Review

Medicine

A Narrative Review of the Gut Microbiota and Its Association with Diseases

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The gut microbiota is vast and diverse, and it is inextricably linked to and interacts with the host. Numerous diseases are associated with the gut microbiota of their occurrence, progression, and prognosis. The gut microbiota has an effect on the occurrence and progression of metabolic diseases through regulating the metabolism of carbohydrates, lipids, and amino acids. Disruptions in the intestinal flora can also contribute to inflammatory bowel disease and certain types of intestinal cancer. Additionally, illnesses of the neuropsychiatric, cardiovascular, and urinary systems, among others, are all associated with the gut microbiota. It is vital to understand the link between gut microbiota and disease in order to prevent, cure, and maintain good health.

Keywords: Gut Microbiota; Metabolic Diseases; Inflammatory Bowel Disease; Neuronal Dysfunction; Cardiovascular Diseases

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THE gastrointestinal system contains around 100 trillion microorganisms, including bacteria, viruses, fungus, and protozoa, and is regarded as a virtual organ of the body (1, 2). Over three million genes are encoded by the gut microbiome, the collective genomes of the microorganisms that live in the gut and create thousands of metabolites that influence the host's fitness, phenotype, and health (3, 4). A growing body of research indicates that the gut microbiota is intimately linked to human health and the emergence and progression of numerous diseases. Apart from influencing the microecology of the gut, these intestinal flora also influence other bodily systems, helping to maintain them at a particular level of normalcy. The impact of gut microbiota on many human body systems has been steadily uncovered. An imbalanced gut microbiota will result in different system dysfunctions, including those of the neurological and cardiovascular systems (5, 6), jeopardizing the body's health. This study examines the relationship between gut microbiota and human diseases with the goal of establishing a foundation for understanding the pathogenesis and treatment of gut microbiota and associated diseases.

Gut Microbiota and Metabolic Diseases

Studies have established that the gut microbiota plays a critical role in the onset and progression of metabolic disorders (7, 8). The gut microbiota interacts with the host to regulate the endocrine system, immunological response, and nervous system function, and dysbiosis results in the development of associated disorders.

Diabetes Mellitus

Diabetes mellitus (DM) is a metabolic disease that develops as a result of alterations in the gut microbiota, which are important in the regulation of the host's energy metabolism and immunological response (9-11). Diabetes patients' gut microbiota differs

from that of healthy controls, which has a degree of influence on patients with type 1 (T1DM) or type 2 diabetes (T2DM). Changes in the structure of the gut microbiota can trigger a moderate chronic inflammatory response in the body, resulting in the destruction and death of pancreatic cells and insulin resistance, hence encouraging the onset and progression of T2DM (12). Clinically, glucagon-like peptide-1 (GLP-1)-based medication is frequently used to regulate blood sugar in individuals with type 2 diabetes. In animal models, it has been shown that a certain species of ileal bacteria can suppress the GLP-1-activated gut-brain axis that regulates insulin secretion and stomach emptying (13). Certain gut microbes are involved in the therapeutic effects and adverse reactions of the anti-diabetic drug metformin, and many other clinical drugs for diabetes also increase the number of bacteria that produce short-chain fatty acids by adjusting the composition of the gut microbiota, thereby enhancing the hypoglycemic effect (14). A novel concept is fecal microbiota transplantation (FMT), which may be used in the future as a therapeutic option for diabetes mellitus (15). Animal studies (16, 17) have shown that restoring insulin resistance and defective islets in diabetic mice is possible.

Obesity

The gut microbiota can influence lipopolysaccharide content and short-chain fatty acid synthesis (18), and a prolonged high-sugar, high-fat diet can alter the organization of the gut microbiota (19). The gut microbiota plays a significant role in the onset and progression of obesity by boosting the generation of short-chain fatty acids, suppressing fasting-induced adipose factor (FIAF), modulating persistent moderate inflammatory responses, and limiting fatty acid oxidation (20). In obese individuals, the Firmicutes/Bacteroides ratios were greater, the Bacteroides ratios were lower, and the quantity of Bacteroides polymorpha, a glutamate-fermenting symbiont, was much lower than in lean persons, and was inversely linked with serum glutamate concentrations (21, 22). By controlling metabolism, the gut microbiota can influence human obesity, and this impact may be utilized to prevent and cure obesity. When the microbiota of obese mice was transplanted into normally raised mice to alter the recipient mice's gut microbiota and microbiome (23), and the recipient mice were then fed a high-fat diet, the recipient mice's liver metabolism was significantly altered (24), with decreased hepatic gluconeogenesis and glucose-6-phosphatase (G6Pase) activity (25). The microbiota of obese mice has an effect on the metabolism of normal mice, and gut microbiota transplantation from healthy individuals may help prevent and treat obesity (26). Thus, the gut microbiota produces a variety of metabolites such as short-chain fatty acids and lipopolysaccharides by regulating the metabolism of sugar, lipids, and amino acids or by interfering with the metabolism of normal substances, thereby contributing to the occurrence and development of metabolic diseases. Meanwhile, the bacterial structure and species composition of the gut microbiota are influenced by the body's metabolism, and their interaction complicates the relationship between gut microbiota and metabolic illnesses (**Figure 1**).

Gut Microbiota and Inflammatory Bowel Disease

Ulcerative colitis (UC) and Crohn's disease (CD) are the two most common clinical manifestations of inflammatory bowel disease (IBD). Although CD and UC patients are both high in lactobacilli and bifidobacteri, the Clostridium flexis group in these two diseases is dramatically reduced (27, 28), suggesting that probiotics should be administered cautiously in the acute phase of IBD patients. FMT may be utilized as a rescue therapy for refractory inflammatory bowel disease in the treatment of IBD. FMT alone is relatively safe and can have short-term effects in young patients with active inflammatory bowel disease (IBD) (29), although adverse events related with FMT and associated safety concerns have lately raised concerns (30). Additionally, FMT can help infants with allergic colitis by reestablishing their gut microbiota (31). The connection between the gut bacteria and the host is critical for the development of CD and UC (32, 33). As a result, in future IBD treatment trials, the treatment of gut flora will become a focal point (34). Meanwhile, the use of probiotics to treat inflammatory bowel disease is a priority, and has yielded promising results (35, 36).

Gut Microbiota and Nervous System and Psychiatric Diseases

Antibiotics, environmental and viral agents, enteric neurotransmitters/neuromodulators, cytokines, and sensory vagal fibers all communicate to the central nervous system (CNS) information regarding the gut's condition (37-41). By activating the hypothalamic-pituitary-adrenal (HPA) axis via sensory nerve fibers and CNS regulatory regions, sensory nerve fibers and CNS regulatory regions can impact the composition of the gut microbiota directly or indirectly via nutritional availability (42, 43). There is a distinct difference between the gut microbiota of schizophrenia patients and healthy individuals (44). Prevotellaceae are reduced in the intestinal tracts of patients with Parkinson's disease, and this difference can be used to make an initial diagnosis of Parkinson's disease (45). The diversity of gut microbiota has varying effects on the autonomic nervous system and central nervous system (CNS) via numerous routes such as the enteric nervous system (ENS) and vagus nerve, and also has an effect on the host's mental state (46, 47). Transplanting the fecal microbiota of depressed patients into rats with a depleted microbiota resulted in recipient animals developing behavioral and physiological characteristics of depression, including anhedonia, anxiety-like behavior, and altered tryptophan metabolism, demonstrating that the gut microbiota community can influence the host's mood (48, 49). Additionally, the gut microbiome plays a critical role in neurodevelopment (50). Emerging data suggests that the development of neurodegenerative disorders such as Alzheimer's disease is inextricably linked to the neuroinflammatory impact of the gut microbiota (51-53). Pain, whether acute or chronic, is a significant issue that has drawn attention to the possible role of gut bacteria in its onset and development (54, 55).

Gut Microbiota and Tumor

Recently, it has been discovered that the gut microbiota is critical for the occurrence, development, prognosis, and disease outcome of intestinal cancers (56-58). At the moment, colon and

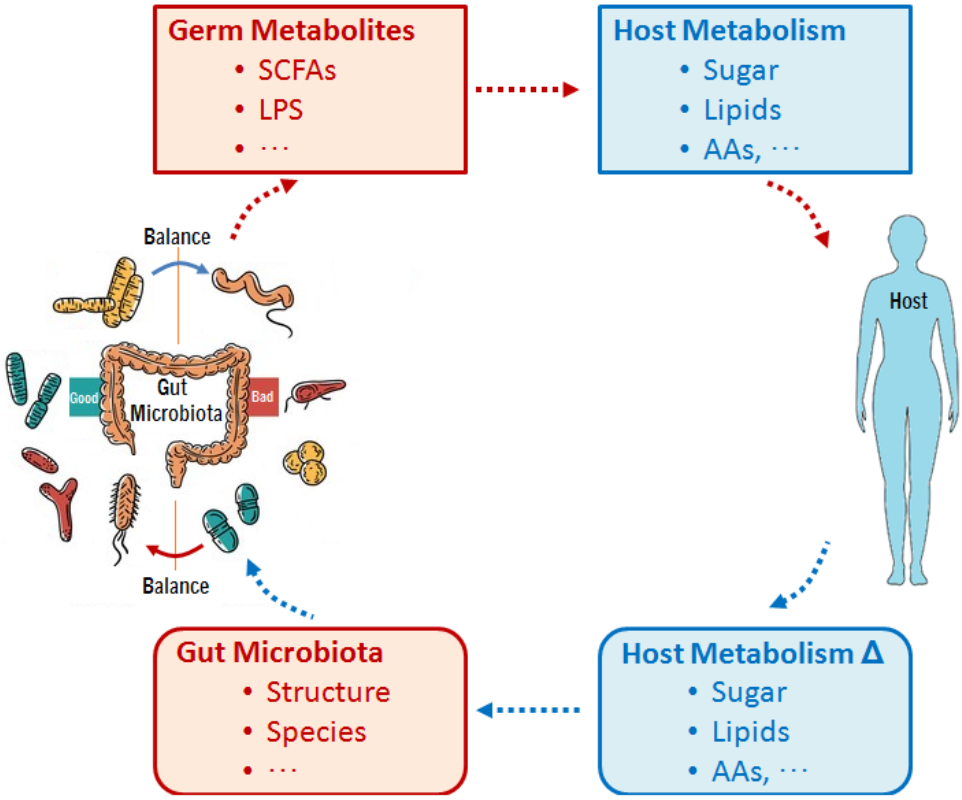

Figure 1. Interaction between Gut Microbiota and Host Metabolism.

rectal cancer staging and prognosis are largely determined by tumor node metastases (TNM) or the Duke System, a crude prognostic guideline that delays the discovery of advanced cancer and has a detrimental effect on the tumor's biological properties (59). The total metabolic profile of colonic mucosa was able to differentiate not only lesions from normal mucosa, but also the morphological and clinicopathological characteristics of colorectal cancer (60, 61), which is beneficial for colon tumor early detection and therapy. Apart from intestinal malignancies, gut microbiota can promote the occurrence and development of other types of tumors, including liver cancer (62), pancreatic cancer (63) and breast cancer (64), via metabolic pathways, hormone or brain-gut axis pathways, immunological pathways, and multifunctional pathways. Because disruption of the gut microbiota contributes significantly to the occurrence and development of cancers, may probiotic supplementation contribute to tumor prevention and treatment? Probiotics have been shown in studies to increase the amount and quality of gut microbiota (65), hence lowering chronic inflammation, the occurrence of sexual responses, and the formation of carcinogenic chemicals induced by gut microbiota dysregulation (66). Lactobacillus reuteri can enhance the activity of mitogen-activated protein kinase; inhibit the nuclear factor kappa B pathway; and promote tumor necrosis factor-induced death of myeloid leukemia cells in tumor treatment (67). These findings supported the use of probiotics in the treatment and prevention of cancers.

Gut Microbiota and Cardiovascular Disease

Gut microbes, like endocrine organs, produce biologically active metabolites via a variety of pathways, including trimethylamine/trimethylamine N-oxide, short-chain fatty acids, and primary and secondary bile acids (68, 69), affecting the host's physiological functions and thus playing a critical role in cardiovascular disease.

Hypertension

Investigating the gut microbiota of hypertensive individuals revealed that the intestinal flora was much less diverse than that of healthy individuals (70, 71), implying that gut microbiota may be associated with hypertension. The gut microbiota has been shown to create short-chain fatty acids via metabolism, so modulating the incidence of hypertension (72), and a high-fiber diet has been shown to alter the makeup of the gut microbiota and its metabolites, thereby lowering blood pressure (73). Of course, the underlying mechanism through which gut microbes contribute to hypertension remains unknown.

Heart Failure

Certain diseases and the gut microbiome interact in people with heart failure. In a study of the gut microbiota of patients with

chronic heart failure, it was discovered that patients with congestive heart failure have particular fundamental bacterial imbalances (74). Congestion of the splanchnic circulation, edema of the intestinal wall, and impaired intestinal barrier function all result in bacterial translocation and bacterial products entering the systemic circulation, aggravating the inflammatory response and promoting the progression of heart failure and atherosclerosis (75). The gut microbiota is intimately linked to the onset and progression of cardiovascular disease, or it may be exploited as a novel method of treating cardiovascular disease (76).

Gut Microbiota and Other Diseases

Apart from the disorders described above, gut microbiota is also strongly associated with the onset, development, and prognosis of a wide variety of other diseases in humans. When 16S ribosomal RNA gene sequencing was used to examine the relationship between the gut microbiome and kidney stones, it was discovered that the number of intestinal microbial species decreased in patients with multiple kidney stones (77), and that changes in microbial abundance affect potassium, sodium, and calcium levels in the blood, as well as chlorine and other trace elements, which provides new non-invasive biomarkers for the diagnosis of kidney stones and aids in the search for a way to prevent them (78). Liver illnesses such as alcoholic hepatitis, non-alcoholic fatty liver disease, and cirrhosis are also strongly associated with alterations in the gut microbiota (79, 80).

Concluding Remarks

The gut microbiome and human diseases are inextricably linked. The imbalance of the gut microbiota has a role in the onset and progression of a variety of systemic illnesses. With the advancement of the gut microbiota genome and related biological research, as well as the application of novel research tools, the mechanism by which gut microbiota contribute to the occurrence and progression of various diseases will become increasingly obvious. Utilizing the gut microbiota as a new target will result in a more safe and effective method of illness prevention and treatment, as well as fresh ideas for the development of several new medications, which is critical for the advancement of medicine.■

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