

Special Issue

Gut Microbial Communities in Health and Disease

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The complex and ancient relationships between animal hosts and the microbial communities that inhabit their digestive tracts have become the focus of intense research in recent years. As a result, our understanding of gut microbial ecology and of the evolutionary and physiologic impacts of gut microbial communities in animal hosts has grown markedly. Indeed, members of the gut microbiota have now been implicated as environmental factors in a wide range of human disease states. This Special Issue of *Gut Microbes* is written by leading researchers in the field and is intended to provide an overview of several important areas of ongoing research on gut microbial communities during health and disease in humans and other animals.

Although gut microbiota has important relevance for human health today, microbial colonization of the gut and other body sites is an ancient and pervasive feature of animal ontogeny. The advent of a primitive gut in early metazoan body plans permitted the capture, concentration, and digestion of exogenous nutrients, and it also provided an attractive nutrient-rich habitat for otherwise free-living microbes. As a result, all animal lineages have established complex strategies for defending against and collaborating with members of their gut microbiota. While some of these strategies can be unique to specific animal host lineages, others are shared among different animals including humans. For this reason, experimental analyses of gut microbiota in diverse animal host models are essential for providing insights into the evolution of gut microbial ecology and host-microbiota interactions, and for identifying conserved mechanisms that might be translatable to

humans and other animal hosts. Because our current information on gut microbial ecology and host-microbiota interactions is derived largely from vertebrate hosts, this Special Issue highlights contributions from several important invertebrate host model systems. Cnidaria possess a primitive gastric cavity and serve as important models for understanding how primitive animals might have interacted with their microbial world. A review article by Thomas Bosch in this Special Issue presents the advantages of Hydra as an experimentally tractable Cnidarian, as well as recent insights into the assembly, composition, and function of Hydra-associated microbiota.¹ The complexity of vertebrate gut microbiotas can pose significant challenges to understanding these natural co-evolved host-microbe relationships. Therefore, animals such as the medicinal leech *Hirudo verbana* that possesses a simple natural microbial community provide useful models to investigate co-evolved symbioses. A review article by Nelson and Graf in this Special Issue describes the anatomy and feeding behavior of the medicinal leech, the composition and roles of its microbiota, and recent insights into the bacterial genetic determinants of gut colonization.² Another important invertebrate host model that possesses a relatively simple gut microbiota coupled with excellent genetic tools is *Drosophila*. Broderick and Lemaitre present a review article in this Special Issue describing our current understanding of *Drosophila* gut microbiota composition, the factors shaping microbiota composition, and the impact of the microbiota on *Drosophila* hosts.³ The study of these animals, together with other major invertebrate and vertebrate host model systems,^{4,5-9} is leading to important

insights into the evolution, ecology, and physiology of gut microbes that will be beneficial in our effort to understand the microbiota's roles in human health and disease.

Our new appreciation for the contributions of gut microbiota to human health and disease in recent years has fueled interest in understanding how gut microbial communities assemble and influence host health during the earliest stages of the life cycle. In this Special Issue, Collado and colleagues review our current understanding of the early ontogeny of the human gut microbiota and the diverse factors that influence gut microbiota composition during early life stages.¹⁰ Using probiotic interventions as an example, they also discuss how manipulations of the gut microbial community during early stages of life can be used to promote later health.

The etiology of many human diseases is known to involve both genetic and environmental factors. The incidence of some human diseases, including obesity, diabetes, and atherosclerosis, has increased alarmingly in recent decades, suggesting a particularly strong environmental contribution. In this Special Issue, Kelsen and Wu review the growing body of evidence that dietary and other environmental alterations can influence the composition and activity of the gut microbiota in mammalian hosts and that such alterations in the gut microbiota might constitute major environmental factors in these human diseases.¹¹ Obesity is ultimately caused by an imbalance between energy intake and expenditure; however, recent studies have also strongly implicated the gut microbiota in obesity-associated metabolic disease. A review by Cani and colleagues in this Special Issue discusses the mechanisms by

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which the gut microbiota can contribute to host energy balance, endocrine signaling, and obesity-associated metabolic disorders such as endotoxemia.¹²

The impact of the gut microbiota on host nutrition is perhaps best understood in the context of the microbial degradation of complex carbohydrates. The degradation of complex non-digestible dietary plant polysaccharides and host glycans in ruminants and hindgut fermenting mammals liberates calories for use by host and microbe, and also has presumably had a profound impact on the fitness and radiation of these animal lineages. An article by Flint and colleagues in this Special Issue reviews our current understanding of the bacterial gene families that contribute these important metabolic activities, the specific capabilities of implicated bacterial taxa, and the impact of these activities on the gut habitat.¹³

A constant tension within host-microbiota relationships in the gut is created by the host's need to defend itself from potentially invasive and pathogenic microbes while tolerating the persistence

of commensal microbial communities within the gut lumen. Although this task is effectively performed by the mucosal immune system in healthy individuals, it is now generally accepted that the inflammatory bowel diseases (IBD) are caused by aberrant host responses to the microbiota. A review by Elson and Cong in this Special Issue provides a framework for understanding IBD pathogenesis by discussing our current understanding of the diverse immune responses to the microbiota that maintain homeostasis and the human genetic variations and underlying mechanisms that confer susceptibility to IBD.¹⁴

The identified contributions of the gut microbiota to IBD, obesity, diabetes and atherosclerosis have underscored its potential to impact intestinal as well as extra-intestinal physiologies. A review by Al-Asmakh and colleagues in this Special Issue presents an intriguing body of evidence indicating that the gut microbiota can affect, and be affected by, the communication between the digestive tract and the central nervous system (CNS).¹⁵

The authors discuss recent studies suggesting that this “microbiota-gut-brain” axis impacts upon a variety of CNS functions, including behavior and mood, and might also contribute to human diseases such as autism.

As exemplified by the diverse animal model systems and biological processes presented in this Special Issue of *Gut Microbes*, the study of gut microbial communities is a vibrant and highly interdisciplinary field that holds great potential for identifying new ways to promote health in humans and other animals. The collective insights provided by this field in recent years have captured the interest and imagination of scientists and the public alike and have revealed intriguing new realms of biological complexity within the digestive tract of every animal. The transformation of these new perspectives into safe and effective approaches for shaping gut microbial communities to promote health will continue to require the integrated and creative contributions of diverse experimental systems and scientific disciplines.¹⁶

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