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Review article

Does the change on gastrointestinal tract microbiome affects host?



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ABSTRACT

During the past decade, studies on the composition of human microbiota and its relation to the host became one of the most explored subjects of the medical literature. The development of high-throughput molecular technologies allowed a deeper characterization of human microbiota and a better understanding of its relationship with health and disease. Changes in human habits including wide use of antimicrobials can result in dysregulation of host–microbiome homeostasis, with multiple consequences. The purpose of this review is to highlight the most important evidence in the literature of host–microbiome interactions and illustrate how these intriguing relations may lead to new treatment and prevention strategies.

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Introduction

The term microbiota refers to an abundant and diverse population of microorganisms such as bacteria and fungi that reside on body sites, with the highest concentration of these organisms found in the gastrointestinal tract. Indeed, humans harbor a complex community of microorganisms that outnumber human cells by tenfold.¹

Standard culture techniques are limited to fully characterize microorganisms within the microbiota, but nowadays, modern molecular techniques termed metagenomics are available to allow deep characterization of the microbiota of the nasal mucosa, oropharynx, skin, urogenital sites, and

lower intestine. These methods rely on polymerase chain reaction amplification of 16S ribosomal RNA-encoding genes of the microbiota, followed by DNA sequencing.²

Projects such as the Human Microbiome Project³ have already done much to define the variability in the microbiota from different body sites and in the microbiomes both within the same human subject and among different subjects. By applying metagenomics, it is estimated that the human lower intestinal microbiota contains at least 1800 genera and 15,000–36,000 species, most of which have never been successfully cultured and the majority of them are classified within Firmicutes and Bacteroidetes phyla.⁴

The human intestinal microbiota matures over the first year of life and has substantial and continuous effects

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Table 1 – Reviews addressing diseases and biological phenomena related to human microbiome.

Topics	Effect of microbiota	Ref.
Inflammatory bowel diseases	In individuals with a genetic susceptibility to inflammatory bowel diseases, abnormal microbial colonization of the gastrointestinal tract might be the origin of such dysregulation.	8
Diabetes and obesity	Studies show the effect of gut microbiota on host metabolism by improving energy yield from food and modulating dietary or the host-derived compounds that alter host metabolic pathways.	9
Neuropsychiatric illness	Recent advances in our understanding of how the intestinal microbiota communicates with the brain via this axis to influence brain development and behavior. This extended communication system might influence a broad spectrum of diseases, including irritable bowel syndrome, psychiatric disorders, and demyelinating conditions such as multiple sclerosis.	10
Colorectal cancer	Potential mechanisms of bacterial oncogenesis are presented, focus is given to the oncogenic capabilities of enterotoxigenic <i>Bacteroides fragilis</i>	11
Asthma	Host's innate sensing systems, combined with recently developed methods that characterize commensal and pathogenic microbial exposure, now allow a unified theory for how microbes cause mucosal inflammation in asthma.	12
Rheumatic diseases	Microbiota may be involved in the pathogenesis of rheumatic diseases including altered epithelial and mucosal permeability, loss of immune tolerance to components of the indigenous microbiota, and trafficking of both activated immune cells and antigenic material to the joints.	13
Antibiotic resistance	Horizontal gene transfer in gut has the potential to influence the evolution of members of this microbial community and to mediate the spread of antibiotic resistance genes from commensal organisms to potential pathogens.	14

on human health and physiological development, including dietary and nutritional processing,⁵ prevention of pathogen invasion,⁶ and immune system maturation (Table 1).⁷

Changing in microbiota

Human behavior influences the composition of microbiota and its continuous changes may be responsible for the modification of the ancient microbiota. Some authors believe that diseases succeed and fail in response to mankind's advances. The appearance and disappearance of infectious and chronic diseases might be related to changes in human ecology, resulting in changes in the microbes that populate our bodies.¹⁵

Human civilizations experienced many transformations, as improvement in sanitization that was implemented to reduce transmission of infections. In order to provide food for an increasing population, food production incorporated new strategies, such as extensive use of pesticides, antibiotics, and hormones in animals and agriculture.^{15,16} The increasing antibiotic use in humans and farming is one of the most important fact that leads to a rapid and sometimes irreversible change on human microbiota.¹⁷

Helicobacter pylori is an example of an ancient human microbiota member that presented a dramatic change. *H. pylori* has been extensively investigated by Dr. Blaser et al. who observed that this bacterium was progressively disappearing during the twentieth century, from individuals in developed countries, with secondary alterations in gastric secretory, hormonal and immune physiology.¹⁸

This bacterium is thought to be related to peptic ulcer and gastric cancer but the sustained acidity in *H. pylori*-negative hosts increases the risk of gastroesophageal reflux disease and its consequences, including esophageal and gastric cardia adenocarcinomas.¹⁹

The stomach also produces adipokine hormones known as ghrelin and leptin, both with multiple roles in energy homeostasis. Patients under antibiotic treatment that eliminated *H. pylori* had increased circulating ghrelin levels.²⁰ There is a

hypothesis that in recent generations of children growing up in developed countries, there has been little gastric *H. pylori*-mediated regulation of those adipokines at the developmental stage, when long-term adiposity is being programmed. It is possible that the disappearance of *H. pylori* might be contributing to the current epidemics of early-life obesity, type 2 diabetes and related metabolic syndromes.

Gordon et al. were also interested in studying the relationship between obesity and microbiome. They analyzed fecal samples of lean and obese twins and observed that obesity was associated with phylum-level changes in the microbiota, reduced bacterial diversity and altered representation of bacterial genes, and metabolic pathways related to glycoside hydrolases.²¹ Cardiovascular risk also has influence on intestinal microbial metabolism, as shown by Hazen et al., who observed an increase in a proatherosclerotic metabolite, trimethylamine-N-oxide (TMAO), in healthy participants after the suppression of intestinal microbiota with oral broad-spectrum antibiotics.²²

Stimulation of the immune system is another important function of the microbiome where the disruption of immune homeostasis may be associated with inflammatory and atopic diseases.²³ Epidemiological studies show that *H. pylori*-positive individuals have lower risk of childhood asthma, allergic rhinitis and skin allergies than those without *H. pylori*.²⁴ *H. pylori*-positive stomach has a rich population of immune cells which regulates immune functions. Stomachs of *H. pylori*-negative hosts have much lower number of these cells, which have systemic, as well as local activities.²⁵ The increase in prevalence of immunological disorders (both of autoimmune and of atopic origin) in the developed world has been associated with changes in microbiome, which gave support to the hygiene hypothesis.²⁶

Microbiome and infectious diseases

The relationship between the microbiome and infectious diseases has yet to be determined. There is a lot of interest

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