professionals.

Dr. Mary Ellen Sanders (MES) is the founding president of a non-profit association of academic and industrial scientists called the International Scientific Association for Probiotics and Prebiotics (ISAPP), and currently serves as ISAPP Director of Scientific Affairs/Executive Officer. She consults internationally in the area of probiotic microbiology.

TOPIC: Do fermented foods contribute to health?

MES: Consumer interest in fermented foods is high—these foods are discussed frequently in media related to food and health, and the US supermarket chain Whole Foods Market recently included fermented foods in its list of the top food trends of 2016. But what do we really know about fermented foods and health?

Patient question: What are fermented foods?

MES: As defined in a recent review article that was an outcome of the 2016 ISAPP meeting, fermented foods are "foods or beverages made through controlled microbial growth and enzymatic conversions of major and minor food components" (Marco *et al.* 2017). These include thousands of foods consumed by populations around the world, from chocolate and coffee to traditional sauerkraut and kimchi. Some fermented foods contain live microbes when consumed, and others do not. (Some processing steps kill or remove the live microbes). A descriptive infographic on fermented foods is available from ISAPP.

Patient question: How do fermented foods differ from probiotics?

MES: It's important to distinguish between fermented foods and probiotic foods. A subset of fermented foods that contain live microbes qualify as "probiotic", but only if the microorganisms are characterized (known) and if research has associated them with a health benefit. The foods in this category include many commercial yogurts and some kefir products that list the bacterial species they contain.

Gut Microbiota Clinical Minute: Do fermented foods contribute to health?

Patient question:
What health benefits are associated with fermented foods?

MES: A limited number of controlled human trials have been carried out on fermented foods (summarized in Table 2 of Marco *et al.* 2017), but direct evidence for health benefits of fermented foods is limited. Clearly, fermented foods provide the nutritional benefits associated with the nutrients contained in the foods. But for the fermented foods that are not also probiotic foods, we know little about extra benefits associated with the presence or growth of the fermenting microbes.

In cohort studies, consumption of fermented dairy foods is associated with weight maintenance (Mozaffarian *et al.* 2011), as well as a reduced risk of cardiovascular disease (Tapsell 2015) and type 2 diabetes (Chen *et al.* 2014). A few randomized, controlled trials have been conducted on different endpoints of metabolic syndrome, providing some causal proof of observations in associative studies. Furthermore, particular fermentation microorganisms in food are associated with certain health benefits. For example, yogurt cultures are known to improve tolerance of lactose by lactose intolerant people.

A vast number and variety of fermented foods exist, and surely they do not all lead to similar health benefits. Researchers have proposed, for example, that, depending

Gut Microbiota Clinical Minute: Do fermented foods contribute to health?

on the raw materials and the microbe(s) responsible for the fermentation, ingestion of a fermented food could in theory inhibit the growth of pathogens in the gut, enhance nutritional value through increased vitamin synthesis or absorption, and/or improve food digestibility, among other things.

Patient question:
By what mechanisms might fermented foods impact health?

MES: Scientists have some insights into how fermentation microbes may impact health. Some produce short chain fatty acids in situ, which are associated with many different health outcomes, including direct inhibition of intestinal pathogens. Some produce B vitamins during growth in the food, increasing the food's nutrient profile. During the fermentation process, some secrete proteins and exopolysaccharides that act as antioxidants, prevent adhesion of intestinal pathogens, enhance immune responses, or improve blood lipids. But research gaps remain and these benefits need to be confirmed.

The number of live microbes contained in different fermented foods at the time of consumption is often unclear, but this question is being investigated for an upcoming review article commissioned by ISAPP.

Patient question:
Do the live microbes in fermented foods support my gut microbiota?

MES: Researchers working on the gut microbiota have long observed that (1) the colonizing microbiota is important to health, and (2) modern diets, compared to diets of early man, are significantly lacking in live microbes. Dietary live microbes provide ongoing exposure of our alimentary canal to a fresh source of microbes. Many of these may not survive through the digestive process – our stomach and upper small intestine are harsh environments. But the ones that do survive, and components of the ones that don't, have the potential to interact with the host, impacting immune, neurological, and other host systems.

SUMMARY:
Fermented foods are associated with positive health effects.

MES: Overall, it appears that many fermented foods are associated with positive health effects, but we lack controlled clinical research to confirm this relationship. The subset of fermented foods that qualify as probiotic may have unique benefits attributable to the live microorganisms. Consuming fermented foods will at least temporarily bolster the live microbes transiting through the gut, and that is likely a good thing. Patients who want to find ways of adding fermented foods to their diet should be advised to seek the advice of a registered dietitian.

References:

Chen, M. *et al.*, 2014. Dairy consumption and risk of type 2 diabetes: 3 cohorts of US adults and an updated meta-analysis. BMC Medicine, 12(1), p.215. Available at: http://bmcmedicine.biomedcentral.com/articles/10.1186/s12916-014-0215-1

Marco, M.L. *et al.*, 2017. Health benefits of fermented foods: microbiota and beyond. Current Opinion in Biotechnology, 44, pp.94–102. Available at: http://linkinghub.elsevier.com/retrieve/pii/S095816691630266X

Mozaffarian, D. *et al.*, 2011. Changes in Diet and Lifestyle and Long-Term Weight Gain in Women and Men. New England Journal of Medicine, 364(25), pp.2392–2404. Available at: http://www.nejm.org/doi/10.1056/NEJMoa1014296

Tapsell, L.C., 2015. Fermented dairy food and CVD risk. British Journal of Nutrition, 113(S2), pp.S131–S135. Available at: http://www.journals.cambridge.org/abstract_S0007114514002359

Read the original post online at:
http://www.gutmicrobiotaforhealth.com/en/gut-microbiota-clinical-minute-fermented-foods-contribute-health/

Beneficial effects of resistant starch for host health

Published on February, 20, 2017 by Andreu Prados.

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.

Dietary fibre is a key nutrient for optimizing gut health and it has been previously documented that a fibre-deprived diet may have a negative impact on the colonic mucus layer and gut microbiota functionality. Resistant starch (RS) is a form of starch that is not digested in the small intestine and is therefore considered a type of dietary fibre.

A recent review by Dr. Stacey Lockyer from the British Nutrition Foundation in London (United Kingdom) and Dr. Anne Nugent from the University College Dublin in Dublin (Ireland) summarises reported health effects of RS and explores the potential mechanisms of action that underpin them.

RS is defined as "a portion of starch that cannot be digested by amylases in the small intestine and passes to the colon to be fermented by microbiota." There are currently 5 types of RS that can be found naturally in plant foods or can be produced or modified commercially and incorporated into food products:

- RS1: a physically inaccessible starch and could be found in coarsely ground or whole-kernel grains such as bread, seeds and legumes.

- RS2: a granular starch found in raw vegetables such as raw potato and green banana, that implies that is rarely or never eaten.

- RS3: formed when starchy foods (e.g. potatoes, pasta, rice) are first cooked and then cooled.

- RS4: includes several chemically modified starches and could be found in food products like commercially produced breads.

- RS5: comprises amylose-lipid complexes that are formed during processing and reforming after cooking (e.g. boiled beans with potatoes, mixed with olive oil) or can be created artificially and added to foods.

The review focuses on human evidence regarding the health effects of RS consumption in several areas including gut health, glycaemia and plasma lipids, satiety and bodyweight.

When it reaches the large intestine, RS is fermented by microbes and produces short-chain fatty acids (SCFAs) that may play an important role in several effects on human health. Besides this, RS may have an

Beneficial effects of resistant starch for host health

impact on gut microbiota composition -especially on those bacterial communities involved in amylose breakdown and butyrate and methane production- and biomarkers of bacterial activity, and therefore it is suggested that RS could be used as a prebiotic. It can be hypothesized that high intake of RS is beneficial for host health, but its role in the interplay between diet, gut, and microbiota is likely more complex.

There is also some evidence that RS can counterbalance the negative effects of high red meat intake on colorectal cancer risk by decreasing pro-mutagenic products that arise during protein fermentation or via protecting against deoxyribonucleic acid (DNA) damage through SCFA production.

When compared with digestible carbohydrate consumption, RS consumption may lead to a reduced glycaemic response, which opens the potential for its use in managing diabetes. Nevertheless, RS appears to have little impact on other metabolic markers such as blood pressure and plasma lipids.

Another area of interest is the role of RS in decreasing appetite. Potential mechanisms involved include SCFA production that stimulates the release of gut hormones that promotes feelings of satiety. The authors concluded in their review that RS consumption does not result in significant changes in bodyweight over the long term, as there appears to be inter-individual variation in responses. In this context, it has been previously reported that colonic propionate produced by gut microbes may affect reward-based eating behaviour and therefore could potentially play a role in managing obesity and unhealthy eating.

Finally, emerging evidence suggests RS as a beneficial ingredient in oral rehydration solutions.

In conclusion, as a type of dietary fibre, RS can contribute to daily fibre intakes and associated health benefits. Although several human studies have reported its impact on different health outcomes, further research is needed in order to elucidate whether it can confer significant benefits that are relevant to the general healthy population and to people with chronic diseases.

Read the original post online at:
http://www.gutmicrobiotaforhealth.com/en/beneficial-effects-resistant-starch-host-health/

New study uncovers a key immune mechanism that modulates the diversity of the gut microbiota

Published on August, 17, 2017 by Andreu Prados.

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.

Previous research has found that the gut microbiome modulates both immune system development and gut homeostasis through its interaction with the host immune cells. Although both innate and adaptive humoral responses target distinct commensal bacteria via mucosal secretory immunoglobulin A (SIgA), little is known about whether secretory immunoglobulin M (SIgM) is also involved.

A new study, led by Dr. Andrea Cerutti from the Hospital del Mar Medical Research Institute (IMIM) (Barcelona, Spain) and the Department of Medicine at Icahn School of Medicine at Mount Sinai (New York, USA), has found for the first time that immunoglobulin M secreted by the human intestine interacts with the gut microbiome to maintain its diversity.

Analyses were undertaken using both mouse and human ileum and colon tissue samples.

The researchers found that the gut mucosa IgM-secreting plasma cells -which account for about 20% of all gut plasma cells- were more abundant in humans than in mice gut and coexisted with a large but previously unrecognized repertoire of gut-specific memory IgM+ B cells that emerged early in life and were clonally related to IgM-secreting plasma cells as well as some memory IgA+ B cells and IgA-secreting plasma cells. According to the authors, "Our identification of clonally related memory IgM+ cells and IgM-secreting plasma cells extends evidence from mouse systemic immunization models indicating that humoral memory is not merely comprised of memory IgG+ and memory IgA+ B cells, but further extends to memory IgM+ B cells."

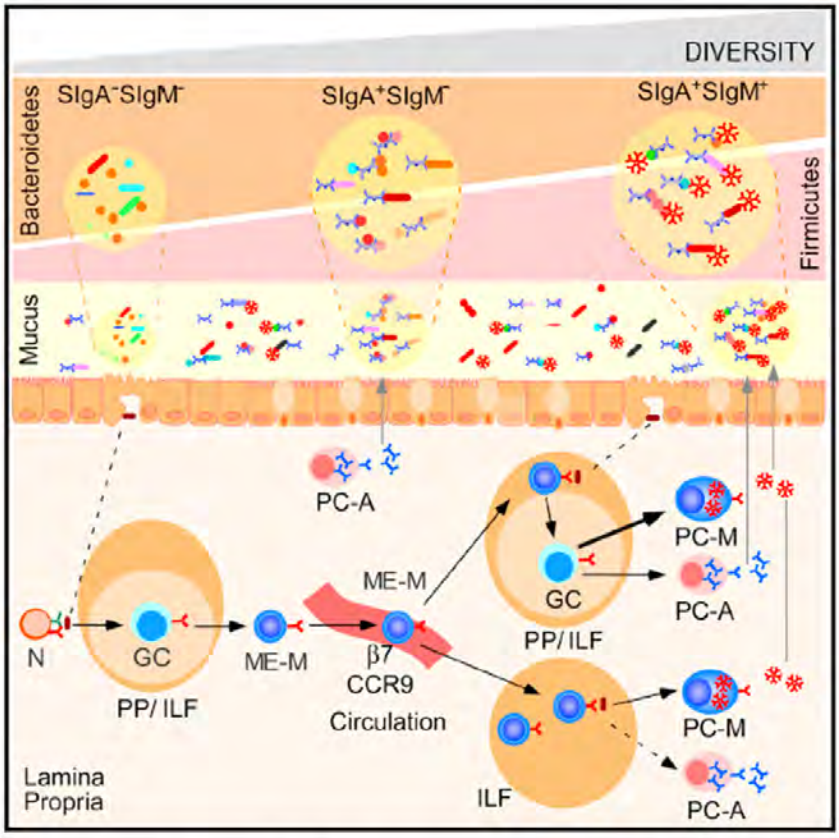
Human gut memory IgM+ B cells underwent proliferation, plasma cell differentiation, IgM secretion, and IgA class switching in response to T cell-dependent and T cell-independent signals. First, human memory IgM+ B cells disseminated in both the ileum and the colon, and afterwards they differentiated to IgM-secreting plasma cells and class-switched IgA-secreting plasma cells by entering germinal centres or progressing through extra-germinal centre pathways. Besides this, memory IgM+ B cells secreted IgM that targeted mucus-embedded commensals, similar to SIgM from IgM-secreting plasma cells. Human SIgM recognized bacteria dually coated by SIgA that exhibited higher diversity when compared to

New study uncovers a key immune mechanism that modulates the diversity of the gut microbiota

SIgA-only-coated or uncoated bacteria. However, murine SIgM could not bind a highly diverse microbiota dually coated by SIgA. On the whole, these data show that human secretory IgM emerges from pre-existing gut memory B cells and plays a role in helping SIgA to anchor highly diverse commensal communities to mucus.

"We have discovered that, in addition to immunoglobulin A (IgA), immunoglobulin M (IgM), secreted by the human intestine, interacts with the intestinal microbiota and actively participates in maintaining its diversity. In addition, we have demonstrated that this immunoglobulin is part of an immunological memory system through which our organism is able to recognise and adapt to its microbial environment," say the first authors of the article, Giuliana Magri and Laura Comerma.

In conclusion, this study demonstrates that IgM has a fundamental role in the regulation of the gut microbiota. Therefore, SIgM may have a role in enhancing host-microbiota symbiosis, similar to SIgA.



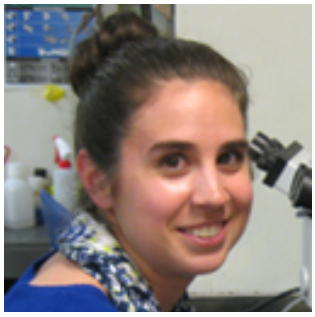
CREDIT: MAGRI G *ET AL.* / IMMUNITY 2017 (CCBY 4.0)

References:
Magri G, Comerma L, Pybus M, *et al.* Human secretory IgM emerges from plasma cells clonally related to gut memory B cells and targets highly diverse commensals. Immunity. 2017; 47(1):1-17. doi: 10.1016/j.immuni.2017.06.013.

Read the original post online at:
http://www.gutmicrobiotaforhealth.com/en/new-study-uncovers-key-immune-mechanism-modulates-diversity-gut-microbiota/

Virus may lead to celiac disease through disruption of intestinal immune homeostasis

Published on April, 10, 2017 by Heather Galipeau.



Heather Galipeau is a Research Associate at McMaster University (Canada) where she is researching dietary and microbial interactions in celiac disease and inflammatory bowel disease. She obtained her PhD in 2015 from McMaster University in Elena Verdu's lab, during which she found that the small intestinal microbial background influences the degree of immuno-pathology triggered by dietary antigens, such as gluten.

Celiac disease (CeD) is a complex immune mediated disorder that is triggered by abnormal immune responses to the dietary protein gluten, which is found in grains like wheat, barley, and rye. Normally, immune tolerance to dietary proteins prevents inflammatory immune responses from developing. However, in those with CeD, the presence of HLA susceptibility genes plus unknown environmental or immune triggers lead to a pro-inflammatory Th1 response towards gluten proteins. While gluten exposure and genetic risk are both required for CeD, only a proportion of genetically susceptible individuals will go on to develop the disease, highlighting a critical role of environmental modifiers. Epidemiological studies have suggested a link between infections or a dysbiotic microbiota and CeD, but mechanistic studies and experimental data to support these associations are lacking. Moreover, the events that lead to the loss of tolerance to these innocuous dietary proteins in the gut, like gluten, are not well understood.

A new study published in Science by Bouziat and colleagues show that reovirus, which are mild or clinically silent viruses that infect humans frequently over the course of a lifetime, can break tolerance to dietary proteins and may constitute an environmental modifier for CeD development. The collection of viruses within the body, known as the virome, is an often forgotten member of the human microbiome. This study helps to highlight the complexity of the gut microbiota and the effects its various components (bacteria, viruses, fungi) have on host immunity. These exciting results also provide evidence that supports the epidemiological link between infections and CeD development.

In a series of elegant experiments, the authors infected mice with two different strains of reovirus. While both strains infected the intestine, induced protective immunity, and were cleared, they differentially modulated immune responses to dietary proteins in the gut. The reovirus strain T1L induced more extensive transcriptional changes in the mesenteric lymph nodes, the site where immune responses to dietary antigens are induced. Interestingly, this was associated with an increase in pro-inflammatory dendritic cells that uptake food antigens, and it promoted an inflammatory Th1 response while inhibiting a tolerogenic, regulatory response. Using a series of in vivo and in vitro experiments with knock-out mice, the authors further showed that the pro-inflammatory Th1 phenotype to dietary antigen induced by T1L was dependent on interferon regulatory factor 1 (IRF1),

Virus may lead to celiac disease through disruption of intestinal immune homeostasis

a transcription factor involved in Th1 regulation. Moreover, in an animal model expressing the CeD susceptibility gene, T1L infection led to a pro-inflammatory dendritic cell phenotype and the loss of tolerance to gluten peptides upon feeding. These exciting findings suggest that reovirus could interact with the host to promote an inflammatory environment at the site where oral tolerance is induced, setting the stage for the generation of inflammatory immune responses to dietary antigens instead of tolerogenic responses.

Viruses have been suggested to play a role in CeD development in humans, and Bouziat *et al*. also showed a trend for higher reovirus antibody titres in patients with CeD compared to controls. The implications of this are critical, as the events leading to CeD and other food allergies are not well understood, and this provides a target for further investigation. The findings also raise the possibility of other gut microbial (viral or bacterial) modulators of oral tolerance. Indeed, an altered microbial composition has been described in CeD patients, with increases in opportunistic pathogens.

Increases in bacterial virulent factors have been reported in CeD patients and the presence of the pathobiont *E. coli* can increase susceptibility to gluten-induced pathology in mice expressing the CeD susceptibility gene. More recently, Caminero and colleagues reported the presence of the opportunistic pathogen *P. aeruginosa* in CeD patients. The study found that proteases from *P. aeruginosa* could participate in gluten metabolism in vivo, leading to the production of gluten peptides with greater immunogenicity. It may be that multiple members of the gut microbiota, including bacteria or viruses, could potentially (independently, through different pathways) play a role in loss of tolerance to gluten or other food antigens.

Together these findings highlight the complex scenario surrounding the factors involved in CeD development. The study by Bouziat *et al.* shows one scenario where subclinical viral infections can lead to the loss of tolerance to dietary antigens like gluten. Importantly, it suggests that members of the gut microbiota can influence immune responses to innocuous proteins in the gut. This scenario may also apply to other microbial members or to other food sensitivities or autoimmune diseases. Deepening our understanding of the events leading to adverse reactions to innocuous antigens will allow for the development of preventative strategies. This is particularly important given the recent increase in prevalence of autoimmune disease, food sensitivities, and food allergies.

References:
Bouziat R, Hinterleitner R, Brown JJ, *et al*. Reovirus infection triggers inflammatory responses to dietary antigens and development of celiac disease. Science. 2017; 356(6333): 44-50. doi: 10.1126/science.aah5298

Read the original post online at:
http://www.gutmicrobiotaforhealth.com/en/virus-may-lead-celiac-disease-disruption-intestinal-immune-homeostasis/

What can the gut microbiota of infants reveal about eczema development?

Published on October, 16, 2017 by Kristina Campbell.

Science writer Kristina Campbell (M.Sc.), from British Columbia (Canada), specializes in communicating about the gut microbiota, digestive health, and nutrition. Author of the best selling Well-Fed Microbiome Cookbook, her freelance work has appeared in publications around the world. Kristina joined the Gut Microbiota for Health publishing team in 2014.

To date, no effective strategy has been identified for reliably preventing the development of eczema and allergy in children at high risk of these conditions. Eczema (atopic dermatitis) is typically one of the first allergic manifestations to appear in infants predisposed to allergic disease. Thus, the condition is of particular interest when it comes to prevention.

Since early life gut microbiota development occurs at a time when key cognitive, metabolic, and immune functions are maturing, some scientists have begun to investigate whether the gut microbiota could be a potential way to predict, from among the population at risk, which children will go on to develop eczema and other allergic diseases.

A new study by a group of scientists from Danone Nutricia Research (the Netherlands), the Laboratory of Microbiology at Wageningen University (the Netherlands), and the Department of Medicine at Imperial College London (United Kingdom) explored how the gut microbiota tracks eczema development in early life—and also whether gut microbiota composition was modulated by a prebiotic early-life dietary intervention.

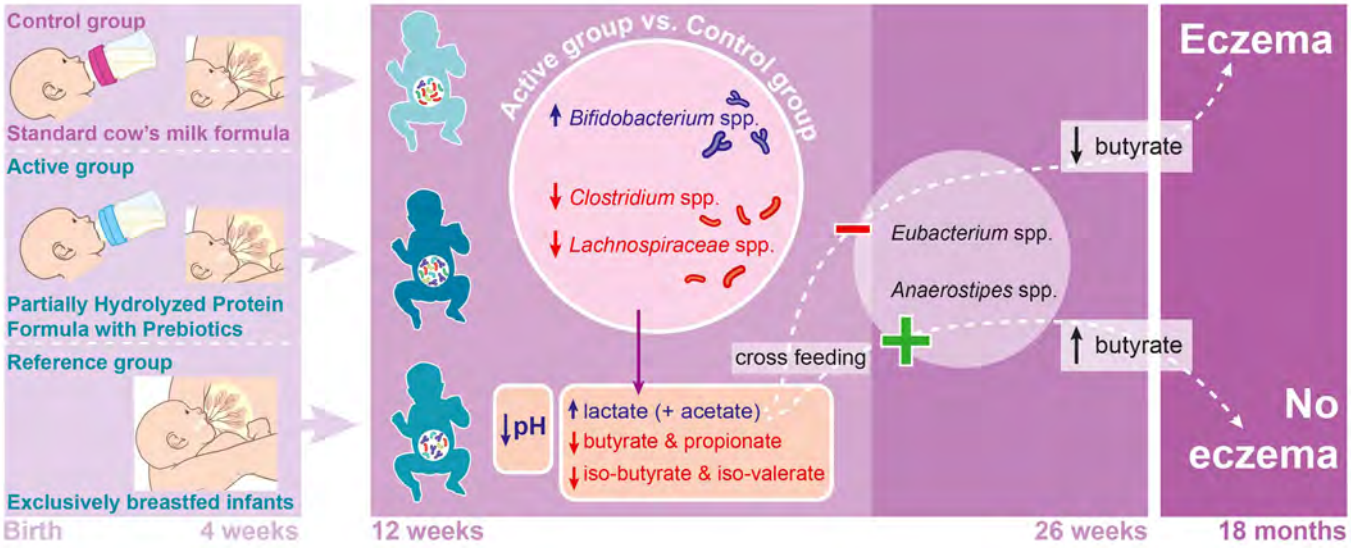
Researchers analyzed the fecal samples of 138 vaginally-born infants at increased risk of allergy (that is, with a parental history of allergic disease); the samples were collected from each infant at 4 and 26 weeks. Stool measurements of pH and lactate, as well as short-chain fatty acids, were also taken at 4, 12, and 26 weeks. The babies who (for various reasons) were not breast-fed consumed either standard cow's milk formula (n=57) or a partially hydrolyzed formula containing specific oligosaccharides (pHF-OS) (n=51). These groups were compared with a reference group of breast-fed infants (n=30).

By 18 months, 52 of the 138 infants (about 38%) showed symptoms of eczema. The infants who went on to develop eczema by 18 months showed compositional differences in their gut microbiota compared to those not developing eczema: at 4 weeks, they showed decreased relative abundances of *Parabacteroides* and *Enterobacteriaceae*, while at 26 weeks they showed decreases in *Eubacterium* and *Anaerostipes* species, which are known to use lactate and to produce butyrate. So unsurprisingly, increased lactate and decreased butyrate were also observed at the 26-week mark in the stool of infants who would later develop eczema.

Previously, a 'parent' study, called the "PATCH trial", had showed immunological changes in infants receiving the pHF-OS intervention,

SELECTED CONTENT

What can the gut microbiota of infants reveal about eczema development?



but no reduced incidence of eczema at 12 or 18 months. In the current study, the researchers followed up with the question of whether this early-life nutritional intervention modulated the gut microbiota composition in a potentially beneficial way.

Researchers assessed the similarity in microbiota composition between groups using a measure of phylogenetic distances and relative abundances of bacterial taxa in pairwise comparisons of samples. At 26 weeks, the infants receiving pHF-OS were more similar in composition to those in the breast-fed group than were the infants receiving control formula. Compared to the control formula group, the pHF-OS group showed increased levels of *Bifidobacterium* species, with decreased levels of *Clostridium* species as well as an unassigned genus of *Lachnospiraceae*. Overall, the authors found, fecal microbiota composition, metabolites, and pH in infants who received the prebiotic-supplemented formula rather than the standard formula were closer to those of breast-fed infants. This trajectory may indicate a benefit, as previous evidence suggests exclusively breast-fed infants have a lower risk for childhood eczema.

This study shows gut microbiota composition in the first six months of life deserves more exploration as a way to predict the development of eczema; furthermore, it shows the potential of a prebiotic-enriched formula to modulate the gut microbiota in a manner that may be beneficial. No specific microbial biomarkers of eczema were identified, however, and further prospective studies are warranted.

References:
Wopereis H, Sim K, Shaw A, Warner JO, Knol J, Kroll S. Intestinal microbiota in infants at high risk for allergy: Effects of prebiotics and role in eczema development. J Allergy Clin Immunol. 2017. doi: 10.1016/j.jaci.2017.05.054

Read the original post online at:
http://www.gutmicrobiotaforhealth.com/en/can-gut-microbiota-infants-reveal-eczema-development/

A large clinical trial in India finds a synbiotic may help prevent neonatal sepsis

Published on October, 19, 2017 by Paul Enck.

Prof. Dr. Paul Enck, Director of Research, Dept. of Psychosomatic Medicine and Psychotherapy, University Hospital Tübingen, Germany. His main interests are gut functions in health and disease, including functional and inflammatory bowel disorders, the role of the gut microbiota, regulation of eating and food intake and its disorders, of nausea, vomiting and motion sickness, and the psychophysiology and neurobiology of the placebo response, with specific emphasis on age and gender contributions.

Sepsis is a life-threatening condition characterized by systemic inflammation; it is one of the major contributors to neonatal mortality, especially in developing countries. The World Health Organization (WHO) estimates that 1 million deaths per year (10% of all under-five mortality) are due to neonatal sepsis and that 42% of these deaths occur in the first week of life. Although exclusive breastfeeding and chlorhexidine antisepsis interventions (on vaginal areas, newborn skin and the umbilical cord) have been proven to benefit neonatal health in low-resource settings, no prophylactic tool is widely used.

A new community-based, double-blind, placebo-controlled randomized trial, led by Dr. Ira H. Gewolb from the Division of Neonatology at College of Human Medicine at Michigan State University (East Lansing, Michigan, USA), has found that a synbiotic consisting of a strain of *Lactobacillus plantarum* and fructooligosaccharide may be effective in preventing sepsis in rural Indian newborns. Synbiotics are combinations of a probiotic -the *Lactobacillus plantarum* strain – with a prebiotic – here the fructooligosaccharide.

The researchers enrolled 4,556 healthy newborns -all of them weighing at least 2,000 g at birth, born at 35 weeks of gestation or later, who were breastfed and had no signs of sepsis or other morbidity- from 149 randomly chosen rural Indian villages and monitored them for 60 days. It is noteworthy that neonatal and infant mortality rates in the studied region are among the highest in India, according to the Department of Health & Family Welfare from the Government of Odisha state.

Infants in the treatment arm (n = 2,278) took a daily dose of the synbiotic (consisting of a capsule containing 109 colony forming units of *Lactobacillus plantarum ATCC* strain 202195 and 150 mg of fructooligosaccharide with 100 mg maltodextrin as excipient) for one week, whereas the placebo group (n = 2,278) took capsules containing only 250 mg of maltodextrin.

Primary outcome was a composite of sepsis (composed of septicaemia, meningitis, culture-negative sepsis, and low respiratory tract infections) or death. Secondary outcomes were other infections (including diarrhoea, omphalitis, local infections, abscess, and otitis media) and weight gain.

SELECTED CONTENT

A large clinical trial in India finds a synbiotic may help prevent neonatal sepsis

The colonizing ability, tolerance and impact on the stool microbiota of administration of *L. plantarum ATCC* strain 202195 in combination with fructooligosaccharide was previously reported in newborns by the same research group. The probiotic strain was initially isolated from healthy volunteers' stool and when administered to infants colonized their gut successfully and remained there for up to 4 months.

Newborn babies who took the synbiotic had a significantly lower risk of developing sepsis. Just 5.4% of the infants who took the synbiotic developed sepsis in their first 2 months of life, compared to 9% of those who received a placebo. The researchers calculated that the reduction of sepsis risk was between 25-50%. Some sepsis cases in newborn babies begin in the gut and the symbiotic may prevent them by either ousting pathogenic microorganisms or stopping commensal ones from entering the bloodstream and causing infections.

Apart from preventing sepsis, the synbiotic also reduced the risk of infection by Gram-positive bacteria (by 82%), Gram-negative bacteria (by 75%), and pneumonia and other airway-related infections (by 34%).

Regarding tolerance and safety, the symbiotic was well tolerated and did not cause any harmful side effects. Only 6 cases of abdominal distention were reported across both groups.

To sum up, this is the first large clinical trial that has found benefits of a symbiotic for sepsis prevention in newborns from a developing country. "We may need to test this in different settings and we are working with the government to do so," says the first author Dr. Panigrahi. In an article in The Atlantic, Ed Yong writes, "Beyond protecting infants… this approach would also reduce the use of antibiotics, and slow the spread of drug-resistant infections. And perhaps best of all, it can be done cheaply. You would need to treat 27 infants to prevent one case of sepsis, and each week-long course costs just one U.S. dollar."

References:
Panigrahi P, Parida S, Nanda NC, *et al.* A randomized synbiotic trial to prevent sepsis among infants in rural India. Nature. 2017. doi: 10.1038/nature23480.

Read the original post online at:
http://www.gutmicrobiotaforhealth.com/en/large-clinical-trial-india-finds-synbiotic-may-help-prevent-neonatal-sepsis/

SELECTED CONTENT

New GMFH "best of" document outlines the latest research on gut microbiota & early life

Published on September, 7, 2017 by GMFH Editing Team.

Gut microbial colonization during early life influences human development by triggering age-dependent immune mechanisms. Although considerable research effort has been made to understand microbial influences on health in early life, many of the processes through which microbial exposures facilitate immune system development remain to be identified. (Prof. Marie-Claire Arrieta)

The GMFH publishing team is pleased to share a new summary document—this one on the latest scientific work on gut microbiota in early life. With an editorial from Prof. Marie-Claire Arrieta, Assistant Professor in the Department of Physiology & Pharmacology and the Department of Paediatrics at the Cumming School of Medicine at the University of Calgary (Canada), this document contains a selection of key scientific studies related to babies and gut microbes, plus a list of resources for further reading.

The GMFH team will continue to keep you updated on this exciting topic—check our website regularly or subscribe to our twice-monthly newsletter!

Read the original post online at:
http://www.gutmicrobiotaforhealth.com/en/new-gmfh-best-document-outlines-latest-research-gut-microbiota-early-life/

GUT MICROBIOTA FOR HEALTH
World Summit 2018

SATURDAY 10 AND SUNDAY 11
MARCH, 2018
ROME (ITALY)
BARCELÓ ARAN MANTEGNA HOTEL

SAVE THE DATE

7th edition
of the primary event on gut microbiota and health,
addressed to clinical researchers and healthcare practitioners

2 days of plenary sessions
and workshops

To view the scientific program and register, stay tuned to
www.gutmicrobiotaforhealth.com

Gut Microbiota & Health · ESNM · ESPGHAN · with the support of · DANONE DAIRY · SANOFI · BIOCODEX

CALL FOR ABSTRACTS:

Submit your abstract for Poster Presentations at GMFH World Summit 2018

SUBMIT

JOIN OUR COMMUNITY TODAY AND STAY TUNED

with the most relevant scientific developments about gut microbiota.

With more than 50,000 members around the globe!

- Gut Microbiota for Health
- @GMFHx
- Gut Microbiota News Watch
- Twice a month newsletter

YEAR AT A GLANCE

January 2018

healthline BEST Blogs GUT HEALTH 2017

PREMIO CONSALUD 2016

2016 WINNER BEST GUT HEALTH BLOGS healthline

www.gutmicrobiotaforhealth.com

ESNM
European Society
of Neurogastroenterology
& Motility

www.esnm.eu
Alser Strasse 4, 1090 Vienna, Austria

Gut Microbiota & Health