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Editorial

EDITORIAL

Outlook on the gut microbiota

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Despite being a rather young research field that only emerged in the last two decades, it has become clear that the gut microbiota is an essential part of our body that strongly influences the processes that regulate our health and wellbeing. In this Special Issue of *Gastroenterology Report*, we have compiled a collection of articles which discuss that microbial signals deriving from our internal bioreactor are by no means restricted to the gut environment, and why it is thus reasonable to consider the gut microbial community as an additional organ to our body.

The intestinal mucosal barrier is the main interface between the gut microbiota and the host [1], thereby being essential in providing tolerance for the commensal bacteria but at the same time protecting against intestinal pathogens. Accordingly, a breakdown of the mucosal barrier is linked to intestinal inflammation and infection. Recent studies have identified that the gut microbiota has an active role in shaping mucosal immunity. Jensen *et al*. [2] discuss the intimate interaction between the gut microbiota and the intestinal barrier in the context of our Western lifestyle. Besides highlighting the immunological response of the host towards the gut bacteria in different regions of the gut, the authors also suggest potential strategies that could restore barrier function in the diseased gut. These strategies include strengthening the mucosal barrier by externally supplemented host-defense peptides or by providing microorganisms or microbe-derived products that stimulate intestinal immunity.

The intestine—specifically the colon—holds the highest microbial density in the body, and thus the majority of microbial metabolites are located within the gut. However, microbial signals can also reach distant organs and, as such, the gut–brain axis that connects enteroendocrine cells in the gut epithelium via the vagus nerve with the central nervous system and the brain has become a major field of research. Gubert *et al*. [3] discuss how microbial signals affect brain function and behavior, and how the gut microbiota can be linked to neuropathologies. Due to the complexity of the phenotypes, human cohort studies have so far mainly remained associative, but several different mouse models suggest indeed some involvement of the gut microbiota in the development of Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, multiple sclerosis, and Huntington's disease.

Identifying the microbial contribution to gut disorders, brain disorders, and other disorders or diseases opens up the possibility to target the microbiota for therapeutic interventions. However, we are just beginning to understand how the microbiota modulates the bioavailability and bioactivity of drugs that are already in clinical use. Even more, it has become evident that many non-antibiotic drugs affect the gut microbiota composition. Wan and Zuo [4] specifically discuss the microbiota–drug interaction for the cases of the anti-diabetic drug metformin, statins, proton-pump inhibitors, levodopa, and digoxin. By only considering this small selection of compounds, it is obvious that the microbial effect on drug efficacy can be exceptionally diverse and be either beneficial or detrimental. The microbial community is thus a factor that should be considered more in the future when evaluating novel therapeutic drugs.

Gut microbiota research has in the past mostly focused on bacteria, mainly due to the availability of sequenced and annotated genomes in cured databases. Yet, besides bacteria, the intestinal microbiota also includes fungi, archaea, protozoa, and viruses. In fact, the number of viruses is estimated to outnumber the bacterial cells by a factor of 10–20, with higher numbers at the mucosa than in the intestinal lumen. Among the viruses, tailed bacteriophages make up the majority of virus particles in

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the gut, and their proficiency for gene transfer likely contributes to the ability of the microbiome to rapidly adapt to changing environmental conditions. Borodovich *et al.* [5] discuss in detail the various mechanisms of horizontal gene transfer through bacteriophages. Specifically, the authors focus on the mechanism of phage transduction, in which a bacteriophage transfers non-viral DNA between bacterial host cells, and what consequences such events could have for the human microbiome.

Phage transduction is not the only process that affects the human microbiome. Mode of birth, breast-feeding or formula feeding, and the surrounding environment appear to be key factors that shape the microbiota early in human life. Taking a global perspective, Wallenborn and Vonaesch [6] present the development of the microbial community with respect to individual, environmental, and geographic contributions. They discuss how the microbiome of an individual needs to be assessed in the context of globalization and industrialization, and how our modern lifestyle affects the microbial composition. At the same time, industrialization has led to an increase in non-communicable diseases, and hence the authors highlight how the microbiota is linked to the most severe global diseases. Since targeting the microbial community is often easier than targeting the host directly, Wallenborn and Vonaesch suggest promising therapeutic interventions that promote a healthy microbiota in order to improve global health.

As will become clear after reading this Special Issue, we are still far from understanding all interactions between the gut microbiota and the human body. However, while early microbiota studies primarily focused on associations between distinct microbial communities and disease phenotypes, more and more mechanistic details are being unraveled. It is thus the hope of the field that the microbiota can be exploited even more as a therapeutic target to develop improved therapeutics for our industrialized society in the future.

Conflict of Interest

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