Gastroenterology 2014;146:1449–1458

Compositional and Functional Features of the Gastrointestinal Microbiome and Their Effects on Human Health



Emily B. Hollister[1,2] Chunxu Gao[1,2,3] James Versalovic[1,2,3]

[1]Department of Pathology and Immunology, [3]Department of Molecular Virology and Microbiology, Baylor College of Medicine, Houston, Texas; [2]Department of Pathology, Texas Children's Hospital, Houston, Texas

The human gastrointestinal tract contains distinct microbial communities that differ in composition and function based on their location, as well as age, sex, race/ethnicity, and diet of their host. We describe the bacterial taxa present in different locations of the GI tract, and their specific metabolic features. The distinct features of these specific microbial communities might affect human health and disease. Several bacterial taxa and metabolic modules (biochemical functions) have been associated with human health and the absence of disease. Core features of the healthy microbiome might be defined and targeted to prevent disease and optimize human health.

Keywords: Gastrointestinal; HMP; Lumen; Metagenomics; Microbe; Mucosa.

The human microbiome comprises diverse microbiologic ecosystems and is composed of a variety of bacteria, archaea, microeukaryotes (eg, fungi), and viruses. Although we have appreciated the diversity of our microbial world for decades, scientists were constrained by the inability to culture many bacteria in the laboratory. Paradigms in biomedical science and medicine are changing in a fundamental way as we explore potential contributions of human-associated microbes to health and expand our understanding of disease susceptibility and pathogenesis. In the early 1900s, scientists studied the abilities of microbes to promote longevity[1] and bacteriophages (bacterial viruses) to treat infections.[2,3] During the 20th century, scientists led military-style assaults on the biosphere with its war on microbes and global campaigns to eradicate infectious diseases. Great progress was made in the discovery and development of novel antimicrobial agents and vaccines to treat and prevent infectious diseases.

In the 21st century, we are attempting to develop a more balanced mindset as we seek to understand the role of the human microbiome in physiology and manipulate it to optimize health and prevent or treat disease. In recent years, we have increased our understanding of microbial communities and their corresponding metagenomes at different human body sites greatly.[4] Here, we review the bacterial component of the human gastrointestinal (GI) microbiome in healthy individuals and discuss what we have learned about its role in health (ie, the condition of being free from disease).

Defining the GI Microbiome in Health

How should biomedical research scientists and gastroenterologists define health and a healthy human microbiome? The microbiome may contribute to human health by increasing relative fitness, resilience, or optimal functioning of the body. The human microbiome has been defined by global ecological parameters such as richness, diversity, and evenness of its microbial communities. Microbial richness and diversity commonly are defined by studies of microbial composition using 16S ribosomal RNA (rRNA) gene sequencing or whole-genome, sequence-based metagenomic analyses; various indices of richness, diversity, and evenness have been used to compare bacterial communities from stool and intestinal biopsy specimens. Greater richness and diversity of bacterial species in the human intestine may be an indicator of health. Reduced bacterial diversity has been observed in the fecal communities of preterm infants who develop necrotizing enterocolitis, compared with those who do not,[5] and reduced GI bacterial diversity during infancy has been associated with an increased risk of allergic disease later in life.[6] In contrast, greater bacterial richness and diversity were found to correspond with better nutritional

Abbreviations used in this paper: GI, gastrointestinal; HGC, high gene count; LGC, low gene count; rRNA, ribosomal RNA.

0016-5085/$36.00
http://dx.doi.org/10.1053/j.gastro.2014.01.052

status, fewer comorbidities, and greater overall health in a cohort of elderly individuals.[7]

In addition to bacterial species counts and estimates of taxonomic diversity, richness of the human GI microbiome also has been characterized on the basis of microbial functional gene richness, determined by metagenomic DNA sequencing.[8] By using this approach, researchers have been able to categorize individuals as either high gene count (HGC) or low gene count (LGC), and these gene counts appear to have implications for health. In a survey of 123 nonobese and 169 obese Danish individuals, LGC and HGC individuals had mean quantities of 380,000 and 640,000 bacterial/phage genes, respectively. HGC individuals generally are considered to have a greater repertoire of microbial metabolic functions, a functionally more robust gut microbiome, and greater overall health, including a lower prevalence of obesity and metabolic disorders.[9]

Beyond microbial richness and diversity, a healthy gut microbiome can be defined by the presence of classes of microbes that enhance metabolism, resilience to infection and inflammation, resistance to cancer or autoimmunity, endocrine signaling, and brain function (brain–gut axis). The microbiome may mediate these effects via secretion of factors that modulate intestinal permeability, the mucus layer, epithelial cell function, innate and adaptive immunity, intestinal motility, and neurotransmission (Figures 1 and 2). The presence of representative core bacterial genera or species, or core metabolic functions/modules, could help to define a healthy microbiome at a given site in the human body, including the GI tract. Examples of bacterial taxa that have been associated with human health and proper GI function include *Bacteroides*, *Bifidobacterium*, *Clostridium* clusters XIVa and IVa (butyrate producers), *Eubacterium*, *Faecalibacterium*, *Lactobacillus*, and *Roseburia*. Bacterial species that might protect against weight gain and are enriched in HGC individuals include *Anaerotruncus colihominis*, *Butyrovibrio crossotus*, *Akkermansia* species, and *Faecalibacterium* species.[9] Core metabolic modules may include pathways involved in central carbohydrate metabolism and cofactor/vitamin biosynthesis. Metabolic

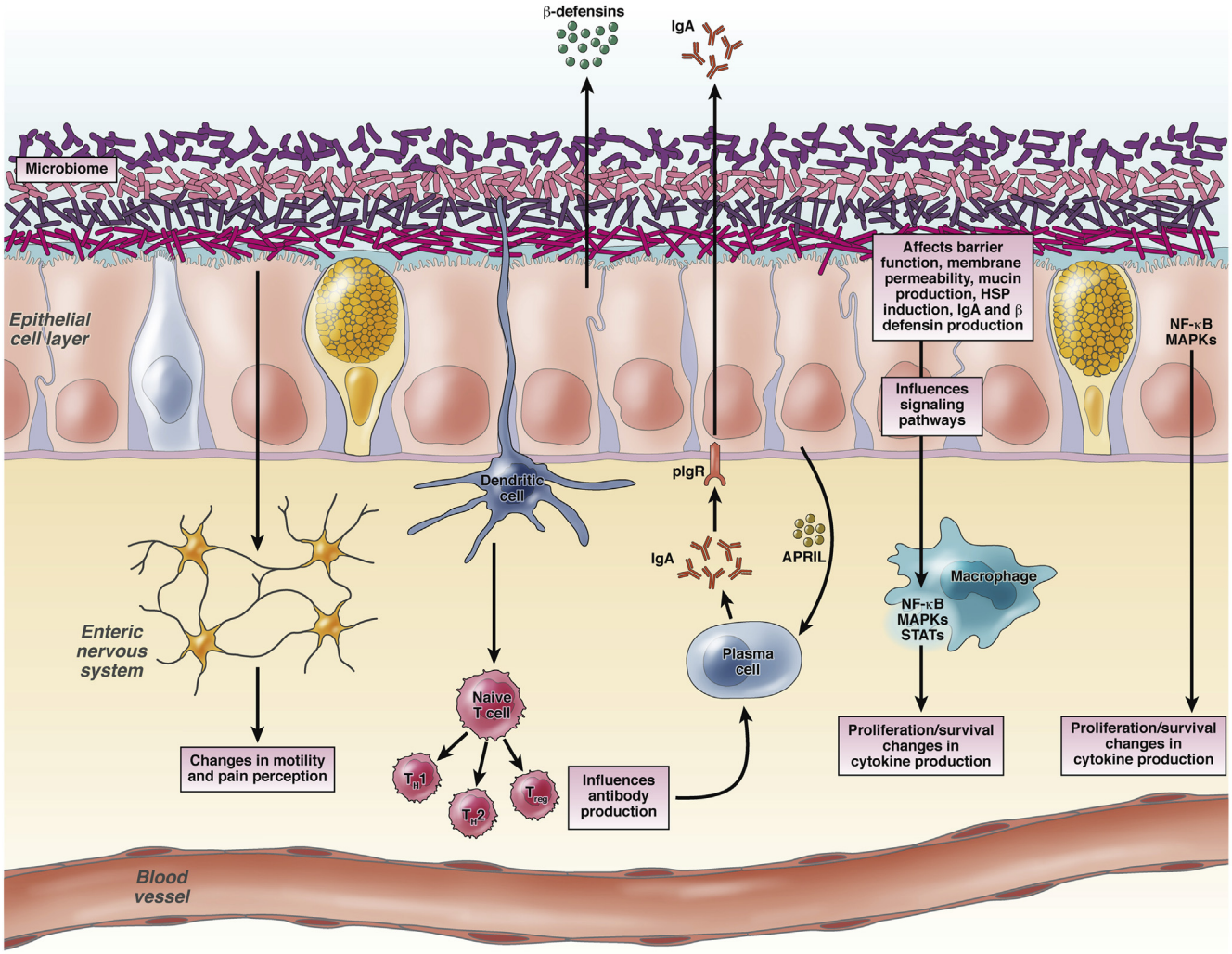

Figure 1. The intestinal microbiome and its effects in the intestinal mucosa. The intestinal microbiome (*top*) lies adjacent to the intestinal epithelium. Specific effects are described in text boxes. APRIL, a proliferation-inducing ligand; HSP, heat shock protein; MAPKs, mitogen-activated protein kinases; NF-κB, nuclear factor kappa-light-chain-enhancer of activated B cells; STATs, signal transducers and activators of transcription.