Diet and the Microbiome

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KEYWORDS

• Diet • Gut • Microbiota • Microbiome • Inflammatory bowel disease
• Irritable bowel syndrome

KEY POINTS

- Diet has a significant impact on the structure-function activities of the gut microbiota.
- Advances have been made in showing how host phenotype is shaped by the gut microbiota, and how diet may provide the selective pressure, in a positive or negative way, to sustain this relationship.
- Diet modification offers the opportunity in a clinical setting to reshape the gut microbiota for the relief of symptoms associated with functional disorders, and the therapeutic treatment of some gastrointestinal and extraintestinal diseases.
- However, studies need to continue to advance from microbiota profiling to function-based approaches and analyses, and more rigorous study designs also need to be used, to better differentiate between the cause and effect relationships of diet-microbiome interactions, and to translate microbiome research to medicine.

INTRODUCTION: WHAT IS THE MICROBIOME?

There are several extant definitions of the term "microbiome," a field of research that has become principally associated with the technological advances in DNA/RNA sequencing and computational biology. As such, the microbiome is still commonly defined as the collective genomic content of all microbes recovered from a habitat or ecosystem (eg, saliva and stool samples, skin swabs).[1] However, although such a definition captures the functional potential inherent to the microbiota (micro-), there

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is a need to place this knowledge in context with the interactions and processes contingent on the physicochemical attributes of their surrounding environment (-biome). This more holistic definition of the microbiome is applied throughout this article, in recognition of diet as a major influence on microbiome dynamics. By doing so, the concept of nutritional ecology is introduced: how the nutrient and its variations across temporal and spatial scales affect the gut microbiota. We contend that nutritional ecology will provide the mechanistic bases for understanding "diet and the microbiome," which will translate into improved diagnoses and treatments for functional and organic diseases.

GENERAL CONCEPTS AND APPROACHES OF MICROBIOME STUDIES

For the interested reader, Morgan and Huttenhower[2] present a well-structured and illustrated general overview of the techniques and approaches underpinning microbiome studies. Over the last two decades, microbiome studies have emphasized the use of polymerase chain reaction techniques targeting regions within the gene encoding 16S ribosomal RNA in prokaryotes (ie, bacteria principally, and archaea). When combined with the rapid advances in DNA sequencing technologies and a combination of ecologic, biostatistical, and computational methods, these 16S rRNA profiling methods have resulted in a taxonomy-based assessment of gut microbial communities resident in different regions of the gastrointestinal tract. Importantly, these approaches have afforded the differentiation of the microbiota to reveal specific microbes and microbial consortia indicative of alterations to gut homeostasis, which are generically referred to as "dysbiosis."[3,4] During the same period the National Institutes of Health Human Microbiome Project[5] has augmented these studies by producing the "reference genomes" of individual microbial species, which has supported the inference of the functional attributes inherent to the 16S rRNA profiles by such methods as PICRUSt.[6] However, and because of the continued advances in sequencing technologies, the time and cost constraints to "shotgun metagenome sequencing" are being relaxed, which affords a scale and depth of sequence coverage that provides an actual (rather than inferred) representation of the functional attributes inherent to the microbiota.[2]

These studies have also substantiated that the microbial communities of the gut are readily differentiated according to their microbial (and gene) density, diversity, and distribution; as affected by anatomic structure, host secretions, and digesta residence times at different sites. Although the esophageal, stomach, and small intestinal microbiota have now been characterised,[7] most studies that have advanced the mechanistic understanding of diet-microbiome interactions have been undertaken using stool/fecal samples and/or tissue samples collected from the large bowel. As such, the term "gut microbiome" has come to define this (terminal) region of the gastrointestinal tract. During the last 5 years in particular, shotgun metagenome sequencing of stool microbiota and the associated metagenome-wide association studies has revealed that the form and function of the stool microbiota is altered in patient cohorts with type-2 diabetes, cirrhosis, and colorectal cancer. These differences have not only provided insights of how microbial metabolism contributes to disease, but the identification of candidate gene and organismal biomarkers of health and disease.[8–11]

Critically, these methods have also shown the gut microbiota of humans (and other animals) is rapidly altered by changes in habitual or available diet, leading to the perception that diet may exert a stronger selective pressure on the gut microbiota than host genetics.[12,13] A particular focus in the last 10 years has related to obesity research, with Turnbaugh and colleagues[14] reporting an enrichment of microbial genes involved in carbohydrate, lipid, and amino acid metabolism in the obese adult