



**GUT MICROBIOTA**  
RESEARCH & PRACTICE  
edited by ESNM

## YEAR AT A GLANCE

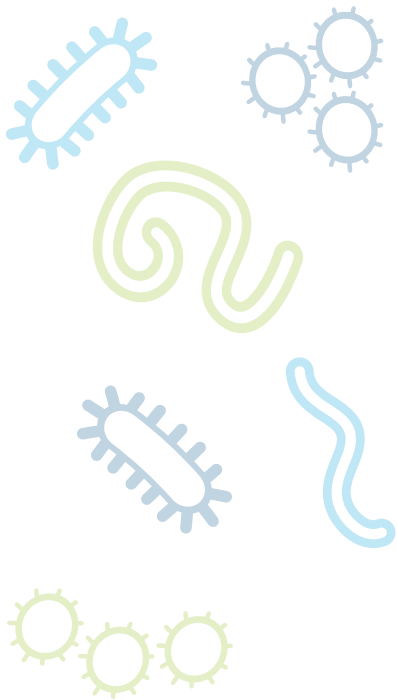
A selection of content from the  
Gut Microbiota for Health 2016

January 2017

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# EDITORIAL



2016 was a year of change for the Gut Microbiota for Health (GMFH) initiative! The European Society of Neurogastroenterology & Motility brought the GMFH Experts Exchange together with its companion website, Gut Microbiota WorldWatch, to create the largest online platform dedicated to gut microbiota research. GMFH now offers a single website with high-quality scientific content, with one section for scientists and healthcare professionals (Research & Practice) and another for the general public (NewsWatch). This year it received a record number of hits—over 35,000 per month—and, in Spain, had the honour of being selected as the “ConSalud Initiative of the Year” for the most outstanding programme focused on health. The GMFH blog was also featured as one of 13 on Healthline’s list of best gut health blogs.

This “Best of 2016” document contains the GMFH publishing team’s curated selections from the Research & Practice section of the website, plus a list of what gathered attention on social media. The publishing team works throughout the year to select the articles of greatest scientific interest from the growing literature on gut microbiota. With publications from both established and early career scientists, the team aims to highlight the research that is important in the unfolding story about the gut microbiome in health and disease.

Harvard’s Wendy Garrett, in her recent review on gut microbiota research, called 2016 “a banner year”<sup>(1)</sup>. Indeed, in 2016, researchers have brought forward some of the most detailed and thoughtful work to date on the roles of the human gut microbiota.



## Obesity and metabolic health

Considerable research efforts continue to focus on the role of the gut microbiota in metabolic disease and obesity. Yet the initially promising studies in mouse models in past years, showing gut microbiota can transfer metabolic phenotype, have not been easily translated into humans. This year brought an increased determination to move beyond gut microbiota composition (the purported increase in the Firmicutes to Bacteroidetes ratio in obesity), as researchers looked at specific influential species, as well as microbiota function, for

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insights about gut microbial influences on parameters of human metabolic health.

One species garnered special interest for its potential metabolism-modulating effects—*Akkermansia muciniphila*. A study this year from Cani, de Vos, and colleagues found new mechanistic information about its role in metabolic disease<sup>(2)</sup>: a protein (called Amuc\_1100\*) isolated from the outer membrane of *A. muciniphila* was responsible for reduced fat mass development, insulin resistance, and dyslipidemia in a mouse model. In addition, the lab tested live and pasteurized *A. muciniphila* in 20 humans with metabolic syndrome, constituting the first safety trial with this potential next-generation probiotic.

## Inflammatory bowel disease

While researchers try to unravel the contributions of genes and the microbiome in the pathogenesis of inflammatory disease, elegant work this year from the lab of Harry Sokol suggested genes may be able to exert their effects on inflammation by acting through the microbiota<sup>(3)</sup>. The researchers studied mice lacking the caspase recruitment domain family member 9 (CARD9) gene, which were more susceptible to experimental colitis. When genetically-normal germ-free mice were colonized with microbiota from CARD9-deficient mice, they too showed increased susceptibility to colitis, as well as defective IL-22 production from

gut immune cells. In these mice, the ability to produce important microbial metabolites from the diet was impaired, resulting in heightened inflammation.

Another study this year underlined the role of fungi, in addition to bacteria, in the pathogenesis of human inflammatory bowel disease<sup>(4)</sup>. And a remarkable advance had to do with predicting the progression towards complicated Crohn's disease (CD)<sup>(5)</sup>: researchers showed in a 100-person cohort that circulating anti-microbial antibodies six or more years before Crohn's diagnosis predicted complicated CD at the time of diagnosis.

## Nutrition

Dietitians and nutritionists are showing increasing interest in the value of microbiota modulation through diet, and 2016 brought some significant insights about how diet-induced microbiota changes may affect health. When it comes to fibre, work from the Sonnenburg lab showed mice with a human gut microbiota that consumed a diet low in microbiota-accessible carbohydrates (MACs) progressively lost microbiota diversity over several generations<sup>(6)</sup>; the loss was not reversible even after dietary MACs were reintroduced. Also, Desai, Martens, and colleagues investigated mechanisms by which fibre may exert its health effects, showing in a humanized mouse study that a fibre-deprived diet

yields a degraded colonic mucus layer and increased enteric pathogen infection<sup>(7)</sup>.

On the role of the gut microbiota in gestation and early life, the Aagaard lab published work this year showing a maternal high-fat diet during gestation and lactation is associated with a distinct gut microbial signature in the neonate at birth<sup>(8)</sup>. Aagaard and colleagues are actively investigating factors that might influence the placental microbiome, and even raised the possibility that some of the adverse health effects attributed to caesarean delivery could actually result from maternal obesity and/or a suboptimal diet during pregnancy<sup>(9)</sup>.

This year the Gordon lab advanced knowledge on growth and gut microbiota in malnourished children: one new study from the group found that oligosaccharides in human breast milk interacted with gut microbes to promote growth and metabolism in malnourished children<sup>(10)</sup>, and another study using both mouse and pig models showed milk oligosaccharides promoted growth and normal metabolism only in the presence of gut microbiota<sup>(11)</sup>.

## Microbiota in the gut-brain axis

The role of the microbiota in affecting the brain through the gut-brain axis is an area of continued scientific promise. Causality is especially difficult to prove in this area because animal

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models cannot account for the unique complexity of the human brain and human behaviour. 'Humanized' mice, however, are providing more insights: for example, a study this year using a particular mouse model of Parkinson's disease (PD) (mice that overexpress alpha-synuclein) found that gut microbiota from humans with PD worsened motor symptoms in the mice<sup>(12)</sup>. Also, a

study by Buffington, *et al.* found that some maternal-diet-induced impairments in the social behaviour of young mice were reversed by the administration of the probiotic species *L. reuteri*<sup>(13)</sup>.

Much more research on gut microbiota was published this year, including work on how gut microbiota could modulate gluten immunogenicity in celiac disease,

and increased support for the hypothesis that both asthma and allergy are linked to features of the gut microbiota in early life. As interest in this area continues to grow, so does the GMFH initiative. We look forward to bringing together our community during the GMFH World Summit in March, 2017, and to following the new developments closely in the year ahead.



## Prof. Dr. Paul Enck

Prof. Dr. Paul Enck, Director of Research, Dept. of Psychosomatic Medicine and Psychotherapy, University Hospital Tübingen, Germany. He is board member/treasurer of the European Society of Neurogastroenterology and Motility and of the German Society of Neurogastroenterology and Motility, and has served as reviewer for many international journals and grant agencies.

### Sources

<sup>(1)</sup> Garrett WS. **A banner year for gut microbiota research.** *Nat Rev Gastro Hep.* 2016. doi: 10.1038/nrgastro.2016.207

<sup>(2)</sup> Plovier H, Everard A, Druart C, *et al.* **A purified membrane protein from *Akkermansia muciniphila* or the pasteurized bacterium improves metabolism in obese and diabetic mice.** *Nature Medicine.* 2016. doi:10.1038/nm.4236

<sup>(3)</sup> Lamas B, Richard ML, Leducq V, *et al.* **CARD9 impacts colitis by altering gut microbiota metabolism of tryptophan into aryl hydrocarbon receptor ligands.** *Nat Med.* 2016; 22(6):598-605. doi: 10.1038/nm.4102.

<sup>(4)</sup> Hoarau G, Mukherjee PK, Gower-Rousseau C, *et al.* **Bacteriome and mycobiome interactions underscore microbial dysbiosis in familial Crohn's disease.** *mBio.* 2016; 7(5):e01250-16. doi: 10.1128/mBio.01250-16.

<sup>(5)</sup> Choung RS, Princen F, Stockfisch TP, *et al.* **Serologic microbial associated markers can predict Crohn's disease behaviour years before disease diagnosis.** *Aliment Pharmacol Ther.* 2016; 43(12):1300-10. doi:10.1111/apt.13641.

<sup>(6)</sup> Sonnenburg ED, Smits SA, Tikhonov M, Higginbottom SK, Wingreen NS, Sonnenburg JL. **Diet-induced extinctions in the gut microbiota compound over generations.** *Nature.* 2016;529(7585):212-215.

<sup>(7)</sup> Desai MS, Seekatz AM, Koropatkin NM, *et al.* **A dietary fiber-deprived gut microbiota degrades the colonic mucus barrier and enhances pathogen susceptibility.** *Cell.* 2016; 167(5):1339-53. doi: 10.1016/j.cell.2016.10.043.

<sup>(8)</sup> Chu DM, Antony KM, Ma J, *et al.* **The early infant gut microbiome varies in association with a maternal high-fat diet.** *Genome Medicine.* 2016; 8:77.

<sup>(9)</sup> Aagaard K, Stewart CJ, & Chu D. **Una destinatio, viae diversae.** *EMBO reports.*

2016; 17(12):1679-1684.

<sup>(10)</sup> Blanton LV, Charbonneau MR, Salih T, *et al.* **Gut bacteria that prevent growth impairments transmitted by microbiota from malnourished children.** *Science.* 2016; 351(6275):aad3311. doi:10.1126/science.aad3311.

<sup>(11)</sup> Charbonneau MR, O'Donnell D, Blanton LV, *et al.* **Sialylated milk oligosaccharides promote microbiota-dependent growth in models of infant undernutrition.** *Cell.* 2016; 164(5):859-71. doi:10.1016/j.cell.2016.01.024.

<sup>(12)</sup> Sampson TR, Debelius JW, Thron T, *et al.* **Gut Microbiota Regulate Motor Deficits and Neuroinflammation in a Model of Parkinson's Disease.** *Cell.* 2016; 167(6):1469-1480.

<sup>(13)</sup> Buffington SA, Di Prisco GV, Auchtung TA, *et al.* **Microbial reconstitution reverses maternal diet-induced social and synaptic deficits in offspring.** *Cell.* 2016; 165(7):1762-75. doi:10.1016/j.cell.2016.06.001.

# SELECTED CONTENT

metabolic conditions

## Yolanda Sanz on gut microbes and metabolic health: The big picture

Published in BIOMARKER, DIABETES, DIET, INFLAMMATION, METABOLIC HEALTH,  
METABOLIC SYNDROME, MICROBIOME

Written on Nov 21, 2016 by Kristina Campbell



*Yolanda Sanz, Professor of Research at the Institute of Agrochemistry and Food Technology (IATA) of the Spanish National Research Council (CSIC) and co-ordinator of the MyNewGut gut microbiome research initiative.*

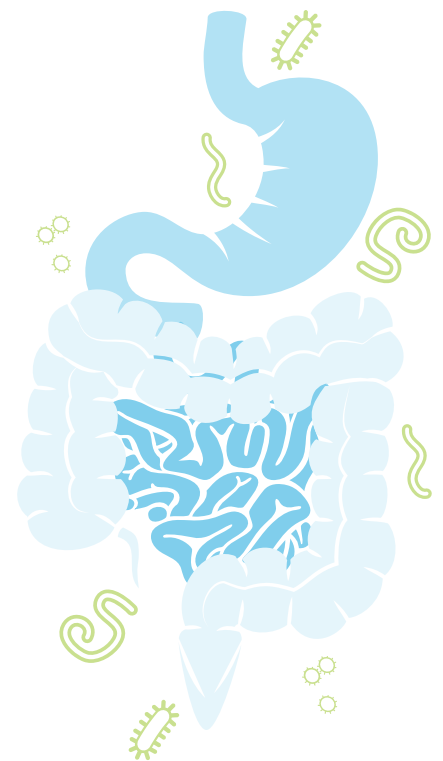
Leading researchers in the field of gut microbiota and metabolic health are set to discuss new insights at an upcoming symposium in Denmark, organized by The Gut, Grain and Greens (3G) Center and the Danish Diabetes Academy. Among the scheduled speakers for this event is Yolanda Sanz, Professor of Research at the Institute of Agrochemistry and Food Technology (IATA) of the Spanish National Research Council (CSIC) and co-ordinator of the MyNewGut gut microbiome research initiative.

Sanz, who plans to present unpublished data from MyNewGut at the symposium (November 24th and 25th), spoke with GMFH editors to share a broad perspective on how research on gut microbiota and metabolic health is poised to affect lifestyle and medical interventions in the years

**We already know metabolic syndrome and diabetes are related to diet. How does gut microbiota add to this knowledge?**

What we now know, with evidence available, is that the microbiota can be one of the factors that mediates the effects attributed to the diet for metabolic health. This means it at least can be considered a secondary consequence of the diet, although a primary role cannot be completely disregarded yet.

“The microbiota can be one of the factors that mediates the effects attributed to the diet for metabolic health.”



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## metabolic conditions

### Yolanda Sanz on gut microbes and metabolic health: The big picture

**Researchers once thought the ratio of Firmicutes to Bacteroidetes was important in obesity, but recent data cast doubt on this idea. What are the next steps?**

The relationship of [the] ratio of Firmicutes and Bacteroidetes with obesity initially was an interesting concept, because it was a way to propose a first hypothesis. But we know that these phyla are very broad, and include many different

species. This means that the functional properties of these species may vary tremendously, so we cannot expect that this could be a good indicator for predicting a disease.

The way to progress from this general concept into a more refined hypothesis, which could be the markers of development of obesity, is to evaluate the role of each of the bacterial species or consortia of bacteria (groups of species)—what

they are doing in rodents, in models of metabolic disease, and later on if possible, to prove and to test the effects in humans.

This is also what we are doing in MyNewGut: those bacteria that we associate with obesity or with metabolic syndrome in humans will be tested in animal models to see specifically which ones play a role and which associations are meaningless.

**What avenues of research are most promising for figuring out the role of gut microbiota in obesity & metabolic syndrome?**

One of the challenges we are facing is that it's very difficult to differentiate the effects of the diet from the effects of the microbiota, because in fact, diet and microbiota have reciprocal interactions.

At least, we know that via these interactions the microbiota exerts effects on metabolic health, and this has been proven in rodents via mechanistic studies. For example, it's known that the microbiota that is altered by the diet could increase the inflammatory tone that also leads to metabolic syndrome and diabetes; and for example, it has been proven that diets rich in saturated fat increase the abundance of some pathobionts that are pro-inflammatory, such as

*Bilophila wadsworthia* or other gram-negative bacteria that provide LPS (which is an inflammatory bacterial component). Very recently it has also been described that insulin resistance and the possible development of diabetes is related to some alterations in the microbiota and its metabolic activities (e.g. synthesis of branched-chain amino acids in particular).

These correlations were shown in humans, and have been proven later on in a more specific way in animal models, by feeding animals with the specific bacteria that were increased in humans with insulin resistance.

The causality has also been proven in the study in humans that involved a fecal transplant of the healthy microbiota into subjects with metabolic syndrome, and it was proven that the glucose tolerance

was also improved. So this study did not point to the role of specific bacteria in the process but, at least, demonstrated the concept that the microbiota matter for metabolic health in humans.

The triggering role of the gut microbiota alterations in the onset of metabolic disease is less well documented, because for finding this out we have to conduct long-term longitudinal studies and track the progression of metabolic disease in subjects that initially are healthy.

Some studies are in progress... We have to bear in mind, however, that these disorders are multi-factorial, so we cannot expect that only the microbiota plays a key role. These roles and these effects, adverse or beneficial, will be played by many factors, many variables, that are interacting together. We do know that some of the key factors are the

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## metabolic conditions

### Yolanda Sanz on gut microbes and metabolic health: The big picture

#### How much will we have to account for personalization in diet-microbiome interactions?

In this field we are just getting started so it's very difficult to quantify what is going to be developed regarding diet-microbe interactions in personalization of treatments or prevention. But the results that we have got so far point to the idea that these interactions will play a role.

In fact, it was recently published that the gut microbiome, together

with some other host factors such as body mass index and other physiological parameters, influence the response to different diets in terms of the glucose levels you reach in blood after the meal. And... the glucose levels in blood can indicate also the risk you have to develop insulin resistance and type 2 diabetes.

So we think that there is enough evidence so far to start foreseeing that gut microbe interactions with the diet will play a role in the personalization of dietary

strategies, but still we don't have very clear ideas about the way we are going to stratify the population as a function of the microbiota. Probably, this will depend on the effect we want to investigate or the effect we want to prevent. For example, it will be different if you are planning an intervention with fibre to look at the response and to reduce glucose response than if you are trying to stratify people for assessing the efficacy of a drug treatment. Because the metabolic activities and the bacteria that could play a role will be different.

“So we think that there is enough evidence so far to start foreseeing that gut microbe interactions with the diet will play a role in the personalization of dietary strategies...”

#### What is the promise of new diagnostics based on the gut microbiota?

The role of the gut microbiota in diagnosis still has to be proven, because for doing so we need longitudinal studies looking at the progression from health to disease. The limitations of defining

a biomarker for use as a diagnostic tool based on the gut microbiota would be related to the fact that there are many, many different factors that can influence the microbiome and the microbiota, so this could reduce the predictive value of these biomarkers or diagnostic tools. But on the other hand, the advantage of these potential early diagnosis tools could

be that these biomarkers could be partially modified by interventions. This means there could be early predictors of development of disease (or the risk of developing disease) that we can modify to prevent disease, and this is the most attractive part of this new vision and these new diagnostic tools.



Read the original post online at:

<http://www.gutmicrobiotaforhealth.com/en/yolanda-sanz-gut-microbes-metabolic-health-big-picture/>



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## metabolic conditions

### New insights into how *Akkermansia muciniphila* improves metabolic health, leading to first human safety trial

Published in DIABETES, DIET, METABOLIC CONDITIONS, OBESITY, RESEARCH & PRACTICE, SCFA

Written on December 5, 2016 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.

Previous studies have identified *Akkermansia muciniphila* as an important bacterium in metabolic health—able to prevent the development of obesity in animal models. Until now, however, its mechanisms were unclear and its effects had never been tested in humans.

Now, a team led by Patrice D. Cani of Université catholique de Louvain (UCL; Belgium) and Willem de Vos of Wageningen University (the Netherlands) published a paper in *Nature Medicine* showing that a pasteurized version of *A. muciniphila* was able to reduce fat mass development, insulin resistance, and dyslipidemia in mice; moreover, the pasteurized bacterium modulated both the host urinary metabolome and intestinal energy absorption. Researchers attributed these effects largely to a protein (called Amuc\_1100\*) isolated from the outer membrane of *A. muciniphila*, which appeared to interact with Toll-like receptor 2.

In the paper, the researchers also reported the first safety testing of *A. muciniphila* in 20 human subjects with excess body weight and metabolic syndrome; for three months, these individuals received either a placebo treatment, pasteurized *A. muciniphila*, or one of two doses of live *A. muciniphila*.

GMFH editors caught up with Patrice D. Cani to learn more about the significance of this work.

**Several bacterial species or consortia are under investigation for their beneficial effects in obesity and diabetes. Why is *Akkermansia muciniphila* unique?**

*A. muciniphila* is unique in the field and potentially interesting as a next-generation bacteria because it resides in the mucus layer, a niche in close vicinity to host cells, but also because it displays beneficial effects on several pathologies. Numerous papers have shown that the direct administration has

proven protective not only against obesity but also against type 2 diabetes, gut barrier disturbances as well as atherosclerosis in various studies. Others have found more *A. muciniphila* in colon cancer for instance, but we do believe that this is due to an opportunistic behavior: more mucus produced is more food for *A. muciniphila*.

Here in our paper we show that pasteurized *A. muciniphila* retains all the beneficial effects on metabolic parameters and is even more potent than the live bacteria.

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## metabolic conditions

### New insights into how *Akkermansia muciniphila* improves metabolic health, leading to first human safety trial

**According to this new work, how was *A. muciniphila* able to exert these beneficial effects?**

Unexpectedly, Hubert Plovier (PhD student in Cani's team) found that pasteurisation doubled the effectiveness of *A. muciniphila* which eventually prevented the development of the diseases.

The teams wanted to understand why *A. muciniphila* behaved differently when live and pasteurised, which led them to their second major discovery. Noora Ottman and Judith

Klievink from the team of Willem de Vos isolated a protein present on the outer membrane of the bacterium. This protein also remains active (stable) after being heated to 70°C. Pasteurisation therefore likely eliminates anything that is unnecessary in the *A. muciniphila* bacterium and retains the protein, which probably explains its enhanced effectiveness. We produced the protein (Amuc\_1100\*) by genetic engineering and then tested it in mice. The results showed it was as effective on diabetes and obesity as pasteurised *A. muciniphila*.

The discovery of this protein is

also really promising as it also has a positive impact on the immune system: it blocks the passage of toxins into the blood, reinforces the immune defences of the intestine, and ameliorates leaky gut syndrome, for instance. Thus, the Amuc\_1100\* protein provides hope for the treatment of other diseases such as inflammation of the intestine that appears, for instance, in cases of stress, alcoholism, liver diseases, and cancer.

Using the pasteurized bacteria or the active protein we have isolated circumvents the putative risk of using live *A. muciniphila* on damaged intestine.

**Short-chain fatty acids (SCFAs) have also been discussed in the context of obesity and diabetes. In this study, did you investigate whether they were affected by *A. muciniphila*?**

It has been previously shown by Willem de Vos that *A. muciniphila* produces SCFAs such acetate and propionate and probably also contribute to reinforcing the gut barrier. But in this study because *A. muciniphila* was pasteurized we did not investigate this parameter.

**What's the next step in finding out whether these bacteria could improve human metabolic health?**

Proof that the positive effects in mice also extend to humans still needs to be confirmed.

The clinical investigation is being carried out in the university clinics of Saint-Luc at UCL study Microbes4U since December 2015. The study is currently underway and we have just passed the first stage, namely proving that the use of the bacteria is safe and not dangerous for the humans that are obese and diabetic (more than 40 patients have been screened for safety).

**If *A. muciniphila* proves useful for achieving a long-lasting shift in the microbiota of humans, do you think complementary dietary strategies will be required?**

We have to be careful and a lot of work still must be done. However, I do believe that body weight loss will be possible only if an adequate equilibrate nutrition is present (rich in prebiotics, polyphenols, omega 3...).

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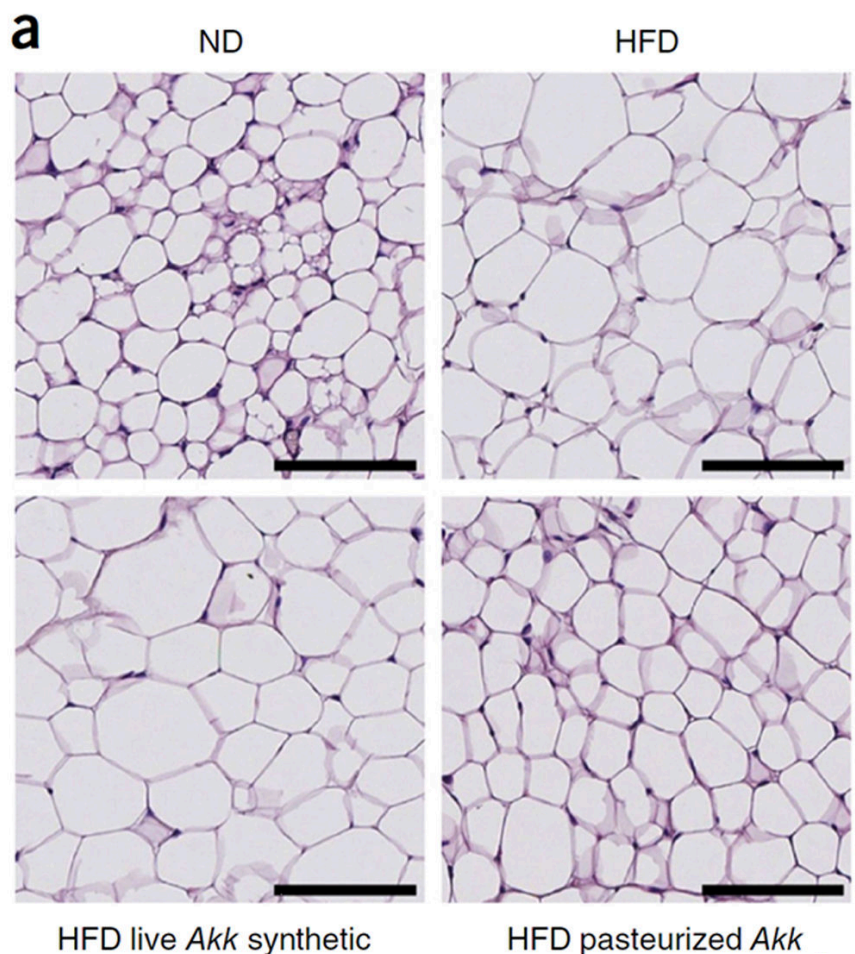
metabolic conditions

## New insights into how *Akkermansia muciniphila* improves metabolic health, leading to first human safety trial

In the years to come (and pending human trials), do you think this intervention could make a difference in the epidemic of obesity in developed countries?

We think that we have to be careful translating all the mouse results into humans. What we really hope is at least to improve metabolic parameters such as low-grade inflammation, glycemia, and cholesterol. If the administration of the bacteria, alive or pasteurized, may change body weight, that is of course interesting.

It is difficult to say that we will cure obesity by using only *A. muciniphila*; however, reducing cardiovascular risk factors or reducing specific markers will likely be the case.



CREDIT: PLOVIER H ET AL./NATURE MEDICINE 2016



### References:

Plovier H, Everard A, Druart C, et al. **A purified membrane protein from *Akkermansia muciniphila* or the pasteurized bacterium improves metabolism in obese and diabetic mice.** Nature Medicine. 2016. doi:10.1038/nm.4236



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nutrition & microbiota

## A fibre-deprived diet may degrade the colonic mucus barrier and promote enteric pathogen infection in mice

Published in ALLERGIES, IMMUNE HEALTH, RESEARCH & PRACTICE, ULCERATIVE COLITIS

Written on December 28, 2016 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 from plant-based foods is the most common fuel for some bacterial species in the gut microbiota and in some contexts has been shown to play a key role in protecting the host against immune-mediated diseases such as food allergies and even neurological disorders. A diet rich in microbiota-accessible carbohydrates (MACs), which are complex carbohydrates found in fruits, vegetables, whole grains, and legumes, has a crucial role in shaping the gut microbial ecosystem. In this context, conserving and restoring the human gut microbiome by increasing consumption of dietary fibre is a current nutritional challenge. However, little is known about the underlying mechanisms by which fibre deprivation impacts the gut microbiota and influences disease risk.

A recent study, led by Dr. Eric Martens from the University of Michigan Medical School in Ann Arbor (USA), has found that a fibre-deprived diet may lead to a degradation of the colonic mucus layer and enhance enteric pathogen infection in mice.

The researchers studied interactions between dietary fibre, gut microbiota and the colonic mucus barrier in a gnotobiotic mouse model, in which germ-free mice were colonized with synthetic human gut microbiota with a known full genetic signature that allowed tracking of their activity over time. The 14 selected species were chosen to represent the five dominant phyla and collectively hold a versatile capacity for degrading indigestible polysaccharides.

Three groups of mice were maintained by constant feeding of one of three

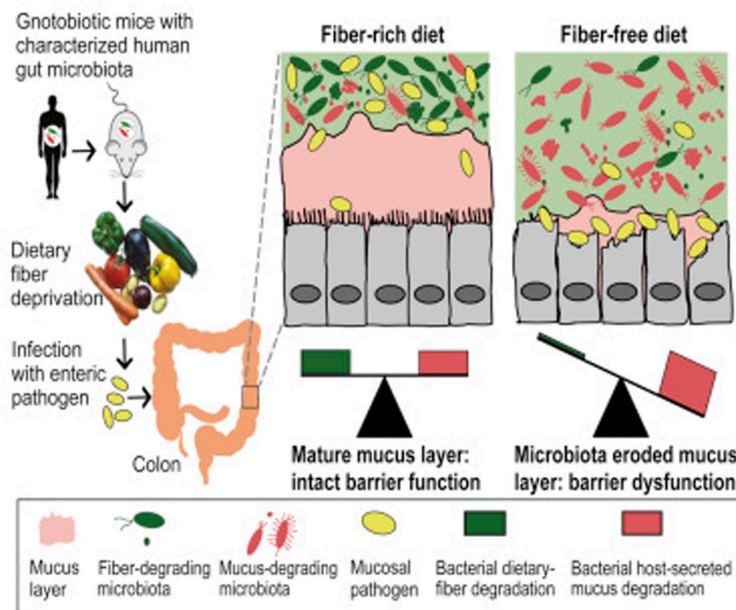
different diets: fibre-rich (contained intact fibre particles present naturally in food), fibre-free, or prebiotic (contained a mixture of purified polysaccharides, matching those used in prebiotic formulations). To imitate fluctuating exposures to dietary fibre in humans, four other groups were alternated between the fibre-rich and fibre-free or prebiotic and fibre-free diets on a daily or 4-day basis. During either chronic or intermittent dietary fibre deficiency, there was an increase in the proliferation of mucus-degrading species such as *Akkermansia muciniphila* and *Bacteroides caccae* and a decrease in fibre-degrading bacteria such as *Eubacterium rectale* and *Bacteroides ovatus* both in faecal samples and in the colonic lumen and mucus layer.

The increased abundance of mucin-degrading bacteria was explained by their ability to degrade

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## nutrition & microbiota

### A fibre-deprived diet may degrade the colonic mucus barrier and promote enteric pathogen infection in mice



CREDIT: DESAI MS ET AL./CELL 2016

mucus as an alternative nutrient, as the lack of naturally complex plant fibre (free-fibre and prebiotic diets) led to a higher expression of carbohydrate active enzymes, sulfatases, and proteases that enable gut bacteria to utilize dietary fibre and mucosal polysaccharides.

The colonic mucus layer thickness from proximal colon to rectum was highest in the colonized group fed the fibre-rich diet. Besides this, mucus production was altered in colonized mice fed the fibre-free

diet and led to altered host intestinal responses. Faecal lipocalin – a neutrophil protein involved in low-grade inflammation – was increased in the group of colonized mice fed the fibre-free diet compared to those fed the fibre-rich diet. Secondly, colon length was shorter in colonized fibre-free diet mice when compared to colonized fibre-rich fed mice. Altogether, these data show that fibre deprivation led the gut microbiota to degrade the colonic mucus barrier and altered some host

responses.

Finally, in order to test whether the reduction in colonic mucus layer thickness was associated with increased pathogen susceptibility, the researchers examined changes in gut microbial communities in response to *Citrobacter rodentium*, a murine pathogen that resembles the human enteric species *Escherichia coli*. When mice were infected with *C. rodentium*, this invading pathogen flourished more in the guts of mice fed a fibre-free diet. Besides this, many of those mice began to show signs of illness and lost weight over time. Measurements of inflamed tissue area in different intestinal segments showed that the colonized fibre-free diet group experienced inflammation that covered significantly more surface area, resulting in more severe colitis by *C. rodentium*. These results show that a fibre-deprived gut microbiota promotes heightened pathogen susceptibility.

To sum up, a fibre-deprived diet may promote expansion and activity of colonic mucus-degrading bacteria, with a consequently negative impact on the colonic mucus layer and increased



#### References:

Desai MS, Seekatz AM, Koropatkin NM, et al. **A dietary fiber-deprived gut microbiota degrades the colonic mucus barrier and enhances pathogen susceptibility.** Cell. 2016; 167(5):1339-53. doi: 10.1016/j.cell.2016.10.043.



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# SELECTED CONTENT

nutrition & microbiota

## New insights on the potential of gut bacteria and breast milk oligosaccharides to prevent childhood malnutrition

Published in BREASTFEEDING, EARLY LIFE & INFANTS, NUTRITION, PREBIOTICS, PROBIOTICS, RESEARCH & PRACTICE

Written on March 30, 2016 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.*

**Childhood undernutrition affects millions of children worldwide and has long-term severe effects, which include stunted growth and impaired cognitive development, among others. A recent study, led by Dr. Jeffrey Gordon from the Centre for Genome Sciences and Systems Biology at Washington University School of Medicine in St. Louis (USA), found that gut bacteria could be considered a useful tool for ameliorating the harmful side effects of malnutrition in mice.**

Having defined a model of normal gut microbial community development in Malawian infants and children, Dr. Laura Blanton and colleagues determined that undernourished children exhibited a persistent immaturity of their gut microbiota. To test whether this immaturity of the gut microbiota was a cause rather than an effect of malnutrition, the researchers took faecal samples from 6- and 18-month-old healthy or undernourished Malawian infants and transplanted them into 5-week-old germ-free mice that were fed a Malawian diet – primarily corn flour cooked with vegetables, peanuts and kidney beans. Mouse growth was tracked over the next month. The immature gut microbiota of the stunted and underweight human donors transmitted impaired growth, altered bone morphology, and metabolic abnormalities in the muscle, liver, and brain to recipient

mice. Independent of the amount of food consumed, these differences in mouse growth were attributed to the composition of their human-derived microbial communities.

Moreover, mice that had received microbiota from healthy children were allowed to live together with mice that had received microbiota from undernourished children. During the experiments, mice ate each other's faeces and therefore exchanged gut bacteria. From observing this, the researchers determined that there were beneficial bacteria that could compensate for growth impairments seen in the mice receiving microbial communities from the undernourished children. When adding two of these bacteria, *Ruminococcus gnavus* and *Clostridium symbiosum*, directly to 'unhealthy' gut microbes and giving this mixture to mice, the growth

Gut bacteria could be considered a useful tool for ameliorating the harmful side effects of malnutrition in mice.

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## nutrition & microbiota

### New insights on the potential of gut bacteria and breast milk oligosaccharides to prevent childhood malnutrition

and metabolic abnormalities were ameliorated. “These results suggest that microbiota may have a role as a cause and also a therapeutic intervention for malnutrition”, says co-author Yue-mei Fan.

These findings show gut microbial communities appear to be a cause of malnutrition in mice, rather than effect, and specific microbes may have a role in directing healthy growth.

In another interesting study from Dr. Jeffrey Gordon’s team, it has been suggested that oligosaccharides in human breast milk may interact with gut microbes in ways that could promote healthy growth and metabolism in undernourished children.

The researchers found that Malawian mothers of healthy infants had significantly higher concentrations of total, sialylated, and fucosylated human milk oligosaccharides (HMOs) than mothers of undernourished infants. As significant amounts of human breast milk were hard to obtain, Charbonneau, *et al.* studied

the effects of sialylated bovine milk oligosaccharides (S-BMOs) rather than HMOs on animal models. To explore the association between S-BMOs and growth in Malawian infants, they colonized young germ-free mice with gut bacteria from a 6-month-old stunted Malawian infant. One group of these mice received a Malawian diet supplemented with S-BMO and a second group received the Malawian diet plus a different kind of sugar commonly added to infant formula, which does not contain sialic acid. A third group received the unsupplemented Malawian diet. S-BMO produced a microbiota-dependent increase in growth by raising lean body mass gain, changing bone morphology, and improving liver, muscle and brain metabolism. The growth promotion effect produced by S-BMO disappeared when it was given to germ-free mice grown under aseptic conditions.

As piglets have physiologic and metabolic properties closer to humans than mice, the

researchers reproduced their results in piglets that were born germ-free and colonized with gut microbiota from an undernourished Malawian child.

These experiments indicate a causal and microbiota-dependent relationship between S-BMO and growth promotion.

In conclusion, the team led by Dr. Jeffrey Gordon found that healthy microbes and breast milk oligosaccharides may promote normal infant growth in a microbiota-dependent way. Thus, it is clear that beyond the gastrointestinal tract, gut bacteria may influence the development of distant tissues including muscle, bone, and brain. In the words of Dr. Gordon: “This is just the beginning of a long journey, an effort to understand how healthy grown is related to normal development of the gut microbiota, and how we can establish whether durable repair of microbiota immaturity may provide better clinical outcomes”.



#### References:

Blanton LV, Charbonneau MR, Salih T, *et al.* **Gut bacteria that prevent growth impairments transmitted by microbiota from malnourished children.** *Science.* 2016; 351(6275):aad3311. doi:10.1126/science.aad3311.

Charbonneau MR, O'Donnell D, Blanton LV, *et al.* **Sialylated milk oligosaccharides promote microbiota-dependent growth in models of infant undernutrition.** *Cell.* 2016; 164(5):859-71. doi:10.1016/j.cell.2016.01.024.



#### Read the original post online at:

<http://www.gutmicrobiotaforhealth.com/en/new-insights-potential-gut-bacteria-breast-milk-oligosaccharides-prevent-childhood-malnutrition/>

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nutrition & microbiota

## Evidence-Based Guidelines for Probiotic Products Now Available to US Doctors

Published in PROBIOTICS, RESEARCH & PRACTICE  
Written on December 5, 2016 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 patients ask about taking a probiotic product to address a symptom, physicians often have difficulty making evidence-based recommendations and are faced with the time-consuming task of finding and comparing results from published clinical studies.**

Making recommendations has recently become easier with the use of a new tool for physicians: the US edition of the Clinical Guide to Probiotic Products. The new guide lists the brand names of probiotic products available in the US, along with each product's strain(s), format, recommended dosage, and CFU (colony-forming units) per dose. Most importantly, the chart details the level of evidence that supports the use of that product for various adult and pediatric health indications.

"Patients often choose probiotics at health food stores, based on what the product label says or what someone at the store tells them," says Dan Merenstein, MD, Research Division Director and Associate Professor of Family Medicine at Georgetown University Medical Center in Washington, DC (USA). Merenstein says the chart will help him steer his patients in the right direction, increasing the likelihood that they will find a probiotic product suited to their needs.

"A lot of people think one probiotic is the same as every other probiotic, and the nice thing here is it shows

they have different indications and they've been studied for different reasons," says Merenstein.

The guide lists both single strain and multi-strain products, and is available online or through a mobile app. The Alliance for Education on Probiotics developed the tool through an unrestricted educational grant, with lead author Dragana Skokovic-Sunjic under the direction of an expert review board. A similar guide for Canada has been available since 2010.

Merenstein also notes that the chart lays out different choices for patients, including 'functional foods' with added probiotics. He says, "One of the beautiful things is that the chart shows there's a lot of products out there. There's a decent amount of evidence and a decent number of products."

Merenstein says, however, the chart will not be relevant to every case he sees as a physician. "Many people take probiotics for general health, just like they take multivitamins," he says. "The chart doesn't address general health, and I think that's a limitation."



Read the original post online at:

<http://www.gutmicrobiotaforhealth.com/en/evidence-based-guidelines-probiotic-products-now-available-us-doctors/>



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gut brain axis

## Hot topics addressed at the 2016 Harvard Probiotics Symposium\_DAY 2

Published in BREASTFEEDING, GUT BRAIN AXIS, METABOLIC CONDITIONS, PROBIOTICS, REPORTS, RESEARCH & PRACTICE  
Written on October 7, 2016 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.

The Harvard Probiotics Symposium, “Gut health, microbiota & probiotics throughout the lifespan: Metabolic & brain function”, was held on September 15th and 16th at Harvard Medical School in Boston (USA).

The second day of the conference, moderated by Emeran Mayer of University of California, Los Angeles (USA), brought to the podium a stellar lineup of researchers on the gut-brain axis. Again, these speakers addressed some key issues in the field:

### How do bacteria affect the brain at different life stages?

Growing evidence (at least from mouse models) suggests gut bacterial composition in early life can have effects on the brain; at the Harvard Symposium, Tracy Bale of University of Pennsylvania (USA) detailed her work showing that exposing mice to stress in early pregnancy changes their vaginal microbiome and induces similar-looking changes in the offspring’s gut microbiota at birth. These changes may alter the brain, for example, by reprogramming the young mouse’s hypothalamus, with various effects on behaviour. Bale also noted that the effects of early prenatal stress in mice are greater and more persistent in males, raising the question of whether there could be sex-specific interventions to

offset these effects.

Later came the opposite end of the lifespan: in the example of Parkinson’s disease, gut microbiota may also exert effects. Filip Scheperjans of Helsinki University Hospital (Finland) presented a talk on Parkinson’s disease and the slowly growing number of studies that link it to gut microbiota compositional differences. He described three studies showing dysbiosis in Parkinson’s disease, but noted that the nature of the dysbiosis was different from study to study. Further research is required to find out whether probiotic interventions could improve motor symptoms themselves, or only the gastrointestinal symptoms (e.g. constipation) associated with the condition.

Growing evidence (at least from mouse models) suggests gut bacterial composition in early life can have effects on the brain.

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gut brain axis

## Hot topics addressed at the 2016 Harvard Probiotics Symposium\_DAY 2

### What are the effects of neurotransmitters produced by gut bacteria?

Bacteria can produce and utilize neurotransmitters for their own

purposes, said Elaine Hsiao of University of California, Los Angeles (USA) as she detailed her lab's work on the gut serotonin system. Recently, her team found a group of bacterial metabolites

that stimulated serotonin in germ-free mice. Hsiao also showed evidence that, in mice, the effects of microbes on gut serotonin influenced both gastrointestinal motility and blood platelet function.



Some of the speakers on day two of the Harvard Probiotics Symposium: Scheperjans, Dinan, Bale, Tillisch and Mayer

### How might probiotics positively influence the brain?

Ted Dinan of University College Cork (Ireland) shared his team's quest to find possible "psychobiotics"—probiotics that produce a health benefit related to the brain. Dinan spoke about a study that found, in healthy humans, the probiotic *B. longum* improved performance on a cognitive test. Yet, he said, another probiotic that seemed to work dramatically in mice had no impact

on stress response or cognition in humans. He highlighted the need for more translational studies of these potential psychobiotics and their specific effects.

Kirsten Tillisch of University of California, Los Angeles (USA) tackled the subject of irritable bowel syndrome (IBS), noting evidence of structural brain changes as well as functional changes in people with the condition. She acknowledged that IBS is still not well understood (and that no good animal model exists),

but that the gut microbiota are probably implicated. Tillisch shared a meta-analysis that supported the efficacy of probiotics for symptoms of IBS, while noting the need for more focused studies of probiotics in three areas: prevention of IBS, treatment of gastrointestinal symptoms, and treatment of psychological symptoms.

Find the stream of live tweets from the Harvard Probiotics Symposium by searching #HarvardMicrobiota16 on Twitter.



Read the original post online at:

[http://www.gutmicrobiotaforhealth.com/en/hot-topics-addressed-2016-harvard-probiotics-symposium\\_day-2/](http://www.gutmicrobiotaforhealth.com/en/hot-topics-addressed-2016-harvard-probiotics-symposium_day-2/)

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gut brain axis

## New insights into the role of gut microbiota in Parkinson's disease

Published in PARKINSON, RESEARCH & PRACTICE  
Written on December 14, 2016 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.*

Recent research has given important insights into the role of gut microbiota alterations in Parkinson's disease (PD). Although motor deficits (including tremor, bradykinesia and rigidity) are the cardinal symptoms of PD, non-motor symptoms (NMS) (constipation, gastrointestinal disturbances, sleep disturbances and sensory alterations, among others) are also apparent and affect PD patients' quality of life more negatively than the motor symptoms. NMS symptoms are often evident before the classic motor symptoms and a recent hypothesis suggests they may be linked to a dysfunction in the communication between gut and brain.

Until now, three case-control studies have assessed gut microbiota in PD: a Finnish study, an American study, and a Japanese study. Although all of them found significant differences between gut microbiota of PD patients and controls, the results differed in terms of differentially abundant taxa and associations of gut microbiota with clinical variables. A recent review gives an in-depth comparison of the three studies (demographic characteristics of both PD patients and controls, antibiotic and probiotic exposure, methodology, relevant findings related to microbiota composition, strengths and limitations). The differences in results may be partially explained by methodological differences between studies regarding geographical regions, ethnicities, disease stages, selection criteria of participants, statistics, and confounder control. Therefore, such aspects should be taken into

account in further studies aimed at establishing the exact nature of the changes involved in alterations of gut microbiota in PD.

Taking things one step further, a recent study, led by Dr. Karl-Herbert Schäfer from the Department of Biotechnology at the University of Applied Sciences Kaiserslautern in Zweibrücken (Germany), has found that gut microbiota dysbiosis in PD may be associated with a shift in short-chain fatty acids (SCFAs), one of the main metabolic products of the gut microbiota.

The researchers analysed SCFA concentrations and gut microbiota composition in faecal samples of 34 PD patients (mean age 67.7 years) and 34 age-matched controls (mean age 64.6 years). A third group of young controls (mean age 33.3 years) was also included to identify age-related alterations.

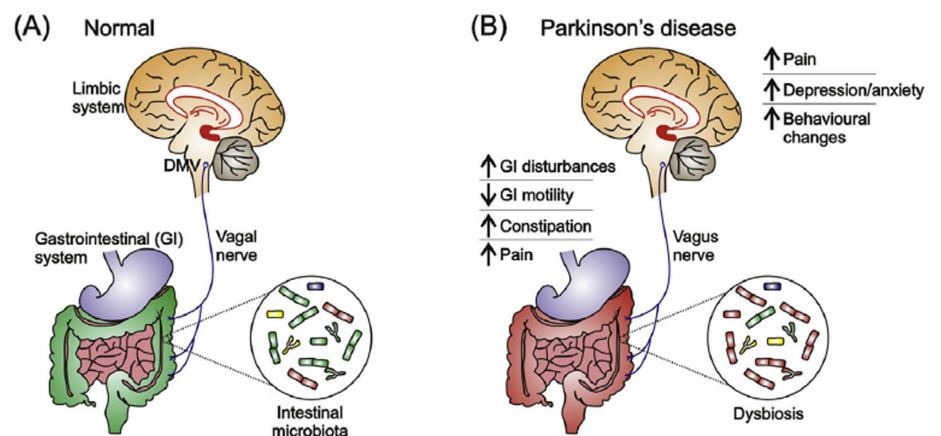
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## New insights into the role of gut microbiota in Parkinson's disease

The bacterial phylum Bacteroidetes and its family Prevotellaceae were significantly reduced in faecal samples of PD patients. By contrast, Firmicutes was the most abundant phylum and showed a similar relative abundance in all groups. *Faecalibacterium prausnitzii*, *Lactobacillaceae* and *Enterococcaceae* (phylum Firmicutes) were significantly reduced in the samples of PD patients compared to age-matched controls. Besides this, *Enterobacteriaceae* (phylum Proteobacteria) and *Bifidobacterium* were more abundant in individuals with PD compared to age-matched controls.

Faecal SCFA concentrations (acetate, propionate and butyrate) were significantly reduced in PD patients compared to controls. Although a causal relationship cannot be inferred yet, the researchers hypothesized that



CREDIT: FELICE VD ET AL./ PARKINSONISM RELAT DISORDER 2016

reduced concentrations of butyrate in the faeces of PD patients may be associated with altered SCFA effects on the enteric nervous system, perhaps contributing to gastrointestinal dysmotility, a frequent NMS in PD.

On the whole, alterations of gut microbiota are present in Parkinson's disease, though it is unclear whether specific features

gut microbiota composition are relevant to disease onset and progression. The exact mechanisms involved and the role of gut microbiota and microbial products in the development of PD and PD-associated NMS are not established yet; future larger studies in this field would add new insights.



### References:

Felice VD, Quigley EM, Sullivan AM, O'Keefe GW, O'Mahony SM. **Microbiota-gut-brain signalling in Parkinson's disease: Implications for non-motor symptoms.** Parkinsonism Relat Disord. 2016; 27:1-8. doi: 10.1016/j.parkreldis.2016.03.012.

Scheperjans F. **Gut microbiota, 1013 new pieces in the Parkinson's disease puzzle.** Curr Opin Neurol. 2016; 29(6):773-80. doi: 10.1097/WCO.0000000000000389.

Unger MM, Spiegel J, Dillmann KU, et al. **Short chain fatty acids and gut microbiota differ between patients with Parkinson's disease and age-matched controls.** Parkinsonism Relat Disord. 2016; 32:66-72. doi: 10.1016/j.parkreldis.2016.08.019.

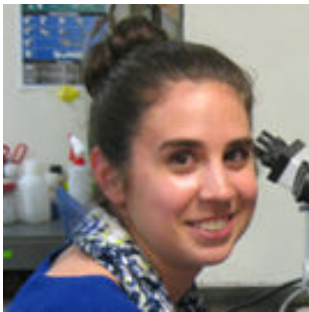
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<http://www.gutmicrobiotaforhealth.com/en/new-insights-role-gut-microbiota-parkinsons-disease/>

## Bacteria from celiac patients influence gluten's digestion and its ability to provoke an immune response

Published in CELIAC DISEASE, DIGESTIVE HEALTH, IMMUNE HEALTH, RESEARCH & PRACTICE  
Written on October 10, 2016 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 is an autoimmune condition involving an immune reaction that is triggered by dietary gluten, found in wheat, barley and rye. Partially digested gluten peptides can trigger symptoms in genetically susceptible individuals, expressing HLA-DQ2 or DQ8 genes. While necessary for disease development, the expression of DQ2/DQ8 is not sufficient for disease development, suggesting a critical role for environmental factors. Alterations in the intestinal microbial composition have been described in celiac disease, but a clear microbial signature hasn't been defined and the pathophysiological significance of these alterations is unknown.

Gluten is highly resistant to digestion by human digestive enzymes; however, digestion of gluten by intestinal bacteria has recently been described. In a recently published paper in *Gastroenterology*, a group led by Dr. Elena Verdú at McMaster University explored how bacteria isolated from celiac disease patients and healthy controls differentially influence gluten digestion and the immunogenicity of gluten metabolism products.

Using germ-free mice colonized with either opportunistic pathogens, such as *Pseudomonas aeruginosa*, or commensals, such as *Lactobacillus*, Caminero *et al* first demonstrated that different bacteria can participate in gluten metabolism *in vivo*, and that they have distinct proteolytic activities.

The present study made use of *Pseudomonas aeruginosa*, an opportunistic pathogen in the small intestine, which was unique to celiac disease patients. The authors showed, *in vitro*, that *P. aeruginosa*, through its elastase activity, degrades gluten to produce immunogenic gluten peptides that can stimulate gluten-specific T cells from HLA-DQ2 celiac disease patients. Interestingly, these *P. aeruginosa*-digested gluten peptides were able to translocate across the small intestinal barrier more efficiently than those peptides digested by human proteases.

Increased antigen uptake can lead to greater antigen availability and may perpetuate immune responses in the small intestine. In contrast to *P. aeruginosa*, *Lactobacillus* spp isolated from the small intestines of

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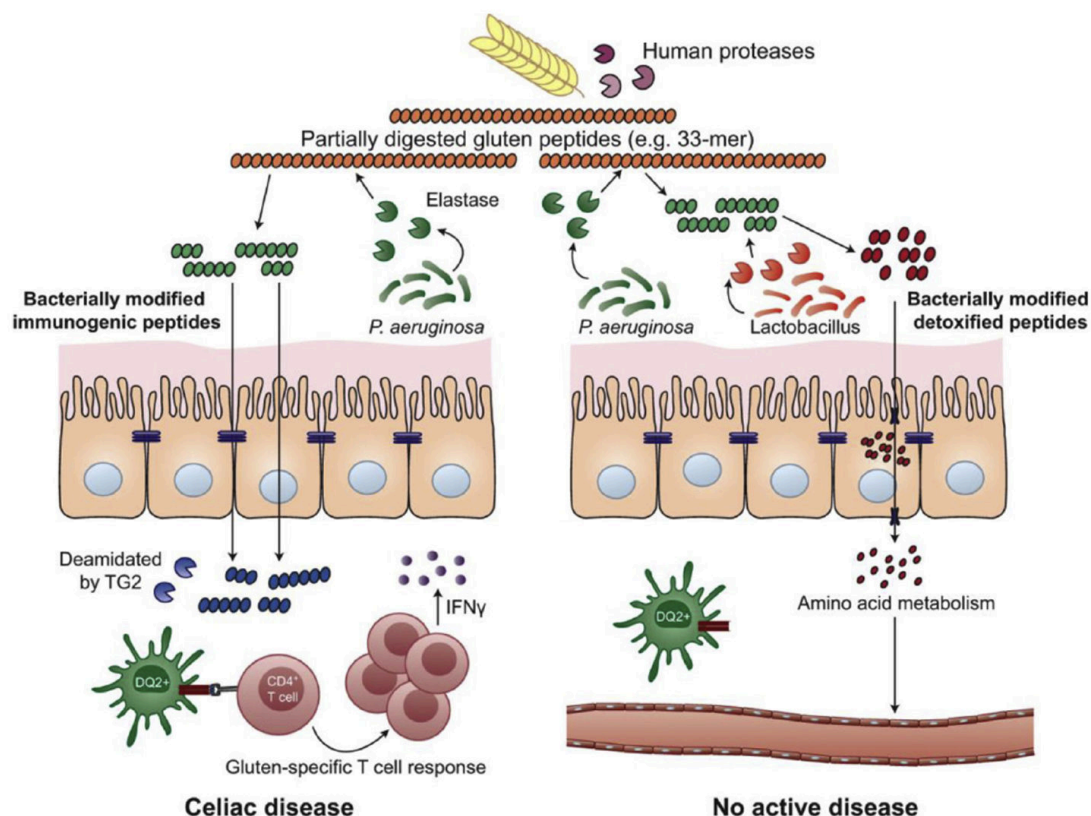
## Bacteria from celiac patients influence gluten's digestion and its ability to provoke an immune response

healthy controls degraded gluten peptides that were generated by *P. aeruginosa* or human proteases into non-immunogenic peptides.

These findings suggest both opportunistic pathogens and commensal bacteria participate in gluten metabolism, but they generate distinct patterns of gluten peptides following digestion, which

are associated with increased or decreased immunogenicity. The authors describe an important mechanism through which opportunistic pathogens, such as *P. aeruginosa*, may modify the pool of gluten peptides in the gut and increase susceptibility to celiac disease. Importantly, the gut is colonized with other bacteria and opportunistic pathogens, in addition

to those described by Caminero et al, that can digest gluten and may also modify celiac disease risk in genetically susceptible individuals. Further insight into how this microbe-gluten-host interaction in celiac disease contributes to pathogenesis may provide exciting new therapeutic interventions, and may also explain the reported dysbiosis in celiac disease patients.



CREDIT: CAMINERO ET AL./GASTROENTEROLOGY 2016

Read the original post online at: <http://www.gutmicrobiotaforhealth.com/en/bacteria-celiac-patients-influence-glutens-digestion-ability-provoke-immune-respons>

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immunity

## Role of gut microbiota diversity in protection from asthma and allergy development

Published in ALLERGIES, ASTHMA, IMMUNE HEALTH, PREGNANCY & EARLY LIFE, RESEARCH & PRACTICE

Written on December 23, 2016 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.*

A recent study led by Dr. Alex Mira (FISABIO, Spain) and Dr. Maria C. Jenmalm (Linköping University, Sweden) and researchers at IATA-CSIC (Spain) has presented an analysis of a total of 192 faecal samples from 28 healthy children and 20 children developing allergic symptoms at age seven, from when the children were 1 and 12 months of age. It has found that children who develop asthma or allergies later in life have altered immune responses to intestinal bacteria in the gut mucosal environment at an early age. The results also suggest that the mother's immune system may play a role in the development of asthma and allergies in children.

Majda Dzidic, first author of the study, corresponded with GMFH editors about the significance of the work.

**What is already known and what have you already found about the role of gut microbiota in allergic diseases? Why do the first 2-3 years of life appear to represent the most critical period for microbiota modulation to reduce children's risk of asthma and allergic disease?**

We believe that the first years of life are crucial when it comes to the maturation of a healthy gut. This early period of childhood is also known as a "critical window of opportunity" [when] the infant's immune system is being instructed on how to react against (and tolerate) the symbiotic microbiota. Mucous membranes are present in the airways and gastrointestinal tract and here they come into contact with large amounts of bacteria and viruses. IgA antibodies, [principal] primary [mediators] of humoral mucosal

immunity, are present in mucous membranes. Here they bind to microorganisms that they recognize and act as a barrier, preventing them from entering the mucosal tissue and creating immune responses that might damage the surrounding tissue. [Besides] the fact that the microbial recognition by maternal and infant IgA antibodies must be appropriately orchestrated for an optimal maturation of the mucosal immune system, the microbiota itself plays a central role in this early immune modulation. So we believe that diversity and composition [of] the bacteria are major drivers for the normal maturation of a healthy mucous membrane. Thus, perturbations in this symbiotic relationship between the immune system and intestinal microbiota, during the early period of life, seem to be highly correlated with the child's risk of asthma and allergic disease development.

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## Role of gut microbiota diversity in protection from asthma and allergy development



**What are the most relevant new findings in your research group regarding the effects of gut microbiota on asthma and allergy development during the first years of life? What does your newest study add?**

This is the first study where the role of mucosal immune responses towards the gut microbiota, in relation to childhood allergy development, has been addressed.

By investigating the bacterial taxa that were targeted or not by IgA antibodies, we could confirm the importance of early life intestinal microbiota for later allergy development. We saw that the children who subsequently developed allergies had a lower fraction of IgA antibodies bound to their intestinal bacteria at one year of age compared to those children who stayed healthy. This was particularly manifested in children who developed asthma during the

first seven years of life. We could also detect the differences in the types of bacteria that were targeted by the immune system of these two groups of children, as early [as] one month of age. These interesting results are suggesting that the barrier function of the mucous membranes is less effective in children who develop allergies later in life and that this can be monitored already during the first year after birth.



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## Role of gut microbiota diversity in protection from asthma and allergy development

### What is the role of the mother's immune system and breastfeeding in childhood allergy development?

Studies and clinical reports suggest that secretory IgA that [originates] from the mother's breast milk is important for immune regulation and protection against many

infections in suckling infants. In this study we were interested to note that the differences in intestinal microbiota IgA responses were obvious in infants as young as one month. This was surprising since the IgA antibodies in children that young come largely from the mother, through breast milk. Moreover, all the infants included in

the study were exclusively breastfed until at least one month of age. So it seems that the immune response of the mother and the antibodies that the child receives in breast milk are connected with the development of allergies. This is something we want to look at in more detail in future work.

### Based on your study, what kind of potential interventions do you suggest to combat the current asthma and allergy epidemic?

We are still far from understanding what is defining a healthy gut microbiome that promotes

tolerance and prevents allergy development. I would say that the interventions enhancing infant mucosal barrier function, such as prebiotic/probiotic supplementation and [encouraging] exclusive breastfeeding during the first months of life (6 months according the WHO guidelines), may

represent efficacious preventive strategies required to combat the asthma and allergy epidemic. Also, we should work on reducing the use of antibiotics and encourage children to play outside, thus increasing the microbial exposure important for healthy immune system development.

### What further steps are you planning to take in the way of using gut microbiota as a biomarker for identifying infants with increased risk of asthma and allergic disease?

We think that the early characterization of IgA coating patterns of intestinal microbiota

may represent a possible way to identify infants with increased risk to develop asthma and allergic disease later in life. Although this needs to be confirmed in larger cohorts, it paves the way to develop diagnostic kits to identify children with high risk so preventive strategies, including those aiming to enhance gut diversity, can be

directed towards that population group. Also, it would be of great interest to detect what factors in breast milk, reflecting the immune response of the mother, are connected with the development of allergies. This is something we are planning to investigate in more detail.



Read the original post online at:

<http://www.gutmicrobiotaforhealth.com/en/role-gut-microbiota-diversity-protection-asthma-allergy-development/>

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