

GUT MICROBIOME AND DYSBIOSIS

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ABSTRACT

Dysbiosis refers to the disruption of the gut microbiota balance and is the pathological basis of various diseases. The main pathogenic mechanisms include impaired intestinal mucosal barrier function, inflammation activation, immune dysregulation, and metabolic abnormalities. These mechanisms involve dysfunctions in the gut–brain axis, gut–liver axis, and others to cause broader effects. Although the association between diseases caused by dysbiosis has been extensively studied, many questions remain regarding the specific pathogenic mechanisms and treatment strategies. This review begins by examining the causes of gut microbiota dysbiosis and summarizes the potential mechanisms of representative diseases caused by microbiota imbalance. It integrates clinical evidence to explore preventive and therapeutic strategies targeting gut microbiota dysregulation, emphasizing the importance of understanding gut microbiota dysbiosis. Finally, we summarized the development of artificial intelligence (AI) in the gut microbiota research and suggested that it will play a critical role in future studies on gut dysbiosis. The research combining multiomics technologies and AI will further uncover the complex mechanisms of gut microbiota dysbiosis. It will drive the development of personalized treatment strategies.

KEY WORDS:

gut microbiota, dysbiosis, disease, precision medicine

INTRODUCTION

The human gut serves an anaerobic bioreactor, hosting a wide variety of microorganisms, including bacteria, fungi, archaea, protozoa, and viruses and others, which are collectively termed the microbiota. They occupy different ecological niches on the mucosal surface of the gastrointestinal (GI) tract. The microorganisms in the gut make up most of the human microbiome, including at least 1000 different species of bacteria and approximately 150 times the number of genes in the human genome. The coevolution between the human host and microorganisms has established a mutually beneficial symbiotic relationship. The immense genetic and metabolic potential of the gut microbiota makes it nearly ubiquitous. The host provides a suitable environment and nutrients for the microbiota, while the microbiota plays a significant role in the host's homeostasis and disease.

DEFINITION

GUT MICROBE

The bacteria and other microbes that live in your gut are known as your “gut microbiome.” They help you digest food and may support immune, heart, and brain health

DYSBIOSIS

Dysbiosis means that having an imbalance in the different types of microscopic organisms living in our body is known as dysbiosis

ETIOLOGY OF DYSBIOSIS

Dysbiosis can be triggered by various infectious agents and environmental factors. For instance, gastrointestinal infections caused by bacteria, viruses, or parasites can disrupt the normal microbial balance. Antibiotic use is another significant factor; while antibiotics are effective in treating infections, they can also kill beneficial bacteria, leading to dysbiosis. Environmental factors such as pollution, exposure to chemicals, and changes in diet can also contribute to microbial imbalances

PATHOPHYSIOLOGY OF GUT MICROBIOTA DYSBIOSIS

- Bacterial dysbiosis in your gut is directly involved in various gastrointestinal (GI) diseases affecting your digestive system, including:
 - Small intestinal bacterial overgrowth (SIBO).
 - Inflammatory bowel diseases, like ulcerative colitis and Crohn's disease
 - Nervous system.
- Gut dysbiosis may be indirectly involved in a variety of other conditions, including:
 - Malnutrition.
 - Malabsorption.
 - Food intolerances.
 - Irritable bowel syndrome (IBS)
 - Fatty liver disease.
 - Metabolic syndrome.
 - Chronic inflammation.
 - Chronic fatigue

DISEASE ASSOCIATED WITH GUT MICROBIOTA AND DYSBIOSIS

GI DISEASES

IBD is a group of heterogeneous chronic inflammatory diseases caused by the interaction of genetic factors, environmental factors, and the gut microbiota. IBD typically including UC and CD. Under healthy physiological conditions, symbiotic microorganisms produce beneficial metabolic products that help maintain an impermeable barrier composed of intact mucosa and epithelium. When genetic/immune driving factors, environmental triggers, and lifestyle/dietary changes lead to the onset of a predisease stage, some symbiotic microorganisms transform into pathogenic bacteria that are better adapted to the ecological niche of the ecosystem. As the disease progresses, IBD patients exhibit active inflammatory mucosal damage. The massive emergence and proliferate of pathogenic bacteria lead to the quantity of symbiotic bacteria significantly decrease and a sharp reduction in beneficial metabolites with persistent inflammatory infiltration. Persistent inflammation and long-term dysbiosis cause immune imbalance and impaired mucosal healing, thereby sustaining inflammation and dysbiosis in a chronic cycle. The intestinal barrier is mainly composed of digestive fluids, symbiotic bacteria, antimicrobial peptides, epithelial cells, and local immune cells. In the case of harmful GI bacteria or related toxins, antigens, and so on break through the barrier and translocate. After being phagocytosed by immune cells, many lipopolysaccharides (LPS) have been released to guide chronic inflammation. At the same time, gut microbiota dysbiosis leads to an imbalance in microbial metabolites, the secretion of inflammation-related cytokines.

METOBOLIC DISEASE

Unhealthy lifestyles have always been the main risk factors for metabolic diseases. The metabolic and immune potential of the gut microbiota determines its importance for host health and disease. Gut microbiota influences the host's energy balance, insulin sensitivity, and fat accumulation through its metabolic products. At the same time, gut microbiota dysbiosis may also exacerbate the symptoms or promote the progression of metabolic.



FIG :1 METABOLIC DISORDES OF GUT MICROBIOTA

THE GUT BRAIN AXIS

Gut brain axis is a communication system that integrates neural, hormonal, and immunological signalling between the gut and the brain, offering the intestinal microbiota and its metabolites a potential route through which to access the brain. This communication system is bidirectional, which enables the brain to command gastrointestinal functions, such as peristalsis and mucin production, and immune functions. Significant progress has been made over the past decade in recognizing the important ways in which gut microbiota relate to brain function. Foster and McVey Neufeld have reviewed key findings, showing that stress influences the composition of the gut microbiota and that bidirectional communication between the gut microbiota and the central nervous system influences a host's stress reactivity. Stress has been shown to influence the integrity of the gut epithelium and to alter peristalsis, secretions, and mucin production, thereby altering the habitat of the intestinal microbiota and promoting changes in microbial composition and/or metabolism

FUNCTIONS OF GUT MICROBIOTA

METABOLISM

As the gut microbiota encode a substantively larger number of genes than its human host, it follows that they can undertake a variety of metabolic functions that humans are unable to do or are only able to do in a limited capacity. The gut bacteria are able to produce a variety of vitamins, synthesize all essential and nonessential amino acids, and carry out biotransformation of bile. In addition, the microbiome provides the vital biochemical pathways for the metabolism of nondigestible carbohydrates, which include large polysaccharides, such as resistant starches, cellulose, hemicellulose, pectins, and gums; some oligosaccharides that escape digestion; unabsorbed sugars and alcohols from the diet and host-derived mucins. This functionality results in the recovery of energy and absorbable substrates for the host and a supply of energy and nutrients for bacterial growth and proliferation. Metabolism of carbohydrates is a major source of energy in the colon.

DEVELOPMENT AND COMPOSITION

Microbial colonization of the human gut begins at birth. The infant's intestines are believed to be sterile or contain a very low level of microbes at birth, but the GIT is quickly colonized during and after delivery. As a neonate passes through the birth canal, he or she is exposed to the microbial population of the mother's vagina. This process influences the development of an infant's intestinal microbiota, which show similarities to the vaginal microbiota of his or her mother. Infants who were delivered through cesarean section showed reduced microbial numbers in the gut at 1 month when compared with those who were delivered vaginally, although these differences do not remain at 6 months of age.

During the first year of life, the composition of the gut microbiota is relatively simple and shows wide interindividual variations. It is believed that the initial gut colonization is instrumental in shaping the composition of the adult's gut microbiota. This fact was demonstrated by Ley et al, who showed that the gut microbiota of their study's mice was closely related to that of their mothers, implicating kinship as a factor in the determination of the composition of the gut microbiota.

The infant's gut microbiota undergoes a succession of changes that are correlated with a shift in feeding mode from breast- or formula-feeding to weaning and the introduction of solid food. Despite the relative similarities of the gut microbiota in mothers and their offspring, microbial succession in the GIT is also influenced by numerous external and internal, host-related factors. External factors include the microbial load of the immediate environment, type of food eaten, and feeding habits, in addition to the composition of the maternal microbiota. Also, dietary and temperature-related stresses can influence the succession of microbes. Internal factors include, but are not limited to, intestinal pH; microbial interactions; environmental temperature; physiological factors, such as peristalsis; bile acids; host secretions and immune responses; drug therapy; and bacterial mucosal receptors.

PATHOGENESIS OF GUT MICROBIOTA DYSBIOSIS

The human gut microbiome is a complex ecosystem, densely colonized by thousands of microbial species. It varies between individuals and is constantly influenced by host genetic and environmental factors, which affect the composition and functional profile. The diversity, metabolic flexibility, functional coordination, and interactions among microbes—microbes and microbes—host in the gut microbiota are crucial for maintaining healthy homeostasis. Due to the combination of natural variations and stress factors can lead to a series of unstable changes, the potential mechanisms of gut microbiota dysbiosis remain unclear. This section will explore the main factors that lead to gut microbiota dysbiosis and analyze the potential mechanisms by which

dysbiosis induces disease, with a focus on the roles of microbial metabolite imbalance, impaired intestinal barrier function, and immune system dysregulation

MECHANISM OF ACTION OF DISEASES

The homeostasis of the gut microbiota plays a crucial role in maintaining normal human health and has a wide range of effects. When the body experiences gut microbiota dysbiosis, it may increase the likelihood of various diseases such as GI disorders, neurological diseases, and metabolic conditions. It has been found that gut microbiota dysbiosis may increase the likelihood of disease development through mechanisms such as microbial metabolic imbalance, impaired gut barrier function, and immune dysregulation

Mechanisms of dysbiosis-induced disease

Disease type	Mechanisms related to dysbiosis	
Gastrointestinal diseases		
IBD	Gut microbiota dysbiosis and abnormal bile acid metabolism	
IBS	Microbial metabolites impair insulin sensitivity	
UC	Sphingolipid metabolism disorders	
CRC	Abnormal bile acid metabolism, especially taurodeoxycholic acid (DCA), and intestinal barrier disruption	
AD	Bile acid metabolism disorders	
AD	Bacteroides fragilis activates microglia and stimulates immune responses	
Metabolic disease		
T2DM	Gut microbiota abundance and bile acid metabolism	
T2DM2	Impaired intestinal barrier integrity and host-microbiome interactions	
NAFLD	Microbiome-derived ethanol promotes NFLD	
NAFLD,	Gut microbiota regulates peripheral immune responses cell cancer	
NAFLD2	The metabolic function of the intestinal flora changes, Bacteroidetes is independently associated with NASH, while Ruminococcus is associated with severe fibrosis	
Obesity	Intestinal microbes degrade inositol and promote lipid absorption	
Obesity	Enterotype-like microbiota Megamonas degrades inositol and promotes lipid absorption	
Obesity	Absence of Tlr9 in B cells causes disturbance of intestinal flora	
Other		
CSU	Low-diversity gut microbiota reduces short-chain fatty acid production and increases lipopolysaccharide levels, promoting mast cell-driven skin inflammation	
Allergic disease	Dysbiosis promotes immune response	
Atopic dermatitis	Arachidonic acid-induced intestinal flora imbalance in infants	
Mastitis	Modulates inflammatory processes and regulates blood-milk barrier permeability	
Mastitis	Gut microbiota dysbiosis leads to endotoxemia, thereby reducing host anti-inflammatory enzyme activity	
Hypertension	Overgrowth of bacteria such as Prevotella and Klebsiella	

CLINICAL MANIFESTATION

- Dysbiosis causes in mouth, on skin, on intestine, on urinary system. If have any sings and symptoms of bacterial, viral, fungal infections. these might include:
- Bleeding gum, tooth decay, cavities
- Atopic dermatitis or acne
- Bloating, gas and poop changes
- Painful urination, genital discharge and itching
- The microbiome can also affect gut health and may play a role in intestinal diseases like irritable bowel syndrome (IBS)Trusted Source and inflammatory bowel disease (IBD)
- The bloating, cramps and abdominal pain that people with IBS experience may be due to changes in the gut microbiome. This is because the microbes produce a lot of gas and other chemicals, which contribute to the symptoms of intestinal discomfort

RISK FACTORS

- The gut microbiome may affect brain health in several ways. Certain species of bacteria can help produce chemicals called neurotransmitters.
- Additionally, your gut is connected to your brain through millions of nerves. particularly the vagus nerve. The communication between the gut and the brain is known as the gut-brain axis.
- Age: The composition of the microbiome changes with age, and older adults may be more susceptible to dysbiosis.
- Gender: Some studies suggest that women may be more prone to dysbiosis due to hormonal fluctuations.

DIAGNOSIS

The diagnosis of dysbiosis typically begins with a thorough clinical evaluation. Healthcare providers will take a detailed patient history, including dietary habits, lifestyle factors, and any previous medical conditions. A physical examination may also be conducted to assess overall health

DIAGGOSIS TEST

Several diagnostic tests can help identify dysbiosis:

- Stool Tests: These tests analyze the composition of gut bacteria and can identify imbalances.
- Blood Tests: Blood tests may be used to check for inflammation or other markers of dysbiosis.
- Imaging Studies: In some cases, imaging studies like X-rays or CT scans may be necessary to rule out other conditions

TREATMENT

- Treatment for dysbiosis depends on the cause. if an underlying disease or condition causes it will need some specific treatment for that condition. If any environmental or lifestyle factors contribute to dysbiosis
- Environmental or lifestyle changes can usually benefit with dysbiosis regardless of other cause involved
- If you have an infection or overgrowth, your healthcare provider might need to target it directly with antibiotics, antivirals or antifungal

Treatment for dysbiosis often involves addressing the underlying causes and restoring balance to the microbiome. Medical treatments may include:

- Antibiotics: In cases where harmful bacteria are overgrown, antibiotics may be prescribed.
- Probiotics: These beneficial bacteria can help restore balance in the gut.
- Prebiotics: These are non-digestible fibers that promote the growth of beneficial bacteria

NON-PHARMACOLOGICAL TREATMENTS

In addition to medical treatments, lifestyle modifications and dietary changes can significantly impact dysbiosis:

- Dietary Changes: A diet rich in fiber, fruits, vegetables, and fermented foods can support a healthy microbiome.
- Stress Management: Techniques such as yoga, meditation, and mindfulness can help reduce stress, which may positively affect gut health.
- Regular Exercise: Physical activity has been shown to promote a healthy microbiome.

CONCLUSION

The gut microbiota in humans evolve throughout life and appear to play a pivotal role in both health and disease. In a healthy state, the gut microbiota has myriad positive functions, including energy recovery from metabolism of nondigestible components of foods, protection of a host from pathogenic invasion, and modulation of the immune system. A dysbiotic state of the gut microbiota is becoming recognized as an environmental factor that interacts with a host's metabolism and has a role in pathological conditions, both systemic—obesity, diabetes, and atopy—and gut-related IBS and IBD, although the specific contribution of the gut microbiota to these diseases is unclear. The heterogeneous etiology of metabolic and gastrointestinal diseases has been associated with different microbes, although little information exists about the causal direction of the association.

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