Microbiota in Clinical Practice: What is New and What is True?

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INCREASING interest in the microbiome can be linked to its great diagnostic and treatment potential, the extent of which is still largely unknown. The session 'The Healthy Microbiota: Does It Exist?', presented at the 31st United European Gastroenterology (UEG) Week in Copenhagen, Denmark, gave an in-depth review of the current landscape of the microbiome in clinical practice.

THE 'HEALTHY' MICROBIOME

Jeroen Raes, Katholieke Universiteit (KU) Leuven, Belgium, opened the session by addressing the surge of interest in the microbiome in recent years. The first big wave of attention was approximately 10 years ago and included research into diseases of the microbiome, but lacked an understanding of what can be considered a 'healthy' microbiome, Raes recalled. He suggested that key features of the research, for example, variation in a clinically relevant population, temporal variation and biomarker stability, factors influencing gut flora composition, clinical endpoints, and effects of the environment in relation to the microbiome, were all largely unknown back in 2012 during this initial wave.

Faecal samples can be considered as a snapshot of a maturing ecosystem and have emerged as one of the most valuable tools in microbiome research. Recent advances suggest transit time is the most important confounder of microbiome studies and should not be underestimated in clinical trials. Transit time should be taken into consideration in any trial as it is the main factor explaining variation in the microbiome between individuals, and should therefore be controlled for. Slow transit times have been associated with a shift from saccharolytic to proteolytic metabolism, which can have significant implications for gut health.

The diversity, composition, and variety of the microbiome in an individual can be determined by several host factors. Factors may include genetics, diet, age, sex, and use of antibiotics. Additionally, the present microbiome may have been affected by historical variables. While experts may not be able to categorically state what should be considered a healthy microbiome, there is knowledge on what is not indicative of a healthy microbiome. The *Bacteroides 2* enterotype can be identified in approximately 10% of the population. It is characterised by dysbiosis, low cell count, low diversity, low anti-inflammatory taxa, high pro-inflammatory taxa/pathobionts, and higher temporal instability.

Population studies are essential in mapping 'normal' variation. There are multiple physiological and lifestyle factors influencing variation, including transit time, diet, low-grade inflammation, age, sex, and drugs.

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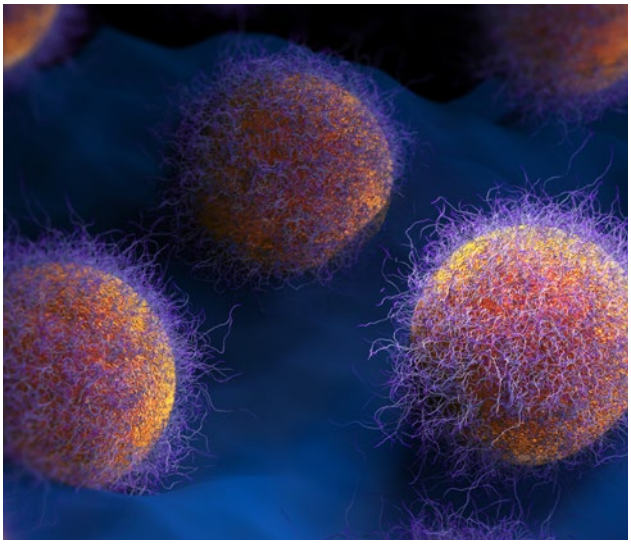

Advances in microbiome research have a major impact on the continuously growing understanding of healthy microbiota. Steering away from the dysbiotic *Bact2* enterotype towards more balanced gut microbiota should be a key target for future microbiome interventions.

THE MICROBIOTA SIGNATURE AND PERSONALISED TREATMENT

Gianluca Ianiro, Gemelli Hospital, Rome, Italy, presented the concept of the microbiota signature, and whether it could be used to guide personalised treatment. The gut microbiome is modifiable and is mainly influenced by the environment. Making changes to environmental factors, such as drugs, diet, lifestyle, or other therapeutics, can advantageously or disadvantageously alter the microbiota in a rapid fashion. Ianiro shared the effects of the modern lifestyle on the microbiome, stating that "Westernisation is causing mass extinction of our microbiota." Ecologically speaking, the diversity of the microbiome is dropping tremendously, driving the prevalence of chronic disorders.

Reassuringly, Ianiro remarked on the ease with which some microbiome interventions can be addressed at the bedside. The current standard for microbiome diagnostics lacks regulation and is even chaotic, Ianiro reported, and international consensus is needed to establish guidelines and standards for microbiome testing and analysis.

THE FUTURE OF MICROBIOME THERAPEUTICS

Haggai Bar-Yoseph, Rambam Health Care Campus, Haifa, Israel, shared the future of microbiome therapeutics with the audience. There is a well-established fascination with the association between the microbiome and disease or health patterns from healthcare professionals and laymen alike. Healthcare professionals must consider where best to intervene to change the natural course of disease towards a more beneficial course.

> **"Westernisation is causing mass extinction of our microbiota."**

Faecal microbiota transplant is a very robust intervention that is relied upon in some clinical scenarios, and can be manipulated through procedure-, recipient-, or donor-related factors. Bar-Yoseph focused on the promise of therapeutics beyond faecal microbiota transplant and other treatments on the horizon. Researchers are exploring microbial consortia, next-generation probiotics, phage targeting, and synthetic biology as potential tools to manipulate the microbiome. These interventions are being actively tested; however, they are not robust enough for the clinic.

Next-generation probiotics offer potential that may be greater than traditional, single-agent interventions or 'old probiotics' historically consumed in food, beverages, or taken as supplements. Also referred to as live biotherapeutics, they do not have a clear history of use, are challenging in strain cultivation, may be genetically manipulated, and are undergoing testing for medical use rather than for dietary supplementation.

There remains much to be discovered in this vast, evolving field of study and the associated health implications. Some interventions are yet to demonstrate the robustness required for clinical implementation, but the exciting possibilities for therapeutic intervention suggest a wealth of forthcoming developments is still to come. ●