

Report



9th edition - 2020

Moving gut microbiome science from the bench to actionable advice: major learnings and paths to explore

Madrid (SPAIN)

Gut microbiome science has exponentially increased over the last two decades, as has the general population's interest in harnessing this knowledge for better health. When it comes to science-backed tools for improving our gut microbiome, according to experts' conclusions from the GMFH World Summit 2020, diet diversity, prebiotics and probiotics are all worth considering.



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ADVANCING GUT MICROBIOME SCIENCE FOR BETTER HEALTH IS NOT STRAIGHTFORWARD: THE MAJOR CHALLENGES AND HOW TO OVERCOME THEM

Gut microbiome publications have exponentially increased over the last decade, with the subsequent impact on both basic science research and clinical practice. While it is clear that the roadmap to clinical translation consists of developing gut microbiome-related solutions for better health, **Colin Hill** from University College Cork (Cork, Ireland) acknowledged during his keynote lecture that higher standards must be rigorously applied to overcome roadblocks when moving from bench to bedside.

To deliver precision gut microbiome-based science, accuracy (and a healthy dose of common sense) is necessary in all steps: from microbiome sampling to specific language used when explaining the benefits of taking care of the gut microbiota. Hill explained that major challenges to be addressed to get the right microbiome science include:

- Using precise language when communicating gut microbiome science;
- Adopting consensus definitions (see the ISAPP consensus documents of probiotics and prebiotics);
- Relying more on actual numbers rather than percentages when clarifying to what extent two or more microbiomes are identical or different;

- Taking into account individuality when interpreting microbiome studies;
- Avoiding defining a gut microbiome as ‘healthy’ or ‘unhealthy’ (any effect of the gut microbiota on host health is likely to depend also on individual host genetics, diet and environment);
- Considering all factors that can shape gut microbiota composition;
- Choosing the right methodology for studying the gut microbiome; and
- Having long-term data regarding the safety of gut microbiota-targeted interventions ■



“The microbiome will prove to be a rich source of therapies and smart food, feed ingredients and diets that will improve the human condition.”

Colin Hill



WHICH HOST AND DIET FACTORS SHAPE THE GUT MICROBIOME?

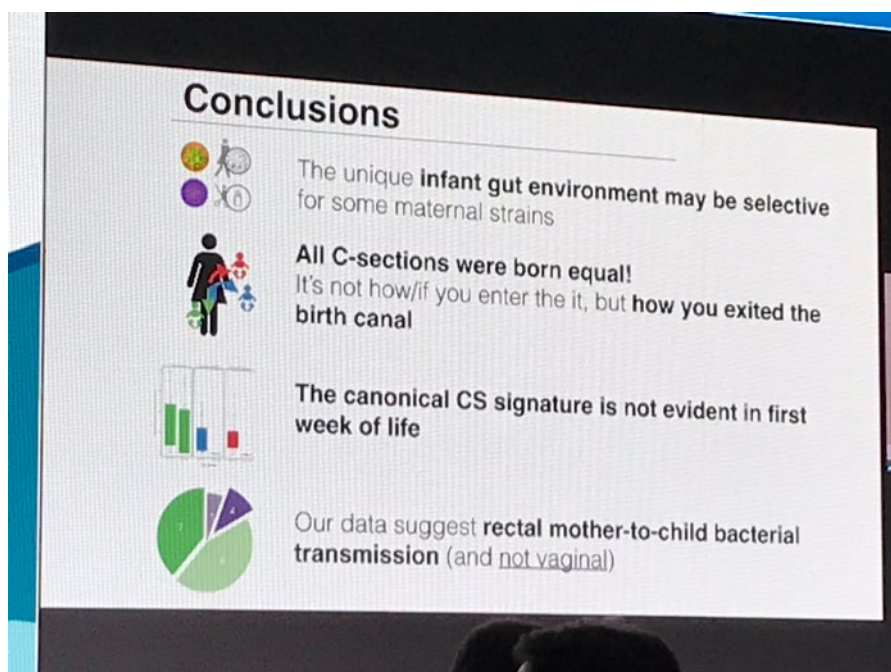
Each person has the gut microbiome they deserve and this is how it changes throughout life

The first three years of life represent the most critical period for dietary interventions aimed at gut microbiota modulation to improve child growth and development and positively affect health. **Moran Yassour** from the Hebrew University of Jerusalem (Israel) focused on the origin and extent of microbe transmission from mother to infant. A longitudinal sampling of gut bacterial transmission in 44 mother-infant pairs enabled Yassour and colleagues to find that two patterns of mother-to-child bacterial transmission exist in the first 3 months of a child's life. **While often the mother's dominant strain (*Bacteroides vulgatus* and *Bifidobacterium adolescentis*) is transmitted to the child, sometimes her secondary strains (often *Bacteroides dorei*) can preferentially colonize the infant gut.** Interestingly, in families where the secondary strain of *Bacteroides uniformis* is inherited, a starch utilization gene that is missing in the mother is available in the newborn for facilitating the metabolism of the mother's milk, explained Yassour. Likewise, the transmission of some antibiotic resistance genes may also be inherited.

Regarding the impact of delivery mode on the child gut microbiome, Yassour explained that, contrary to common belief, the impact

of a C-section on the infant's gut microbiome is barely noticeable during the first weeks of life and when the procedure is performed (that is, before or during labor) affects children's gut microbiome in the same way. In this regard, the high number of shared strains between C-sections and vaginal deliveries suggests that **rectal mother-to-child transmission, rather than vaginal bacteria, appear to be what affects newborn gut colonization efficiency.**

Rectal mother-to-child transmission, rather than vaginal bacteria, appears to affect newborn gut colonization efficiency.



Paul O'Toole from University College Cork (Ireland) covered diet-microbiota health interactions in elderly people (aged >65 years). In this population, lifestyle and habitual diet can outweigh age-related gut microbiota changes. Specifically, elderly people living in their

Diet keeps the gut microbiome fit in the elderly: it is not the quantity of calories per se that matters, but the quality of the diet.

homes and looked after by caregivers show the highest diversity in their gut microbiota, with subjects residing in long-term care facilities (consuming a diet with a low diversity of food components) showing the least diverse microbiota. Furthermore, these microbiota changes correlated with increased frailty and increased values of markers of inflammation, explained O'Toole.

The gut microbiota composition profile groups change according to the duration of stays in long-term residential care and O'Toole's research group was interested in exploring whether modulation of the gut microbiota through diet could lead to healthier aging. A dietary intervention in elderly subjects and young healthy controls showed how an intake of prebiotics with a high content of resistant starch for 6 months can modulate specific gut microbiota taxa (such as *Ruminococcaceae*, *Parabacteroides*, and *Phascolarctobacterium*) and reduce inflammation in the elderly. In the light of these findings, **it might be possible to improve the loss of certain taxa in the gut microbiota of frail long-stay older people through prebiotic supplementation.**

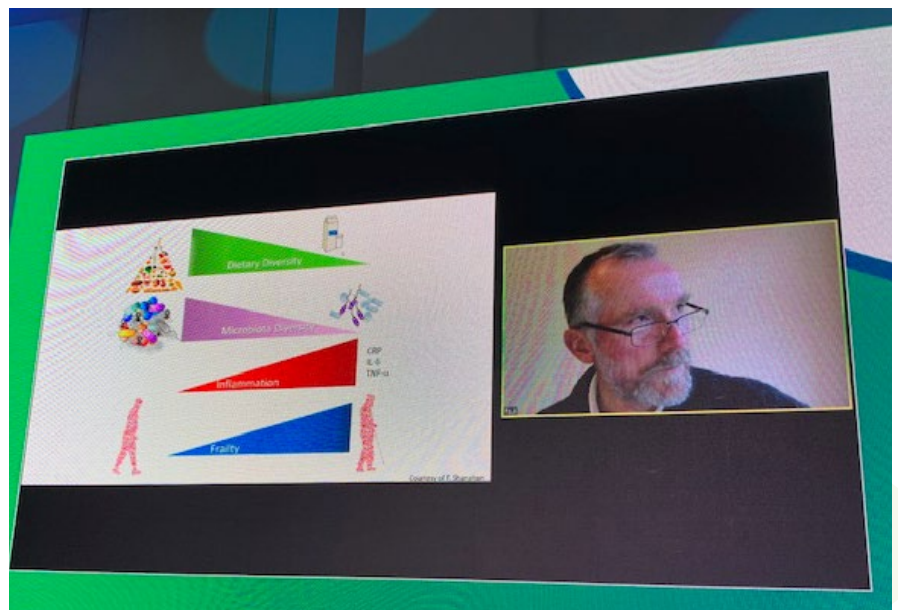
In another study presented, O'Toole and colleagues showed **that adherence to the Mediterranean diet (MedDiet) for 1 year in 612 elderly non-frail and pre-frail European subjects led to a higher abundance of different taxa that are positively associated with markers of lower frailty and better cognitive function but also negatively**

correlated with inflammation, in a manner independent of body mass index and age. It was also possible to identify 44 Operational Taxonomic Units (OTUs) that were more abundant when the MedDiet was strictly observed (named "diet positive"), whereas 45 OTUs were negatively associated with adherence to the diet (named "diet negative"). In conclusion, the study supports the fact that diet quality matters more than the quantity of calories per se, even in subjects of advanced age, and gut microbiota can explain the benefits of a highly diverse and balanced diet.



“Our findings show the benefits of following a Mediterranean diet to modulate the gut microbiota, which, in turn, has the potential to promote healthier aging.”

Paul O'Toole



Your allies for looking after your gut microbiota: fermented foods, probiotics and prebiotics

Different dietary strategies are currently undergoing a surge in po-

Not all fermented foods are a source of probiotics. Learn more about the impact of kefir and major non-dairy fermented foods on the gut microbiota and gastrointestinal health [here](#).



“The most widely investigated fermented foods are fermented milks and kefir, with human evidence suggesting beneficial effects on lactose malabsorption for yogurt and functional constipation, lactose malabsorption and *Helicobacter pylori* eradication for kefir”

Kevin Whelan



Fermented foods, probiotics & prebiotics

Foods or beverages produced through controlled microbial growth, and the conversion of food components through enzymatic action

Fermented foods

Live yoghurt
Kombucha
Tempeh
Sourdough
Beer
Wine

Fermented milks (some)
Kefir (some)

Live micro-organisms that, when administered in adequate amounts, confer a health benefit on the host

Probiotics

Capsules
Powders

A substrate that is selectively utilised by host micro-organisms conferring a health benefit

Prebiotics

Inulin-type fructans
Galacto-oligosaccharides

Resistant starch?
Pectin?

Synbiotics

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pularity, as a means of improving gastrointestinal health by shaping the gut microbiota. **Kevin Whelan** from King's College London (United Kingdom) summarized human intervention studies investigating the impact of fermented foods, probiotics and prebiotics on gastrointestinal health and disease. **The most widely investigated fermented foods are fermented milks and kefir, with human evidence suggesting beneficial effects on lactose malabsorption for yogurt and functional constipation, lactose malabsorption and *Helicobacter pylori* eradication for kefir.** There is limited clinical evidence for the effectiveness of kombucha, sauerkraut, soya fermented foods (miso, natto and tempeh), kimchi and sourdough in gastrointestinal health and disease, explained by a variable microbial composition in fermented foods and the lack of human studies.

Beyond fermented foods, probiotics are also a way to deliver beneficial

bacteria and yeast within the gastrointestinal tract. However, Whelan acknowledged that not all probiotics work in the same way and careless use of this word as a generic descriptor without specifying the content (genus, species and strain) or clinical indication often makes for a superficial imprecise term. In addition, **humans' response to probiotics is highly individualized and clinicians should focus on health outcomes rather than whether a probiotic colonizes or has detectable effects on the indigenous microbiota.** Probiotics have been shown to be beneficial in constipation, irritable bowel syndrome (IBS) and ulcerative colitis, whereas their role in Crohn's disease is controversial.

Prebiotics, meanwhile, act by selectively stimulating the growth of some gut bacteria. The most studied prebiotics are inulin-type fructans (inulin, oligofructose) and galactooligosaccharides, while resistant starch and pectins are consid-



The vegan diet.

red candidate prebiotics. Similar to what happens with probiotics, Whelan explained that **the response to a prebiotic is largely affected by the background gut microbiota profile and habitual dietary fiber intake.** Science-backed indications for prebiotics include constipation and IBS.

A 16-week plant-based diet can boost the gut microbiome, helping with weight loss and overall health

A wealth of data has shown the benefits of plant-based diets for preventing and managing diabetes, with gut microbiome research connecting the dots between inflammation, insulin resistance and diabetes. **Hana Kahleova** from the

Physicians Committee for Responsible Medicine (USA) presented the results of a randomized clinical trial looking at changes in gut microbiota in response to a low-fat vegan diet. In 147 participants who were overweight and insulin resistant but who had not yet been diagnosed with diabetes, Kahleova and colleagues looked at their fecal microbiota, body composition and insulin sensitivity at baseline and after randomizing them to follow a vegan diet or to stay on their usual diet for 16 weeks.

The vegan diet led to a 5.8kg reduction in body weight, which was mainly due to a reduction in fat mass analyzed using dual energy X-ray absorptiometry. More interestingly, **metabolic outcome improvements were also related to changes in the gut microbiome.** Specifically, an increase in the butyrate-producing bacterium *Faecalibacterium prausnitzii* – which has been found to be depleted in patients with type 2 diabetes and has also been linked to increased inflammation and increased insulin resistance – in response to the vegan diet was associated with changes in body weight, fat mass and visceral fat. In addition, the vegan diet led to less of a drop in *Bacteroides fragilis* compared with the Western diet, and that too was related to changes in weight loss, fat mass and insulin sensitivity ■



“Our study highlights the importance of fiber intake for diabetes prevention because *Faecalibacterium prausnitzii* feed on fiber and produce short-chain fatty acids with positive metabolic benefits.”

Hana Kahleova

THE GUT MICROBIOME-IMMUNE SYSTEM BALANCE: WHY DOES IT MATTER?



The neonatal period spanning birth to weaning represents the most critical period for dietary interventions aimed at microbiota modulation.

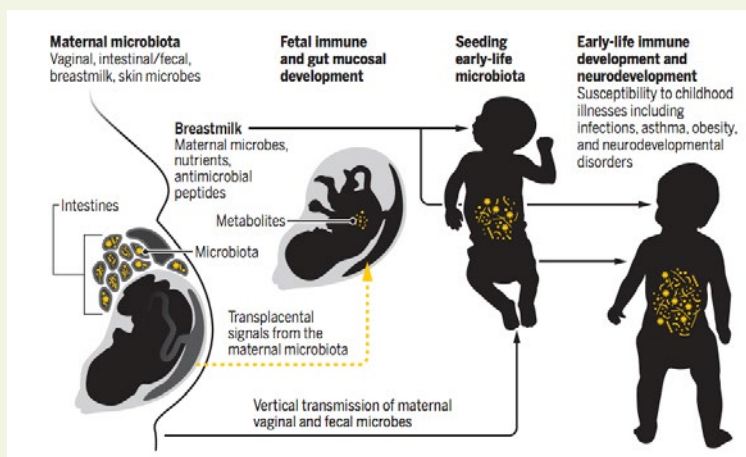
Kathy McCoy from the University of Calgary (Canada) covered the influence of maternal gut microbiome on the training and maturation of the neonatal immune system, even before birth. McCoy started by providing evidence supporting the theory that seeding of early-life microbiota with maternal microbes leaves a lasting imprint on the offspring. Studies in mice have covered the critical role of colonization by maternal microbes in early life for normal immune development, including innate immune cell production, antibody production, immune regulatory functions, epithelial barrier

integrity, and even tryptophan and nucleotide metabolism in offspring. *“As the early-life microbiota is seeded by vertical transmission, the education of immunity in offspring is critically dependent on maternal commensals,”* acknowledged McCoy. In addition, the maternal microbiome can also have an impact on disease development later in life. It seems that an altered microbiota can increase intestinal permeability and thus promote the development of a pro-inflammatory milieu that stimulates beta-cell autoimmunity in the predisposed host. For example, differences in human milk oligosaccharide-utilizing bacteria provide a route to differences in immune education that may predispose the body to immune and metabolic-related conditions such as diabetes.

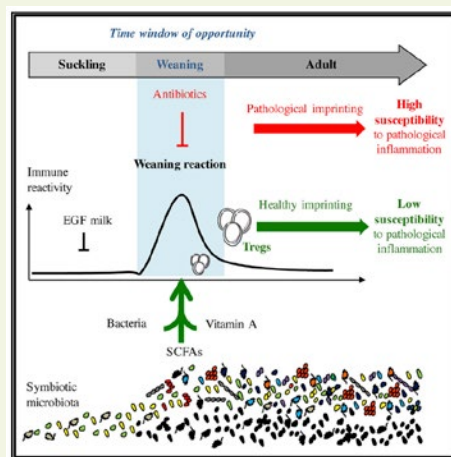
“As the early-life microbiota is seeded by vertical transmission, the education of immunity in offspring is critically dependent on maternal commensals”

Kathy McCoy

G rard Eberl from Institut Pasteur (Paris, France) presented findings in mice showing how important an



Effects of the maternal microbiota on early life immune development
Source: McDonald B & McCoy KD, Science. 2019; 365(6457):984-5.



Time windows for immune development by microbiota.
Source: Al Nabhani Z et al., Immunity. 2019; 50(5):1276-88.

adequate response by the immune system to the expanding gut microbiota during the gradual switch from a diet composed exclusively of milk to a diet that includes other foods is for health later in life. However, **an altered gut microbiota during the weaning period (e.g., secondary to antibiotics or due to a high fat diet) may hinder adequate development of host immune responses, which leads to increased susceptibility to immune-related diseases such as allergy later in life.** The right food intake during this weaning period also matters for a balanced activation of the immune system. For example, compounds of dietary origin such as retinoic acid, whose metabolism is affected by the gut microbiota, appear to shape the developing immune system. By contrast, microbial exposure after weaning does not alter the development of immune responses, highlighting the critical window of weaning for preventing immunopathologies in adult life.

The gut microbiome and the immune system in inflammatory bowel disease: what is the chicken and what is the egg?

Harry Sokol from Saint Antoine Hospital (Paris, France) updated major learnings on using gut microbiota as a therapeutic tool in inflammatory bowel diseases (IBDs). Although specific gut microbiome signatures have been defined in IBDs, the role of the microbiota in the onset of IBD

in terms of host genetic susceptibility is unknown. Sokol shared observational data showing associations between four major genetic variants linked to an increased risk of IBD and gut bacterial populations. Within them, a link between *NOD2* genes and a reduction in both the *Roseburia* and *Faecalibacterium prausnitzii* genera was replicated in three independent cohorts. Overall, these findings show that **the gut microbiota might be a potential mechanism underlying the association between IBD and genetic variants.** In addition, gut microbiota-derived metabolites are gaining interest as potential targets for precision therapeutic modulation in IBD. Increased tryptophan metabolism has been associated with the activity of IBDs, generating aryl hydrocarbon receptor agonists that have a wealth of effects on mucosal immunity and homeostasis.

Finally, Sokol shared the findings of a recent randomized controlled trial as the first to evaluate the use of fecal microbiota transplantation in maintaining remission in Crohn's patients. The authors found a higher rate of steroid-free remission in Crohn's patients treated with FMT as well as improved lesions and inflammatory markers. Although further studies on larger patient populations are needed, the results of this pilot trial are promising for the many patients suffering from Crohn's disease. ■



“In order to develop a balanced immune system, mice and humans need to be exposed to microbiota during the neonatal period spanning birth to weaning”

Gérard Eberl



Learn more about the contribution of gut microbiota-derived metabolites in IBD [here](#).

FOOD INTOLERANCES AND FUNCTIONAL GUT DISORDERS ARE CLOSELY CONNECTED: WHY IT IS TIME TO FOCUS ON THE SMALL INTESTINE?



Although the small intestine is a harsh environment for microorganisms to thrive, its involvement in driving immune responses and digesting macronutrients makes it worthwhile to explore in the context of food sensitivities and enteropathies. **Alberto Caminero** from McMaster University (Hamilton, Canada) presented findings suggesting the gut microbiota's involvement in the processes underlying gluten or wheat sensitivity. Certain small-intestinal bacteria, such as *Pseudomonas*, produce elastases that contribute to gluten degradation. However, in mice expressing genes associated with coeliac disease (HLA-DQ8), bacterial elastase can synergize with gluten to induce severe inflammation. Similarly, non-gluten proteins present in wheat, such as α -amylase trypsin inhibitors (ATIs), can induce an innate immune response, causing bar-

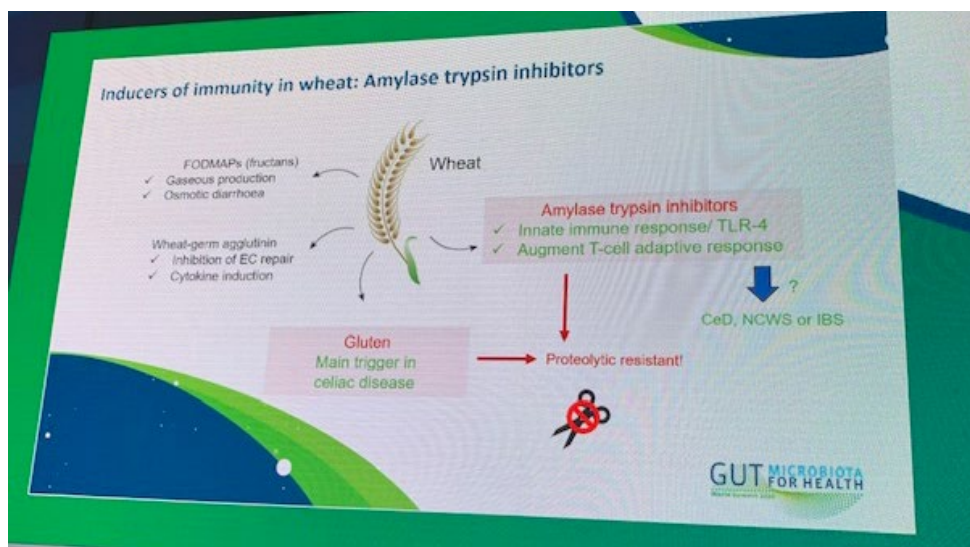
rier dysfunction in the absence of mucosal damage. Interestingly, *Lactobacillus* can degrade ATIs, leading to a reduction in its pro-inflammatory effects. These findings open the potential of gut microbiome-modulating strategies through gluten and ATI-degrading bacteria in patients with wheat-related disorders.

Purna Kashyap from Mayo Clinic (Rochester, USA) focused on the small intestinal microbiome in functional gastrointestinal disorders. Small intestinal bacterial overgrowth (SIBO) has been suggested as a culprit of common functional gastrointestinal symptoms, including IBS and intestinal bloating. However, there is no gold standard for diagnosing SIBO and Kashyap showed that **high-throughput sequencing analysis of the duodenal microbiome, rather than diagnosing SIBO using the traditional**

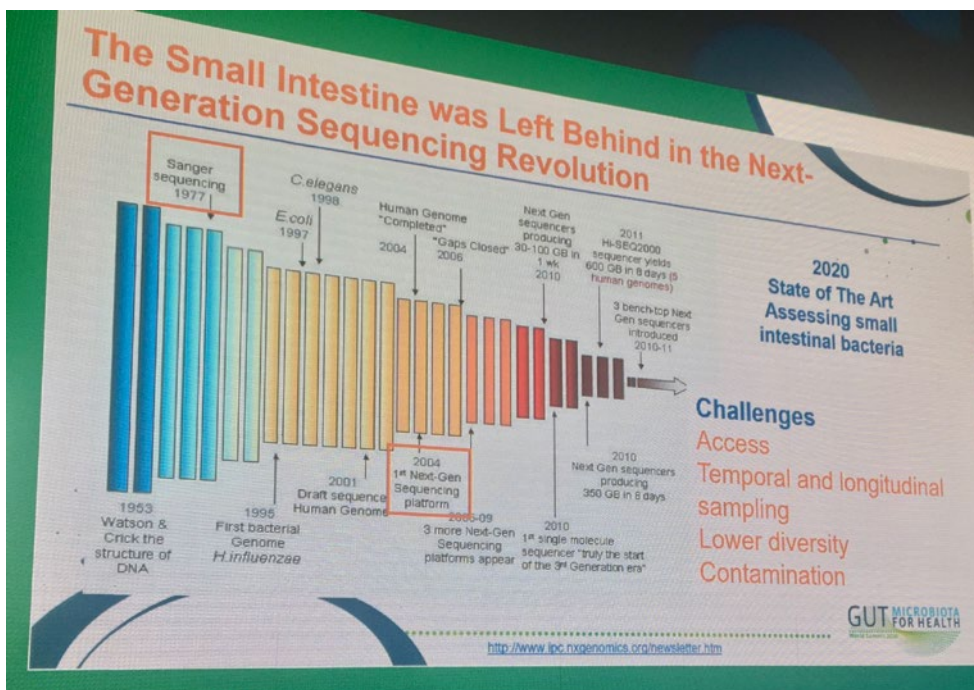
“Understanding the basics of bacterial-diet interactions will help us better treat patients with food sensitivities and enteropathies, such as celiac disease”

Alberto Caminero

Learn more about current research on how changes in the gut microbiota play a role in food sensitivities: [here](#).



Wheat components involved in increased intestinal inflammation in patients with celiac disease or other wheat-related disorders (e.g., non-celiac wheat sensitivity and irritable bowel syndrome).



“Small intestinal bacterial overgrowth (SIBO) has been suggested as a culprit of common functional gastrointestinal symptoms, including IBS and intestinal bloating.”

aspiration and culture of small intestinal contents, correlates with functional symptoms in 126 individuals who had various gastrointestinal symptoms. Indeed, asymptomatic individuals commonly met criteria for SIBO. In addition, metabolic pathways involved in metabolizing simple sugars were enriched in symptomatic individuals, whereas complex carbohydrate degradation pathways were decreased. These findings led the investigators to hypothesize that dietary factors might be relevant to alterations of the duodenal microbiome and prompted them to examine the effect of fiber content in the diet on gastrointestinal symptoms and the small intestinal microbiome in 16 healthy individuals. **Switching to a low-fiber and high simple sugar diet for 7 days increased small intestinal permeability and induced IBS-type symptoms (such as bloating and abdominal discomfort)**

that resolved on resumption of the subjects’ habitual high-fiber diet. This means diet affects the small intestinal microbiome and may be a factor determining SIBO.

Beyond dietary fiber, Kashyap acknowledged that other dietary components and drugs may modulate the small intestinal microbiome. For example, consumption of a high fat diet can profoundly alter the microbiota in the small intestine, which increases fat absorption in mice. Although the long-term impact of these results in the clinical setting remains to be seen, it turns out that it is time to move away from SIBO for predicting functional gastrointestinal symptoms and to focus on the small intestinal microbiome as a key protagonist in functional gastrointestinal symptoms ■

“It is time to move away from SIBO for predicting functional gastrointestinal symptoms and to focus on the small intestinal microbiome as a key protagonist in functional gastrointestinal symptoms.”

THE MICROBIOME CANNOT BE IGNORED WHEN LOOKING AT HOW DRUGS ACT IN THE BODY

It is not only antibiotics that can have an impact on our gut bacteria; a quarter of drugs designed to act on human cells do too.

Medication, together with diet, stands out as a major environmental factor that influences gut microbiota composition. Rinse K. Weersma from the University of Groningen (Netherlands) highlighted that **the identification of a causal impact of proton pump inhibitors (PPIs) and the anti-diabetic drug metformin on the gut microbiome provides firm evidence of gut microbiome perturbation by drugs other than antibiotics.** PPIs have the potential to alter the gut microbiota by reducing acidity in the stomach that leads to an overrepresentation of oral microbes in the gut; increasing the risk

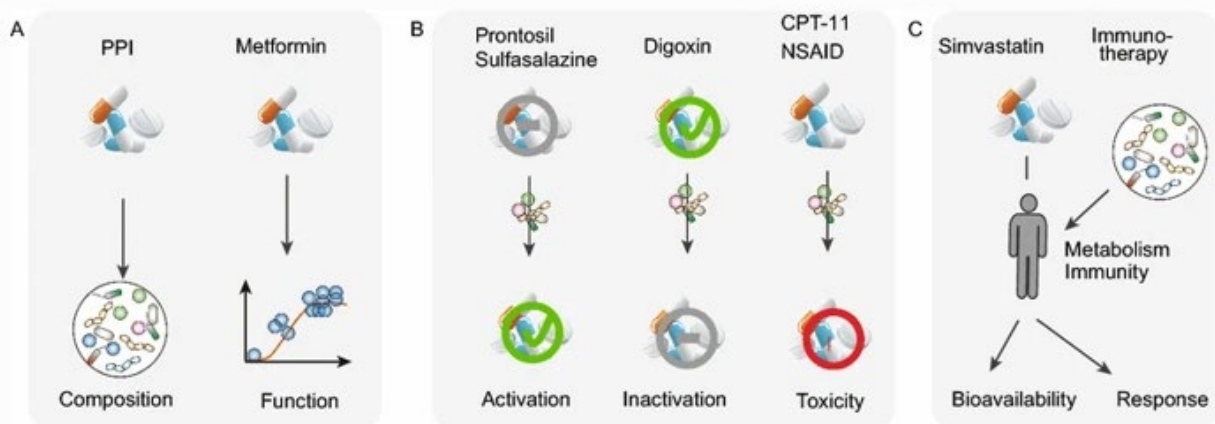
of enteric infections caused by a decreased colonization resistance for *Clostridioides difficile* infection due to a reduction of stomach barrier function; and altering gut microbiota functions (e.g., increased purine deoxyribonucleoside degradation as a source of carbon in PPI users). Notably, long-term effects tied to chronic PPI consumption include an altered response to immune checkpoint inhibitors in cancer and the development of childhood obesity.

Meanwhile, Athanasios Typas from the European Molecular Biology Laboratory (Heidelberg, Germany) focused on the impact of non-antibiotic drugs on gut microbes. Typas's group found that **nearly one quarter of more than 1,000 commonly used drugs had antibiotic effects, which are reflected in side effects in humans.** Drugs that have the most profound effect include anti-cancer drugs, antipsychotics and



“Microbiome studies should be corrected for medications use, including proton pump inhibitors, metformin, laxatives, selective serotonin reuptake inhibitors and antibiotics.”

Rinse K. Weersma



Different scenarios in which drug-gut microbiome interactions can occur:
Source: Doestzada M et al., Protein Cell. 2018; 9(5):432-45. doi: 10.1007/s13238-018-0547-2.

antihypertensive drugs. As specific therapeutic classes target not only human cells but also gut microbes, this might imply the role of polypharmacy as a strong driver of antimicrobial resistance. Typas also showed that the detrimental effects of antibiotics on the gut microbiota are not limited to their ability to stop the growth of gut microbes and include collateral damage such as the lysis of gut commensals. In this regard, experimental research has started exploring selective antidotes for avoiding the side effects of wide-spectrum antibiotics on Gram-negative gut commensals, while retaining activity for pathogens.

The next frontier in medicine: harnessing living bacteria in our body as a non-invasive way to detect and treat disease

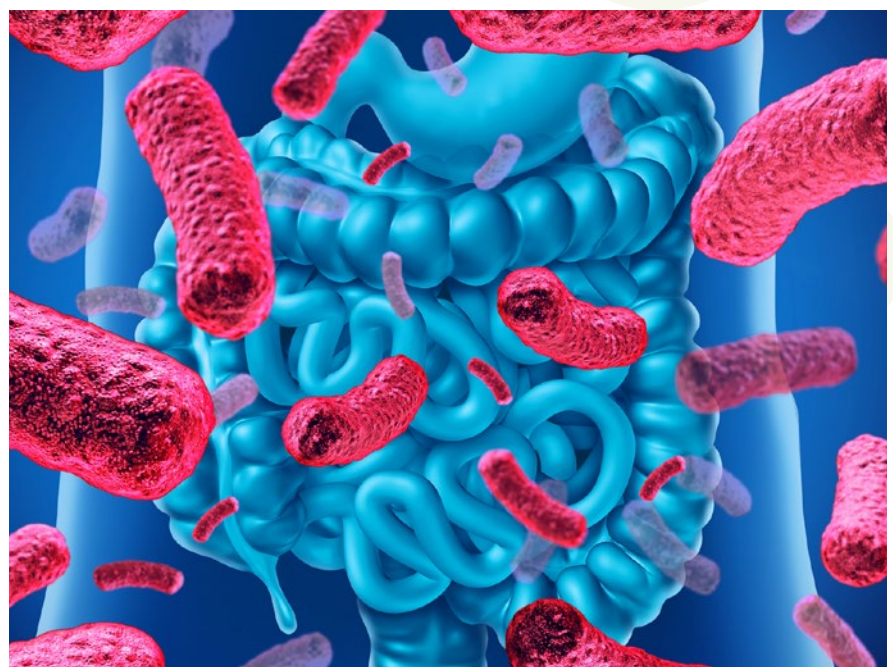
David Riglar from Imperial College London presented the potential of engineering living bacteria in our body as non-invasive tools for detecting and treating disease. The Riglar lab uses a combination of synthetic biology, imaging and sequencing-based approaches to better understand the function of the gut and its microbiota during health and disease. Riglar explored the potential of living engineered probiotics for probing and controlling the gut environment. For example, studies have shown engineered gut bacteria can survive in the mouse gut and sense, record

and respond to in vivo signals, such as in the healthy or diseased gut. **The unique abilities of living organisms with the potential to improve how we care for patients include being able to integrate and respond to new signals; accessing parts of the body inaccessible to standard technology; producing and delivering biological therapeutics directly to the site of disease; and showing a durable performance (lasting even longer than 6 months) within the gut.**

On the whole, **the use of live, engineered probiotics represents a new frontier in managing gut diseases and as a novel mechanism for drug delivery.** Major challenges include the availability of libraries and conditions to be tested in order to better understand bacteria behavior within the complex gut environment ■

“Selective antidotes are being developed as a means of stopping the impact of antibiotics and human-targeted drugs on gut commensals, while not affecting antibiotic effects on pathogens.”

Athanasios Typas



The use of live, engineered probiotics represents a new frontier in managing gut diseases and as a novel mechanism for drug delivery.

GUT MICROBES SHOW THE WAY TOWARDS BETTER MENTAL HEALTH

John F. Cryan from University College Cork gave an overall glimpse of the role of intestinal microbiota in regulating the gut-brain axis across lifespan. The role of the gut microbiota in brain and behavior is supported by initial findings in which germ-free mice showed alterations in neuron myelination and activity, dendritic growth and even blood-brain-barrier permeability. In other words, the brain does not develop appropriately without microbes. Mode of delivery is among the most studied factor playing a pivotal role in regulating early brain development, with enduring neurobehavioral effects. More interestingly, C-section-induced effects on behavior can be reversed by targeting microbiota with probiotics, at least in animal models. As for later in life, Cryan explored the gut microbiota's influence on brain development through adolescence, which is a time of enormous developmental change. Cryan explained that gut microbiota undergoes a shift in structure and balance during adolescence and external sources of stress during this period may

have an impact on the intestinal microbiota and subsequent mental illnesses in the developing teen. In addition, as we age, changes in the gut microbiota and associated increases in gut permeability, inflammation and arterial dysfunction may be important mediators of impairments in the behavioral, affective and cognitive functions seen in aging.

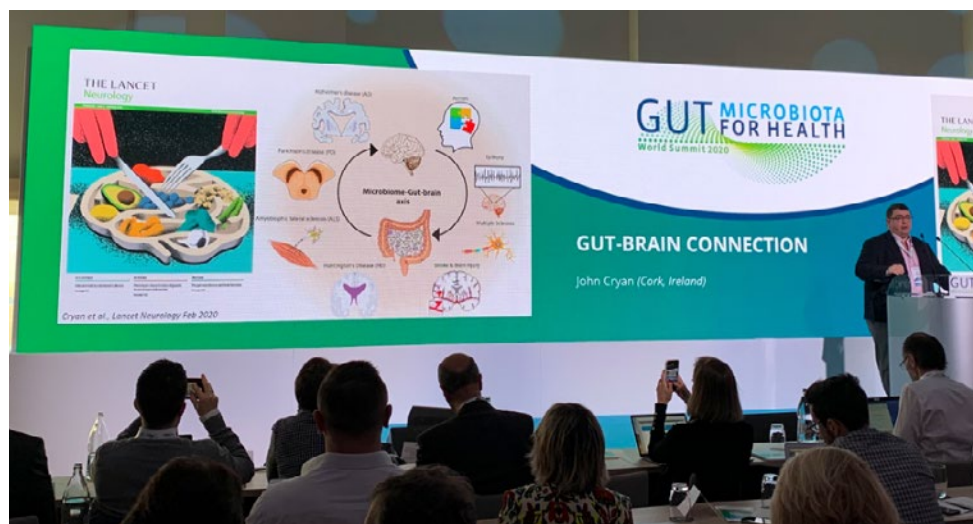
Due to the close interaction between gut microbiota and the brain, scientists have started exploring means of influencing the gut microbiome for the benefit of mental health. While the term psychobiotic was introduced by Irish scientists in 2013 and originally referred to a subset of probiotics that could produce a health benefit in those with psychiatric illness, more recently, the definition of psychobiotics has expanded to include other means of influencing the microbiome for mental health benefits. Psychobiotics, therefore, can include a range of substances that affect microbiota-gut-brain axis signaling, including probiotics, pre-



“Gut bacteria are directly linked to our mental health. We have coined the term psychobiotic for means of influencing the microbiome for mental health benefits, including probiotics, prebiotics, synbiotics and postbiotics.”

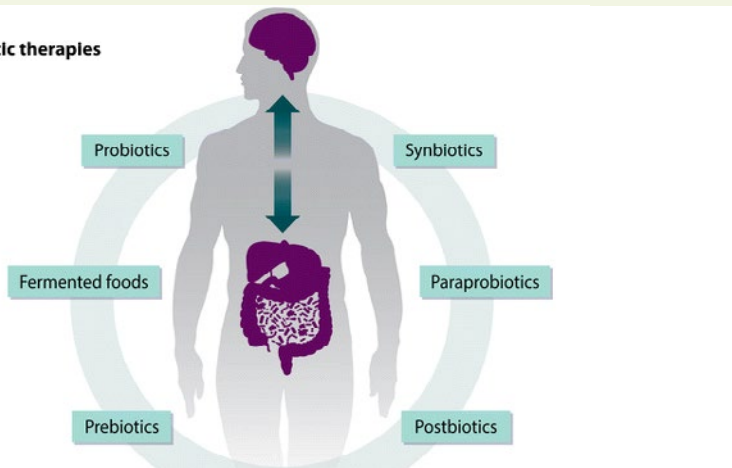
John Cryan

“Psychobiotics, therefore, can include a range of substances that affect microbiota-gut-brain axis signaling, including probiotics, prebiotics, synbiotics and postbiotics.”



“Serotonin of microbial origin can have an impact on host functions, including gastrointestinal motility and platelet function.”

Potential psychobiotic therapies



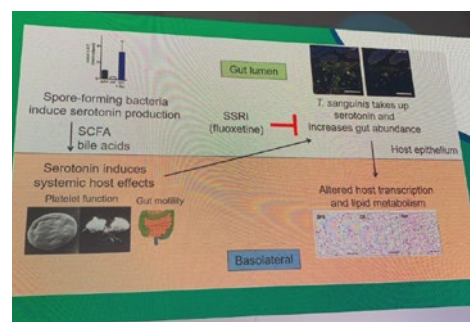
Ways of targeting the gut microbiome for mental health benefits.
 Source: Long-Smith et al., *Annu Rev Pharmacol Toxicol.* 2020; 60:477-502.

biotics, synbiotics and postbiotics. These substances can be delivered through supplements, functional foods, and improvements to dietary intake. For instance, targeting the gut microbiome by using dietary prebiotics can reverse neuroimmune alterations in middle-aged mice. In addition, the consumption of probiotic *Bifidobacterium longum* 1714 has been associated with reduced stress and improved memory in healthy adults. Current unknowns include dose responses and the long-term effects of psychobiotics' anxiolytic and antidepressant effects.

Serotonin acts as a node for gut microbiota-brain interactions

When going deeper into the communication across the microbiome-gut-brain axis, there is also evidence to suggest that serotonin may be an important mediator. **Jonathan B. Lynch** from the University of California, Los Angeles updated how the gut microbiota influences body functions by modulating serotonin levels. Although

more than 90% of the body's serotonin is synthesized in the gut, Lynch showed the important contribution of indigenous spore-forming bacteria dominated by Clostridiaceae and Turicibacteraceae from the mouse and human microbiota in promoting serotonin synthesis. This implies that serotonin of microbial origin can have an impact on host functions, including gastrointestinal motility and platelet function. In the opposite way, specific dominant members of the gut microbiota are well equipped to respond to intestinal serotonin, with an impact on host lipid metabolism that is not completely understood. These results reveal that certain gut bacteria modulate host physiology and its regulation could have therapeutic implications ■



GUT MICROBIOME DATA WILL HELP CLINICIANS MOVE TOWARDS CUSTOMIZED PATIENT HEALTH MANAGEMENT

Joël Doré from the French National Research Institute for Agriculture, Food and Environment discussed the progress toward clinical insights from gut microbiome data. Although it is known that a disrupted host-microbe symbiosis is a common thread in chronic conditions, Doré acknowledged that harnessing available gut microbiome datasets to develop diagnostic, preventive and therapeutic tools is not straightforward. In this regard, a good starting point is grouping people according to low or high richness enterotypes depending on species diversity/gene count in their gut microbiota. While a gut microbiota showing high richness is considered a marker of health, people with low gut microbiota richness appear to be at higher risk of metabolic conditions such as diabetes and obesity, may show a reduced response to treatment (e.g., dietary intervention in obesity), and may even be more prone to exper-

riencing complications associated with liver cirrhosis. This means that nutritionists or clinicians can have an idea of healthy individuals or patients' lower or higher risk of metabolic conditions or response to certain treatments based on their gut microbiota richness assessed using full shotgun metagenomic sequencing.

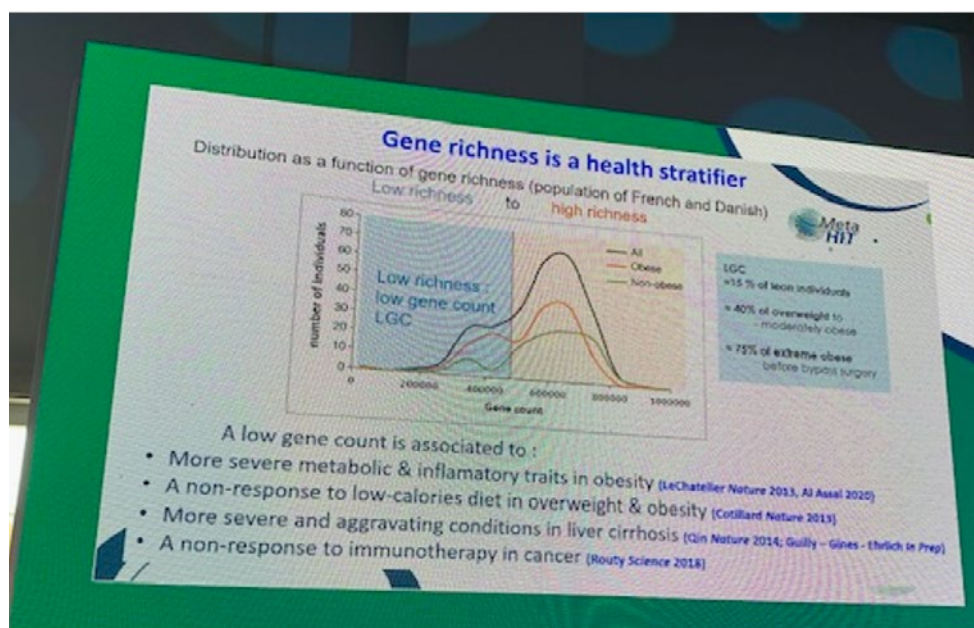
For gut microbiome data to become useful in the clinical setting, however, it is important to standardize sample collection and analysis. Only with well documented microbiome standards that allow for robust and reproducible analysis will reliable data that provide a clear picture of the microbiome help guide clinical decisions. In this regard, the International Human Microbiome Standards project has developed standard operating procedures to optimize data quality and comparability in the human microbiome ■



“Gut microbiota richness might help clinicians make better decisions in terms of clinically managing the patient.”

Joël Doré

“A gut microbiota showing high richness is considered a marker of health, people with low gut microbiota richness appear to be at higher risk of metabolic conditions such as diabetes and obesity.”



Conclusion

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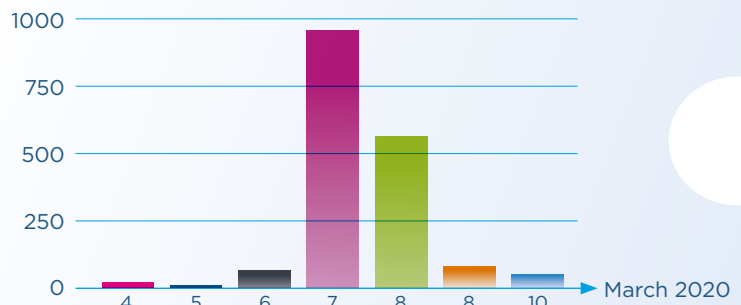
While initial studies in the human microbiome field focused on describing alterations in gut microbial communities in disease states compared with healthy individuals, during the last decade we have gained insights regarding how the microbiome shapes health and disease across lifespan. This has led to the development of gut microbiome-targeted strategies that will allow clinicians to make better decisions in terms of clinically managing the patient. Scientists agree that the recipe for achieving a healthier gut microbiome that can aid gut-related conditions and systemic indications include nutrition, prebiotics, probiotics and fermented foods.

▶ Plenary sessions replay available [here](#).

Gut Summit 2020 was accompanied by interactive conversations on Twitter. We thank the 580 participants who played an active role in the #GMFH2020 conversation.



Tweet Activity of #GMFH2020



9.882M Impressions

1,670 Tweets

580 Participants

19 Avg Tweets/Hour

3 Avg Tweets/Participant



KEY DEFINITIONS

Amylase trypsin inhibitors (ATIs): non-gluten proteins present in wheat that may promote intestinal inflammation, increased intestinal permeability and gut dysmotility. Research in mice has shown *Lactobacillus* can degrade wheat ATIs to reduce intestinal dysfunction induced by immunogenic wheat proteins.

Dysbiosis: an imprecise term used for defining a perturbed microbial ecosystem compared with the healthy state or homeostasis. Instead of being measured by species richness or diversity, scientists highlight that functional diversity, stability and resilience also matter when assessing the health of the microbiota and the host. Instead of dysbiosis, scientists acknowledge that the terms “different”, “altered” or “adapted” are more accurate when referring to a dysbiotic gut microbiota composition and/or function.

Enterotype: name for a type of microbiome classification described in 2012 based on the proportions of certain microbes, in particular *Bacteroides*, *Prevotella*, and *Ruminococcus*. As communities of gut bacteria may form a spectrum rather than falling into distinct groups, a new definition classifies gut microbiota enterotypes into two entities based on species diversity/gene count. One of the enterotypes is low richness (more prevalent in patients with more severe conditions) and the other is high richness (considered a marker of health).

Fermented foods: foods or beverages whose production involves extensive microbial growth. The fermented foods containing live organisms that have been characterized and have clinical evidence of a health benefit are considered probiotics. For example, many fermented milks have probiotic activity for conditions relating to the digestive tract and the immune system.

Full shotgun metagenomic sequencing: a bioinformatics technique that identifies which microbes are present in a sample and their functional potential. It gives more reliable functional predictions compared with 16S rRNA sequencing.

Germ-free: a host without a microbiome. Generally refers to mice and rats that were born and reared in a sterile environment for research purposes.

Inflammatory bowel disease (IBD): an umbrella term used to describe disorders characterized by an excessive swelling of the wall of one section of the digestive tract. Types of IBD include Crohn’s disease, ulcerative colitis and pouchitis. Both genetic and environmental factors potentially affect microbiota composition, which plays a role in IBD pathogenesis.

Irritable bowel syndrome (IBS): a common functional disorder affecting up to 20% of people worldwide, with a higher prevalence in women. It is indeed the main motivation behind gastroenterology conditions. Researchers believe it may originate from an unbalanced gut microbiota.

Lipopolysaccharide (LPS): the major component of the outer membrane of Gram-negative bacteria. When found

in the blood, it is a sign of gut barrier impairment, with subsequent long-lasting effects that go beyond the gut (e.g., obesity has been linked to an increased intestinal permeability, favoring the shift of LPS from the gut lumen to the bloodstream).

Microbiome: this term is used for two concepts. One to refer to the collective genomes harbored by microbes, and another for referring to the entire habitat, including the microorganisms and their genomes. Nowadays, this term is commonly used to refer to the microorganisms themselves.

Microbiota: the community of micro-organisms living in a specific environment. For example, ‘the gut microbiota’ refers to all microbial communities within the intestinal tract.

Microbiota-gut-brain axis: a network comprising the gastrointestinal tract, the gut microbiota, the enteric nervous system and the brain. Bidirectional communications between the gut and the brain regulate important functions, including immunity, digestion, metabolism, satiety and stress reactions.

Operational taxonomic units (OTUs) or phylotypes: similar bacterial individuals based on a predetermined similarity threshold (e.g., 97% similarity).

Postbiotics: bacterial metabolites with a direct effect on host nutrition, metabolism and immunity (e.g., short-chain fatty acids).

Prebiotics: these are substrates that are selectively utilized by host microorganisms conferring health benefits. Not all food fibers are considered prebiotics as selective utilization by gut bacteria is a requirement for a prebiotic.

Probiotics: live microorganisms that, when administered in adequate amounts, confer a health benefit to the host.

Psychobiotics: targeted interventions of the microbiome for mental health benefits. It refers to probiotics, prebiotics and other means of influencing the microbiome for the benefit of mental health.

Short-chain fatty acids: fatty acids with two to six carbon atoms that are produced by bacterial fermentation of dietary fibers (e.g., acetate, propionate and butyrate).

Small intestinal bacterial overgrowth (SIBO): a poorly understood entity characterized by an excessive growth of bacteria within the small intestine. These excessive bacteria have been linked to functional gut disorders such as IBS.

Synbiotics: synergistic combination of prebiotics and probiotics.

Taxa: a scientifically classified group. Ways of classifying the members of a defined microbiome, in decreasing order: Phylum -> Class -> Order -> Family -> Genus -> Species -> Strain.