

SHORT REPORTS FROM WORKSHOPS

Gail Hecht (Chicago, USA)
& Francisco Guarner (Barcelona, Spain)

- Patients with LGC had increased diversity, but not significantly on weight or resistance
- Subjects with higher diversity and microbial richness had a better profile



Managing Gut Health Through Nutrition

A report from the workshop "Gut microbiota targets in nutrition"

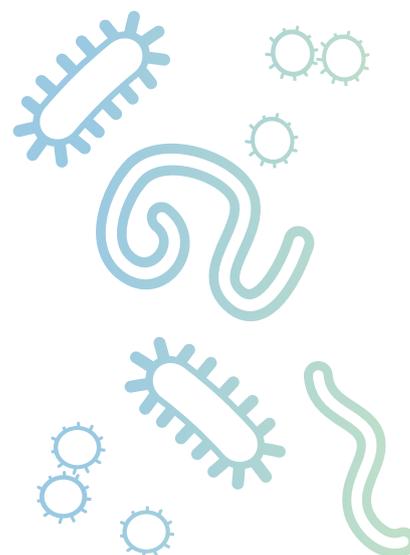


Rome | March 2018



During the Gut Microbiota for Health World Summit 2018, held in Rome on March 10th & 11th, 2018, a specific workshop on nutrition and gut microbiota was provided for experts and healthcare practitioners specializing in nutrition and gastrointestinal disorders.

The workshop, chaired by Karine Clément, provided an overview of how the gut microbiota could relate to the prevention and treatment of obesity, and of potential gut microbiota targets in gluten-related disorders.



Dr. Karine Clément

Dr. Karine Clément is Professor of Nutrition and former Director of the Institute of Cardiometabolism and Nutrition (ICAN) linked to the University of Pierre and Marie Curie in Paris and head of a research group at the Institut National de la Santé et de la Recherche Médicale (INSERM). She was the chair of the session.



Dr. Hervé Blottière

Dr. Hervé Blottière is the current Director of Research at INRA, the French National Research Institute for Agricultural and Food Research. He also serves as a member of the GMFH Digital Scientific Board.



Dr. Elena Verdú

Dr. Elena Verdú is researcher and Associate Professor at the Division of Gastroenterology, at the Department of Medicine at McMaster University (Canada) and Canada Research Chair in Inflammation, Microbiota and Nutrition. She serves as a member of the GMFH Digital Scientific Board.

Diet and gut microbiota interactions relevant to clinical care in metabolic disorders

Hervé Blottière gave a critical overview of the gut microbiota and gut-targeted therapies in prevention and treatment of obesity.

Complex gene-environment interactions occur in obesity, and changes in dietary composition have been related to changes in the composition of gut microbial populations. Functional differences in gut microbial populations may matter: in a study of 38 obese and 11 overweight individuals, subjects who at baseline had a low abundance of gut bacterial genes presented with more pronounced low-grade inflammation and a dysregulated metabolic status as compared to those with a high gene count. A **dietary intervention** consisting of a diet rich in proteins, fibres and carbohydrates with a low glycaemic index led to an increase in microbial gene abundance of about 30%



Kristina Campbell, microbiome sci...
@bykriscampbell

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Blottiere of @Inra_France gives a comprehensive summary of gut microbiota in cardiometabolic diseases and promising new methods for modifying weight & metabolism through the gut microbiota
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in the subjects with the initially low-gene-count microbiota, together with improvements in metabolic and inflammatory parameters. These results suggest that **diet can improve gene richness in the gut microbiota and gene richness may have predictive potential for the efficacy of dietary intervention in obese or overweight patients.**



"Diet should be viewed as a means to prevent the potentially durable alterations of symbiosis observed in immune-mediated metabolic and inflammatory diseases," emphasized Blottière.



GutMicrobiota Health
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Key question: Can the gut microbiome be a treatment for human metabolic disease? Consider that these metabolic diseases can look very different, depending on the patient. Blottière: "There are many obesities."
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The ways in which new laboratory methods have opened avenues for finding new gut microbiota-derived diagnostic markers, and the identification of new pathways related to chronic metabolic diseases, was also covered. According to Blottière, **"gut microbiota derived metabolites from diet may play a key role in the regulation of host metabolism."** Some have studied the relationship between the diet, the gut microbiome and cardiometabolic disorders (CMDs), and the transfer of resident gut microbiota from mice or humans into germ-free mouse models has helped identify that dietary intake of choline and its metabolization by the gut microbiota, is associated with cardiovascular outcomes in mice and humans. Trimethylamine N-oxide (TMAO) –a metabolite derived from phosphatidylcholine (also called lecithin, which can be found in cheese, meats and eggs) conversion by the gut microbiota– might represent a novel biomarker for metabolic alterations and chronic CMDs.

Diet and gut microbiota interactions relevant to clinical care in metabolic disorders

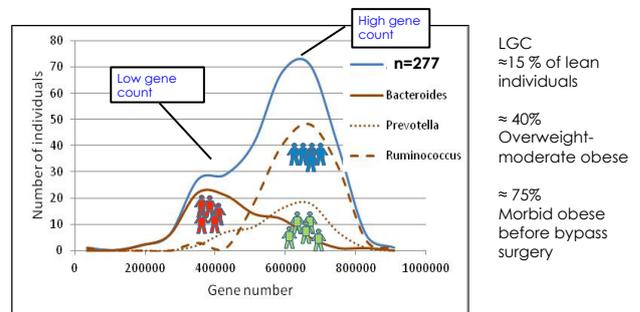


"Low gut microbial richness (assessed by a low gene count) in humans has been associated with a higher risk for cardiometabolic disease, despite the same overall body mass index," explained Blottière.

Finally, there is potential for manipulation of the gut microbiota for the treatment of obesity and associated health complications, both as a unique therapy and as part of other weight loss interventions. Among approaches being considered in modulating gut microbiota for weight loss, prebiotics and probiotics are the most prominent but their potential in clinical care deserves further studies in humans. Regarding faecal microbiota transplantation, Blottière noted that it deserves further human studies in order to justify its use in a clinical setting in the treatment of metabolic disorders.

Blottière wrapped up his talk by highlighting that in order to consider the microbiome as a treatment for human metabolic disease, several questions should be asked, including:

HUMAN GUT MICROBIOMES DIFFER AT THE LEVEL OF GENE RICHNESS (DIVERSITY)



58 « species » significantly linked to gene count

Le Chatelier, et al, Nature 2013; Cottillard et al, Nature, 2013



Who will benefit the most from pre- and/or probiotic interventions?

Patient phenotypes, heterogeneity and plausible healthy states of obesity should be taken into account. The fact that there are many obesities hampers the effective targeting of the gut microbiome for treating human metabolic diseases.

What gut microbiota targeted intervention is more effective based on current experimental and clinical data?

Possible interventions include food, prebiotics, probiotics, metabolites, faecal transfer or maybe a combination of several of these.

Why should we carry out these interventions?

The efficacy relative to cost must be considered.

What should be targeted in the host?

Possible targets include the microbiome, gut barrier, derived-molecules, or host targets, or maybe a combination of these.

When should these interventions be carried out?

It's important to consider which periods of time are most appropriate for intervention (whether as prevention or treatment).

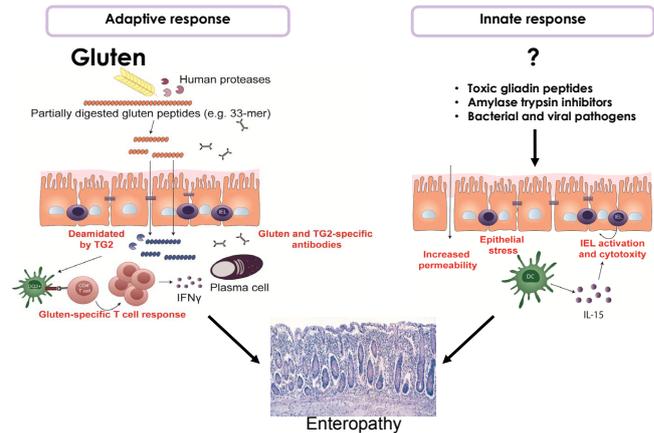
Gut microbiota targets in gluten-related disorders

Elena Verdú (Hamilton, Canada) summarized the current evidence for altered gut microbiota composition in coeliac disease (CD) and discussed the role of host-microbial interactions on host responses to gluten.

Current research points towards alteration in gut microbiota composition and function in CD, some of which can precede the onset of disease and can persist when patients are on a gluten-free diet. Verdú noted that **although nowadays the gluten-free diet is the only treatment for people with CD, it is still an imperfect therapy, and focusing on environmental factors such as gut microorganisms may lead us to new therapeutic solutions in the future.**

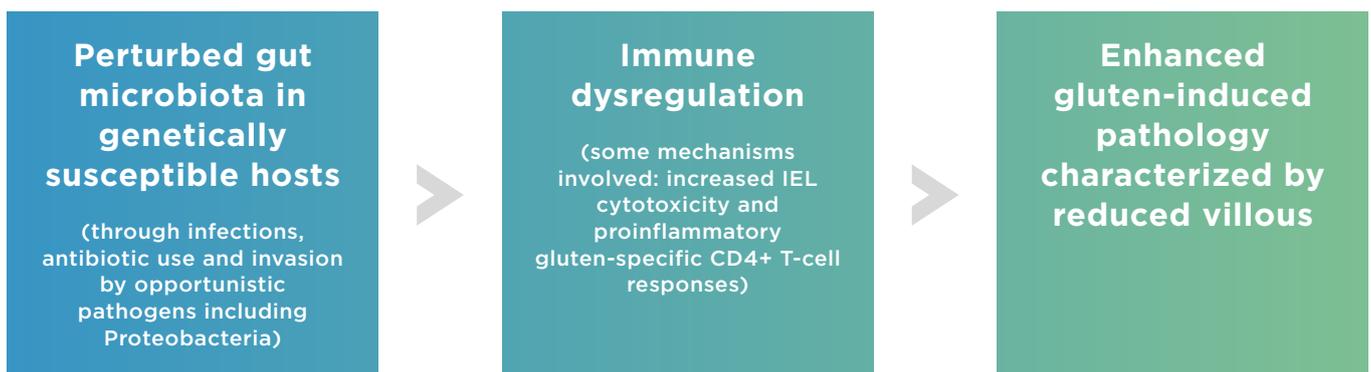
Regarding the relationship between the gut microbiota and CD, Verdú showed clinical associations of CD pathogenesis with infectious disease and antibiotic treatments that can potentially perturb the gut microbiota. Besides the timing of gluten introduction to the infant's diet, additional environmental factors could also determine CD risk, such as type of delivery at birth, milk-feeding practices, intestinal infections, and/or use of antibiotics. When focusing on the period early in life, alterations in the developing

Pathogenesis of the celiac enteropathy



intestinal microbiota and immune markers may precede CD onset in infants at familial risk of developing the disease.

Verdú also described her lab's insights into a possible mechanism linking gut bacteria to coeliac disease pathogenesis. **When small intestinal microbes from a patient with CD interact with gluten, they can trigger a different immune reaction than microbes from a person without CD.**



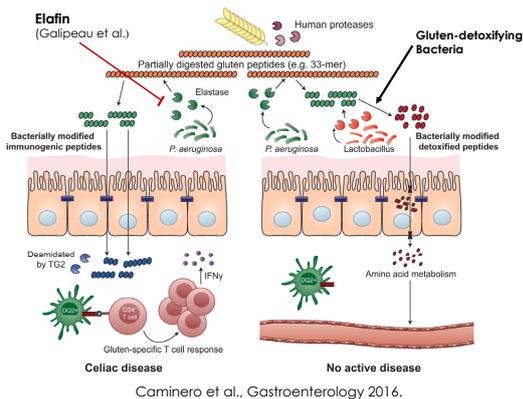
Learn more about the role of duodenal bacteria in affecting gluten breakdown and immunogenicity in a previous GMFH post based on a study led by Verdú.

Emerging research is exploring the potential role of probiotics for CD based on the fact that some probiotics have been found to digest or alter gluten peptides. Among probiotics that could provide better

effectiveness in the treatment of CD, Verdú mentioned *Bifidobacterium longum* CECT 7347 and *B. infantis*. Although these studies are exploratory, the findings suggest that certain probiotics could help improve the health status of CD patients who tend to show alterations in gut microbiota composition and a biased immune response even on a gluten-free diet.

Gut microbiota targets in gluten-related disorders

Gluten metabolism by small intestinal bacteria could play a role in CeD risk, and this interaction is a therapeutic target!



"Gut microbiota and its metabolites may be the missing element to have a better understanding

of celiac disease and we still need more mechanistic and clinical studies in order to have confidence recommending probiotics for celiac disease," pointed out Verdú.

According to Clara Belzer talk "Novel probiotics: *Akkermansia Muciniphila* And *Eubacterium Hallii*", during the summit, probiotics not only could help improve the health status of CD patients who tend to show alterations in gut microbiota but there are evidence-based adult indications for probiotics in gastroenterology and hepatology, in particular:

- Improvement in global IBS symptoms, severity of abdominal pain and quality of life, especially in constipation-predominant IBS.
- Primary and secondary prophylaxis of hepatic encephalopathy and improvement in immune and biochemical markers (e.g. aminotransferases) and histological activity score in non-alcoholic fatty liver disease.

Some next-generation probiotics such as *Akkermansia muciniphila* will be on the market in a few years with the aim to improve host metabolic health.

On the whole, the nutrition workshop led to the conclusion that the **gut microbiota is an important player in metabolic health** and although the mechanisms are not fully understood, further research will allow consideration of personalized gut microbiota-targeted interventions for both metabolic disorders and gluten-related disorders. Scientific insights covered during the workshop illustrate the **relevant role of diet and nutrition in managing not only gut health, but also other disorders in distal organs that are related to the gut. The gut is the cornerstone of health, diseases and well-being and the impact of diet and lifestyle on gut microbiota and human health assists in maintaining health. Nutrition is the main factor that affect the composition of the intestinal microbiota and may help preventing or restoring its imbalance.**



Kristina Campbell, microbiome sci...
@bykriscampbell

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Karine Clément: Now we know that in obesity, there's disease in the tissues, abnormalities in the signalling, and differences in the gut microbiota (or microbial gene richness) -- so the solution to improve health will probably be complex
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