Review Article

Role of Gut Microbiome in Chronic Diseases

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ABSTRACT

Gut microbiota (GM) dysbiosis has adverse health effects on the human body, leading to various chronic diseases. The underlying mechanisms of GM on human diseases are incredibly complicated. Whether these relations underlie causal effects in humans remains to be established. In the last two decades, considerable interest has been shown in understanding the development of the gut microbiota and its internal and external effects on the intestine, as well as the risk factors for cardiovascular diseases (CVDs) such as metabolic syndrome. The intestinal microbiota plays a pivotal role in human health and disease. Recent studies revealed that the gut microbiota can affect the host body. The realization of this latter action of the microbiota has altered the concept of pharmaceutical-microbiota interactions, shifting the influencer role from medicines to an appreciation of microbiome-medicine interplay. This review systematically summarizes the effect of gut microbiota and their bacterial metabolites on the development of chronic diseases. An imbalance in gut microbiota can also increase susceptibility to diseases.

Keywords: Homeostatic imbalance, xenobiotic, drug pharmacokinetics, drug metabolizing enzymes, IBS, microbial dysbiosis, and atherosclerosis.

INTRODUCTION

Gut health

The human intestinal microbiota of healthy adults contains more than 5% of the total bacterial population, with *Faecalibacterium prausnitzii* being the most abundant bacterium. The importance of this highly metabolically active commensal bacterium as a component of the healthy human microbiota has been increasingly described in numerous studies over the past five years. Several human disorders have been associated with dysbiosis linked to changes in the abundance of F. prausnitzii.[1]

The strain Bifidobacterium longum 35624® is derived from a healthy human's gut epithelium and can survive the journey through the gastrointestinal tract. It possesses specific genetic traits, one of which results in the production of a distinct exopolysaccharide. Clinical trials have demonstrated the effectiveness of this strain (compared to a placebo) in easing the common symptoms (abdominal pain, bloating, gas passage, and bowel irregularities) in IBS patients.[5]

Gut microbiome

The human gut microbiome, comprising up to 100 trillion microbes (microbiota) and their genomes functions symbiotically with the host superorganism it inhabits. These unique populations of bacteria, viruses and fungi are crucial not only for the innate maintenance of health, but also in processing exogenous compounds (medicines) intended to rectify homeostatic imbalances. The realization of this latter action of the microbiota has altered the concept of pharmaceutical-microbiota interactions, shifting the influencer role from medicines to an appreciation of microbiome-medicine interplay. The microbiota, and in particular microbiome-encoded enzymes, now represent plausible intermediate targets to alter drug pharmacokinetics (absorption, distribution, metabolism and elimination) to consequently enhance clinical response and vice versa. This movement also produces organic or toxic metabolite to disclose microbiota is temporarily convenient. This is an attractive prospect that this is an improvement during work in microbiomes patient clinical outcomes will be discussed in relation to the current literature.[2]

Drug metabolism involves enzyme-catalyzed biochemical processes that convert lipophilic drugs into more polar and easier-to-excrete metabolites, leading to the termination or alteration of the drug's biological activity. Drug-metabolizing enzymes are abundant in the liver and play an important role in xenobiotic metabolism.

Microbiome

The collective genome of gut microbiota is termed microbiome and is approximately 100 times the number of genes compared to the human genome (Gill et al., 2006). Furthermore, recent estimates suggest that the number of cells in the human body (3*10) is comparable to the number of bacterial cells (3.8*10), with the total mass of bacterial cells being approximately 0.2 kg. Research on the metabolic capabilities of gut bacteria is expanding regarding their impact on health, medicinal properties and toxicity. The microbiota, co-evolving with the host, is now considered as a virtual organ with properties that are valuable for integrating with the host physiology. The US National Health Page understood Initiative and human

microbial projects. Gamma, microbiomes, and all aspects that affect human genetic and physiological differentiation Distribution of conversion of microorganisms in the body. It also includes research on related microbias.For human health and illness. Another important European Union project on metagenomics of the human gut (MetaHIT) targets the gut microbiota and associated microbial metabolic activities in human health.[1]

The difference between the composition and the function of the intestinal microbiome is linked. Various chronic diseases, gastroenteric inflammation, and Metabolism conditions for neurological, cardiovascular disease, respiratory disease. The purpose of the review of this story is to explain the relationship between the composition of microbial flora and various kinds of chronic diseases. It is associated with meals and regular food ingredients.[2]

Background

The development of gut microbiome research:

In the past 10 years, we have witnessed an exciting discovery that connects the configuration and functions of human intestinal microorganisms to the public diseases and expression types. For the research of the association changes in documents of various abundance intestinal bacteria for people with gastrointestinal tract expressive type containing inflammatory bowel disease, irritable bowel syndrome and colon rectal cancer, and including other systems and organ diseases like Cardiovascular, metabolic status, automatic immunity and mental disorders. In addition to the analysis of the association, intervention research and research on animals are not only proven, not only relevance, but also causal relationships of intestinal micro-biome due to several diseases. Influence of internal and external factors the composition of the intestinal microorganisms increases. Eases.[3]

Childhood obesity is recognized as one of the most serious global health problems in modern society. Assuming that the number of infants is about 43 million, the incidence and prevalence of obesity are equal to the prevalence of obesity. Over the past two decades, the proportion of people with cobblestones has increased, from 6.7% in 2010.Obese children are more likely to be obese as adults, increasing their risk of early death and future health problems.

Over the past decade, emerging evidence from animal and human studies has revealed links between our gut bacteria (collectively known as the gut microbiota) and host metabolism and obesity. Infancy is a critical period in the development of com-Mensal intestinal bacteria with a gradual increase in colonization with Bacteroidetes Philo over time1, † 1, † 1,2,3, return to the top birth. On the initial colonization, especially with members of this philomel, depends on a few early. Life influences, including birth regime, food for babies and the use of antibiotics. The introduction and increased use of next-generation sequencing and metabolomics technologies have increased our ability to study the development of the gut microbiota, its metabolic functions, and its relationship to later health outcomes during this important early period of life.[4]

Incidence and Prevalence of chronic diseases and alteration of gut microbiome

Urbanization-related increases in the prevalence of chronic diseases are linked to abnormalities in the gut microbiome's makeup. Based on 16S rRNA sequences, the decline in microbial diversity only suggested an imbalanced gut ecology; it did not give us additional specific details regarding strains (species) or specific microbial roles. In general, there are also insufficient functional investigations. We suggest that a targeted and innovative framework for the fine-scale investigation of particular roles of gut microbiomes in the pathophysiology of chronic diseases during urbanization is required, as lowering the prevalence of chronic diseases and ensuring the health of inhabitants are essential for economic and social development.

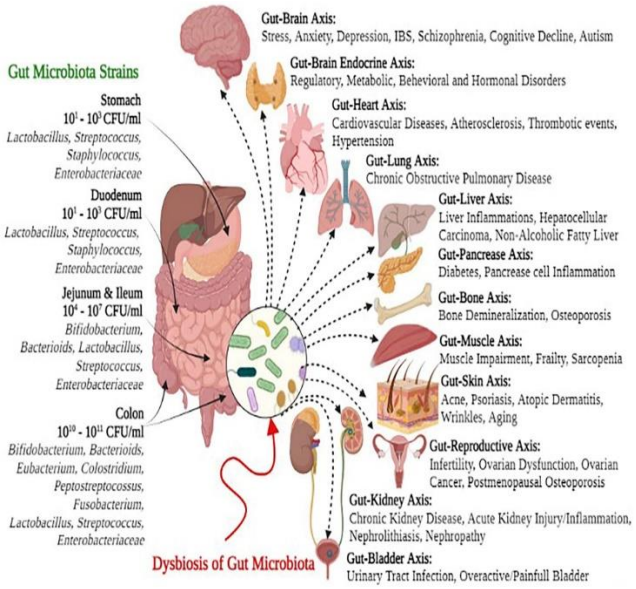

Figure 1: Human gut microbiota in health and disease

Gut microbe-gut inflammation/bowel disorders

Irritable bowel syndrome (IBS)

Irritable bowel syndrome (IBS) typically involves abdominal pain, discomfort, and changes in bowel habits. While the exact cause is complex, recent insights into the underlying mechanisms of IBS suggest that disruptions in the usual gut microbiota may contribute to the mild intestinal inflammation linked to the condition. The family Enterobacteriaceae includes various pathogenic bacteria, such as Escherichia, Shigella, Campylobacter, and Salmonella as shown in Fig 2. The by-products produced by these potentially harmful bacteria have been linked to several typical symptoms of IBS, such as abdominal pain, bloating, and diarrhea.[2]

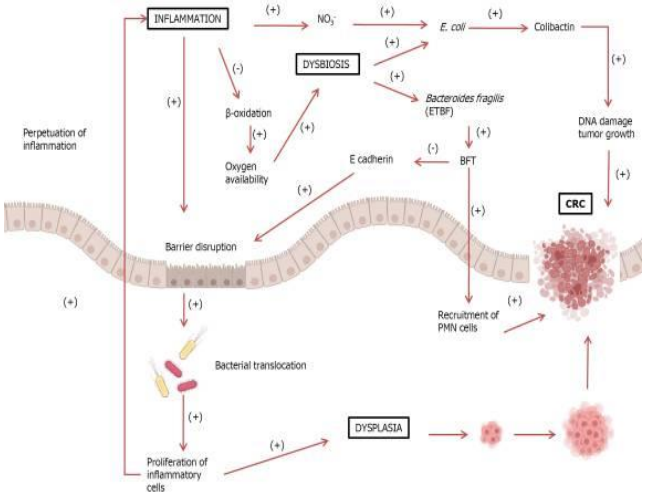

Figure 2[7]: Enterobacteriaceae pathogens drive inflammation, dysbiosis, and colorectal cancer progression.

The disruption of the intestinal barrier due to an increased inflammatory response can allow bacteria to move into the intestinal lumen. These bacteria then trigger an immune and inflammatory response, which perpetuates the inflammation. Inflammatory cells can also lead to dysplasia, contributing to the development of colorectal cancer (CRC).

Under normal circumstances, epithelial cells create an anaerobic environment by reducing oxygen availability during β-oxidation. However, during chronic inflammation, β-oxidation decreases, increasing oxygen availability. This change also results in the formation of nitrate (NO^{3-}), promoting dysbiosis and the growth of proteobacteria like *Escherichia coli* (E. coli). E. coli produces colibactin, which has the potential to damage DNA and encourage tumor growth. Additionally, the growth of Bacteroidetes fragilis may occur, leading to the production of Bacteroides fragilis toxin (BFT). This toxin breaks down E-cadherin, a key component of the zonula adheres responsible for cell adhesion, further disrupting the barrier. Furthermore, BFT stimulates epithelial cells to recruit polymorphonuclear leukocytes (PMN) cells, which promotes the development of CRC.

Altered bacterial metabolites can be further affected by dysbiosis; a reduction in butyrate-producing bacteria such as F. prausnitzii has been linked to a decreased concentration of SCFAs in both patients with IBD and in animal models of intestinal inflammation. The diminished levels of SCFAs can impact the differentiation and expansion of Treg cells as well as the growth of epithelial cells, ultimately resulting in the disruption of intestinal homeostasis.

Several researchers have noted a relative rise in Proteobacteria, particularly *Escherichia coli* (E. coli), in patients with inflammatory bowel disease (IBD). The precise mechanisms that increase Proteobacteria during inflammation are not fully understood; however, Rizzatti et al., suggested two mechanisms: The oxygen hypothesis and the presence of nitrate. In a healthy colon, epithelial cells use beta oxidation to deplete oxygen in the lumen, creating an anaerobic environment. Conversely, during an inflammatory episode, the beta-oxidation capacity of colonic cells decreases, leading to increased oxygen availability, which in turn promotes dysbiosis and the growth of Proteobacteria. Nitrate produced as a by-product during the inflammatory process provided a growth advantage to the commensal bacteria E. coli in the large intestine, allowing it to become the predominant species.[5]

Gut microbiome and autoimmune disease

Autoimmune diseases (AIDs) develop due to a combination of genetic predisposition and environmental influences, with a particular focus on the impact of disrupted gut microbiota. Various autoimmune diseases have been linked to alterations in the composition and function of gut microbiota, and there is growing evidence indicating that imbalanced gut microbiota plays a role in their immune-related development.[2]

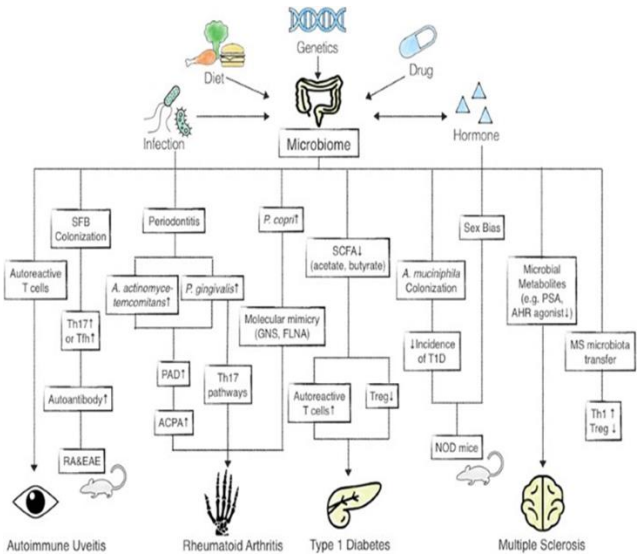

Figure 3: Factors influencing the gut microbiome

Rheumatoid arthritis (RA)

Rheumatoid arthritis (RA) is a systemic autoimmune inflammatory disease that causes joint damage. Recent research has shown that various environmental factors contribute to the development of intestinal/oral dysbiosis and the onset and progression of arthritis. These factors include diet, smoking, and infections. Studies have found that germ-free mice are shielded from developing experimental arthritis, indicating a potential involvement of the microbiome in the disease's pathogenesis Rheumatoid arthritis.[2]

The gut microbiota can control not just the immune system in the intestines, but also to significantly impact immune responses throughout the body.[7] Deficient development of the GALT and abnormal systemic and central immunity result from a lack of gut microbiota.[5]

Chronic kidney disease

Chronic kidney disease (CKD) is a widespread public health issue that impacts around 10% of the population. The "Microbiome-centric theory of CKD progression" suggests that initial adjustments in the gut microbiome may become problematic in the later stages of CKD, leading to complications associated with the disease. The dysbiosis observed in CKD patients is increasingly seen as a potential target for treatment, although the field is still in its early stages. This review will explore recent developments in the study of the gut microbiome and its potential to transform the management of CKD-related complications. [8]

Higher concentrations of urea in the blood are a result of progressive renal failure. When intestinal bacteria are exposed to urea through GI secretions, they convert urea to ammonia via bacterial urease. This elevated urea concentration leads to the overgrowth of bacterial families containing urease. Patients with end-stage renal disease (ESRD) compared with healthy controls experience an expansion of bacterial families producing uricase and indole- and p-cresyl-forming enzymes. It is intriguing to consider how changes in appetite due to renal failure may impact the consumption of foods that can alter the microbiome. Reductions in resistant starch content associated with changes in appetite could contribute to the acceleration of chronic kidney disease (CKD) progression. Notably, research has shown that a high-salt diet can impact the gut microbiome in ways that may interact with the progression of CKD. Mice fed a high-salt diet have been reported to experience decreases in several species of bacteria, including those of the genus Lactobacillus. Additionally, a high-salt diet has been found to alter the frequency of Th17 lymphocytes, which could be improved by reintroducing Lactobacillus species.[8]

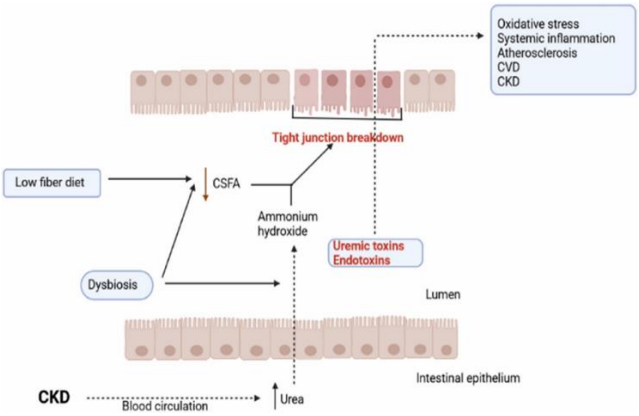

Figure 4: The role of gut microbes in chronic kidney disease

Intestinal microbials is related to human health. Microbial colony formation occurs with the maturity of the immune system, fig. 1. Blood urea levels increase and urea influx into the intestinal lumen in patients with CKD. Dysbiosis of the gut microbiota increases the number of certain urease-containing bacteria, and urease activity is increased by ammonium hydroxide. In contrast, the low-fiber diet of these patients reduces the production of SCFAs by gut bacteria, which are nutrients for colonocytes. When the amount of short-chain fatty acids decreases with increasing ammonium hydroxide and the intestinal epithelial barrier (tight junctions) is damaged, uremic toxins and bacterial derivatives such as endotoxins can penetrate through the damaged epithelium and enter the circulation, causing inflammation and oxidative processes such as cardiovascular disease and CKD. Short-chain fatty acids. Cardiovascular disease: cardiovascular disease; CKD: chronic kidney disease.[9]

The host endocrine system is influenced by gut microbial metabolites, such as SCFAs produced through the fermentation of dietary fiber. For instance, propionate, an SCFA, induces the release of glucagon-like peptide 1 (GLP1) and the gut hormone peptide YY (PYY) from primary intestinal cultures of mice through a mechanism dependent on the free fatty acid receptor 2 (FFAR2).[11] Dialysis patients exhibit chronic inflammation throughout their entire gastrointestinal tract, from the esophagus to the colon. The low phosphorus and low potassium dietary restrictions in CKD patients lead to inadequate intake of vegetable fiber and beneficial bacteria, while also causing urea to enter the gut from the bloodstream. This changes the composition of the gut microbiota and encourages the proliferation of a bacterial community that generates uremic toxins like p-Cresyl and indoxyl-sulfates. Bacteria with urease enzyme break down urea into ammonia, and convert it into ammonium hydroxide (NH4OH), which then breaks down tight junction proteins. In a study involving rats with CKD, significant decreases in claudin, occluding, and zona-occludent (important molecules for epithelial tight junctions) were observed in the intestinal tissue [9]

Mental health disorder

The gut–brain axis (GBA) facilitates communication between the central nervous system (CNS) and the human GI tract, involving neuronal, endocrine, and immunological mechanisms in a two-way connection. The gut is often referred to as the “second brain” due to its housing of the enteric nervous system (ENS), a neural network enabling the gut to function independently from the brain.

Previously, functional gastrointestinal disorders (FGIDs) were viewed as purely functional disorders without scientific confirmation of a clear pathogenetic mechanism. According to Rome IV, the phenotype of FGIDs arises from an altered transmission of nerve and biochemical signals within the gut microbiome–brain axis, influenced by both genetic and environmental factors. As a result, FGIDs have recently been renamed as disorders of gut–brain interactions. There is documented overlap between disorders of gut-brain interactions and central nervous system disorders, and it has been shown that about one-third of IBS patients experience depression.[10]

In cases of depression, the phyla most impacted are Firmicutes, Actinobacteria, and Bacteroidetes, with a notable rise in the Bacteroidetes/Firmicutes ratio among MDD patients. This is characterized by an abundance of the Bacteroides genus and a scarcity of the Blautia,

Faecalibacterium, and Coprococcus genera. Patients with MDD also consistently exhibited an increase in Eggerthella and a decrease in Sutterella.[11] The latest findings indicate that the gut microbiota (GM) has the potential to influence the brain and contribute to these conditions.[12]

Early Evidence of Association of Gut Microbiota and Mental Health

Researchers have speculated about the impact of gut microbiota on the mental health and behavior of individuals after discovering the connection between microbiota, the gut, and the brain. A previous study on rodents that were germ-free (GF) - meaning they had no exposure to microorganisms - showed that they had learning deficiencies and experienced impacts on anxiety behavior and sociability. A preclinical study on healthy mice that had undergone vagotomy and were given *Lactobacillus rhamnosus* demonstrated the role of microbiota in modulating the neurochemical behavior of the brain. The administration of L. rhamnosus (JB-1) was found to modulate the GABAergic system in mice, resulting in beneficial effects on mental health by reducing depression-related and anxiety-like behavior. Furthermore, changes in the levels of gut microbial metabolites, such as SCFAs, SBAs, D-lactate, ammonia, tryptophan, and histamine, have been directly associated with various neurological conditions like Parkinson's disease (PD), Anorexia Nervosa (AN), Alzheimer's disease (AD), autism spectrum disorder (ASD), chronic stress, and depression. Additionally, these metabolites can break down into neuroactive catabolites, for example, tryptophan breaks down along the kynurenine pathway to produce many catabolites that are neuroactive.

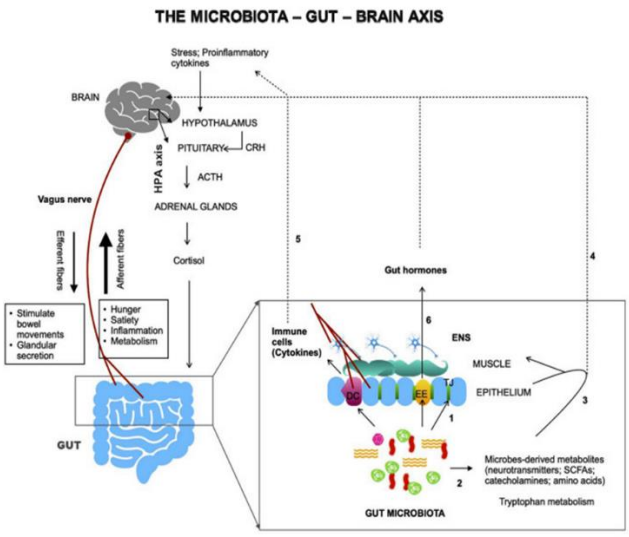

Figure 5: The Microbiota-Gut-Brain Axis

The gut-brain axis is a two-way communication network involving the neural pathway (vagus nerve, enteric nervous system), the immune pathway (cytokines), and the endocrine pathway (HPA axis, gut hormones). Gut microbiota influences this axis through various direct and indirect mechanisms (1–6, as outlined in the passage). HPA stands for hypothalamic–pituitary–adrenal axis, while EE refers to enteroendocrine cells, DC to dendritic cells, TJ to tight junctions, and SCFAs to short chain fatty acids. Solid arrows represent local interactions, and dashed arrows indicate interactions via circulation.[13]

Cardiovascular disease

Several researchers have documented a connection between CVD characteristics and variations in the prevalence of microbial taxa, as well as gut bacterial richness or diversity. Initially, bacterial DNA was identified in atherosclerotic plaques with patterns that correspond to taxa linked to disease conditions. Additionally, alterations in microbial composition have been observed in individuals with various CVD risk factors such as hypertension, dyslipidemia, insulin resistance, and other metabolic characteristics.[14]

Hypertension

High blood pressure is a common contributor to cardiovascular diseases globally. The initial indication of the involvement of gut microbiota in the development of hypertension was observed in a study involving antibiotic treatment and its effect on blood pressure in rats. Subsequently, studies have revealed reduced levels of microbial richness, biodiversity, and evenness in the fecal microbiota of animal models and human patients with hypertension. Furthermore, the severity of hypertension has been linked to the presence of specific bacterial species associated with hypertension, increased Firmicutes/Bacteroidetes ratios, higher levels of opportunistic pathogenic taxa (e.g., Klebsiella spp., Streptococcus spp.), and reduced populations of acetate-/butyrate-producing bacteria. Research has shown similarities in microbial characteristics between prehypertensive and hypertensive populations, with noticeable overgrowth of Prevotella and Klebsiella bacteria in both groups. The abundance of the butyrate-producing genus Odoribacter and butyrate production are inversely correlated with blood pressure levels in women at higher risk of developing pregnancy-induced hypertension and preeclampsia.[15]

Atherosclerosis and coronary artery disease

Atherosclerosis, a chronic inflammatory condition, is characterized by vascular cell dysfunction and the accumulation of low-density lipoprotein particles in plaques (Davignon and Ganz, 2004; Libby et al., 2002). Staphylococcus species, Proteus vulgaris, Klebsiella pneumoniae, and Streptococcus species have been found in both atherosclerotic lesions and the gut of the same individual, indicating the potential involvement of gut microbiota (GM) in the development of atherosclerosis. Certain types of gut bacteria have been identified as new contributors to the advancement of atherosclerosis. Eastern Poland's middle-aged men with inappropriate total cholesterol and LDL-C levels exhibit high levels of Prevotella, low levels of Clostridium, and Faecalibacterium, while Chinese patients with atherosclerotic cardiovascular disease show a decrease in Bacteroides and Prevotella, and

an increase in Streptococcus and Escherichia (Jie et al., 2017).[16]

A recent set of transplantation studies aimed at proving a direct connection between host thrombosis potential[14] and gut microbial cutC (a prominent microbial gene responsible for choline→TMA transformation.[12, 13] provide an exemplary illustration of this (Figure 2). In these investigations, a human commensal (C. sporogenes) that had been genetically modified to either have or not have a functional microbial cut C gene coexisted with germ-free (GF) mice that had been colonized with a synthetic polymicrobial community devoid of choline→TMA functional capacity.[14]

The gain-of-function C.sporogenes mutant increased circulating TMA and TMAO levels within the host, accelerated the rate of thrombus formation, and shortened the time to the cessation of blood flow following arterial injury in vivo, despite only being present in the large intestine gut microbial community at a very low abundance (just ~0.1%).[14]

The gut microbiota metabolizes dietary precursors like choline and carnitine into trimethylamine (TMA) through specific genes, which include members of the choline utilization gene cluster (Cut)C/D. TMA is then oxidized into TMAO by host hepatic flavin monooxygenases (FMOs), leading to metabolic and functional changes in the host, such as cardiovascular and renal end-organ damage.[14]

Microbial Dysbiosis in Airway Disease

Chronic Respiratory Diseases

The latest research has shown that various long-term lung conditions such as asthma, COPD, and cystic fibrosis are closely connected to an imbalanced airway microbiota. This imbalance typically occurs due to a decrease in bacterial diversity and the overgrowth of certain harmful bacteria. Patients with chronic lung disorders have a specific airway microbiota profile. In comparison to healthy individuals, individuals with asthma or COPD show a higher presence of Proteobacteria (especially Haemophilus, Moraxella, and Neisseria spp.) and Firmicutes (Lactobacillus spp.), while the proportion of Bacteroidetes (specifically Prevotella spp.) is significantly reduced. The lung microbiota of cystic fibrosis patients is characterized by a significant increase in typical cystic fibrosis pathogens from the Proteobacteria phylum, including Pseudomonas, Haemophilus, and Burkholderia, as well as an additional growth of the Actinobacteria phylum. Not only is the airway microbiota affected during these chronic lung disorders, but changes in the composition of the intestinal microbiota have also been observed, particularly in the context of asthma and cystic fibrosis.[16]

Several research projects have focused on the influence of the microbiota in the gut and lungs on long-term respiratory conditions like chronic obstructive pulmonary disease (COPD), asthma, and CF. The severity and exacerbations of COPD are linked to reduced diversity in lung microbiota and an increase in Proteobacteria. The presence of a more diverse pulmonary microbiota and a lower risk of exacerbation in patients with genetic mannose binding lectin deficiency suggests a potential causal relationship. In addition to the lung flora, gut microbiota may also play a role in exacerbations, as indicated by the higher gastrointestinal permeability in COPD patients admitted for exacerbations. The level of circulating gut microbiota-dependent trimethylamine-N-oxide has been associated with mortality in COPD patients, although the impact per se is not confirmed and may be influenced by comorbidities and age. Further research is necessary to explore the role of GLA in COPD and to establish causality.

The gut microbiota affects the immune systems of both the gut and the lungs through local or long-distance interactions, involving various pathways such as CD8+ T cell, Th17, IL-25, IL-13, prostaglandin E2, and NF-κB-dependent pathways. Similarly, the lung microbiota impacts mucosal immunity and contributes to immune tolerance through processes like neutrophil recruitment, production of pro-inflammatory cytokines via TLR2, and release of antimicrobial peptides like β-defensin 2 stimulated by Th17 cells. Additionally, the lung microbiota influences the gut immune system, although the specific mechanisms are not fully understood, with some evidence linking intestinal microbial disruption to Th17 cell mediation after lung infection with influenza virus. Factors like diet, medications, and probiotics are well-known to influence the composition of gut and lung microbiota.[17]

Modulation of gut microbiota

Probiotic Species

Microorganisms known as probiotics, such as bacteria, yeasts, and molds, can enhance the health of the host when administered in sufficient amounts. The most commonly utilized bacterial genera as probiotics are Lactobacillus, Bacillus, Bifidobacterium, Streptococcus, and Enterococcus.

Lactobacillus

Most probiotic species studied in biomedical research have focused on the lactic acid bacteria group. Lactobacillus has been identified as the primary probiotic within the lactic acid bacteria group in studies of gut microbiota. Various tools and techniques, including targeted, culture-dependent methods and metagenomics sequencing, have been used to investigate the impact of probiotic species on the composition, diversity, and function of the gut microbiota. Despite this, only a small number of studies have shown the connections between probiotic species and changes in gut microbiota composition. An analysis of 8-week-old Swiss mice fed a high-fat diet using metagenomics revealed that treatment with a probiotic mixture of Lactobacillus and Bifidobacterium (L. rhamnosus, L. acidophilus, and Bifidobacterium bifidum) resulted in significant alterations to the gut microbiota

composition and improved insulin sensitivity. Several authors have noted that mice on a high-fat diet treated with probiotic species had reduced populations of Firmicutes, Actinobacteria, and Bacteroides compared to untreated mice. Similar research on obese mice indicated that various Lactobacillus probiotic strains (L. acidophilus IMV B-7279, L. casei IMV B-7280, B. animalis VKL, and B. animalis VKB) increased the gut microbiota composition in mice on a high-fat diet. Furthermore, the gut microbiota composition of obese mice treated with L. casei, L. delbrueckii subsp. bulgaricus, and B. animalis showed a significant decrease in microscopic fungi. Probiotic Lactobacillus species may enhance gastrointestinal barrier function by promoting the growth of certain harmful bacteria. This can lead to increased intestinal permeability through the upregulation of the intestinal tight-junction protein occluding. Following alterations to the gut microbiota composition through probiotic treatment, mice on a high-fat diet exhibited increased expression of the tight-junction protein, proglucagon mRNA, and reduced intestinal expression of the pattern recognition receptors CD-14 and NOD1. Moreover, this led to a decrease in circulating lipopolysaccharide levels and an increase in glucagon-like peptide 1. Additionally, probiotic-treated mice demonstrated increases in lipoprotein-lipase-dependent triglyceride storage in adipose tissue and adipocyte triacylglycerol accumulation. Probiotic Lactobacillus strains have been shown to enhance gastrointestinal barrier function by promoting the proliferation of harmful bacteria in nonalcoholic fatty acid liver diseases and IBD. [18]

Prebiotics:

Prebiotics are “selectively fermented ingredients that cause specific changes in the gastrointestinal microbiota's composition and/or activities that confers benefits upon host well-being and health”. The polyphenols, polyunsaturated fatty acids (PUFAs), and carbohydrates, including galactooligosaccharides (GOS), Xylo oligosaccharides (XOS), fructooligosaccharides (FOS), fructans,and inulin, possess prebiotic properties.

Additionally, prebiotics prevent harmful bacteria from adhering to intestinal epithelial cells. For example, Ribeiro et al. demonstrated that prebiotic-rich olive pomace powders have antioxidant and anti-adhesive capabilities against infections in addition to encouraging the microbiota to produce SCFAs.

Postbiotic:

A variety of health benefits for the host are included in postbiotics, which are defined as cell fractions, inactivated microbial cells, and cell metabolites produced with probiotic live cells during fermentation. They are safer than live microorganisms since postbiotics are found in the conditioned/supernatants media of bacterial culture.

The two ways that postbiotics protect the intestinal epithelium are by 1) selectively suppressing tumor cells and 2) preventing intestinal epithelial cell death and boosting IgA production

Postbiotic metabolites generated by certain bacteria, such L. plantarum, have been demonstrated to have anti-proliferative and cytotoxic effects on tumor cells, including CRC cells. The tumoricidal effect of probiotic cell-free supernatant therapy with L. fermentum against CRC cells in a three-dimensional culture system was evaluated by Lee et al.

Antibiotics:

Antibiotic use has been demonstrated to have detrimental effects on the gut microbiota, including decreased bacterial biodiversity, the selection of organisms resistant to antibiotics, and altered metabolic processes. These effects can lead to antibiotic-associated diarrhea and recurrent C. difficile infections. Antibiotics may reduce the size and number of tumors by influencing the gut microbiota, despite mounting evidence that they raise the risk of colorectal cancer. For instance, in a mouse model of intestinal neoplasia, DeStefano Shields et al. found that enterotoxigenic B. fragilis colonization could be entirely and permanently eradicated by cefoxitin antibiotic treatment.

Antibiotics are also protective in preserving the intestinal mucosal barrier. Given that consuming large amounts of red meat raises the chance.

Fecal microbiota transplantation:

Microbiota transplantation of the feces One of the most intriguing and cutting-edge biotherapeutic techniques is fecal microbiota transplantation (FMT). such as transplanting stool from healthy people into patients. In addition to treating C. difficile infection (CDI), it demonstrated encouraging potential for the treatment of cardiovascular disorders, non-alcoholic fatty liver disease, obesity, IBD, and diabetes. FMT may prevent intestinal colonization of antibiotic-resistant bacteria (ARB) in individuals with blood disorders, according to prospective clinical trial research. Patients' ARB was fully (75%) and partially (80%) decolonized because of FMT. FMT aims to restore the diversity of the gut flora. It has been demonstrated that FMT can improve several GI illnesses and restore microbial equilibrium by introducing a healthy and disease-free microbial population into an unbalanced community.[18]

CONCLUSION

In conclusion, the gut microbiome plays a pivotal role in the development and progression of chronic diseases. An imbalance of the gut microbiota, or dysbiosis, has been linked to various conditions, including obesity, diabetes, inflammatory bowel disease, and mental health disorders. Modulating the gut microbiome through dietary interventions, probiotics, prebiotics, postbiotics, FMT and Antibiotics offers promising therapeutic strategies. Further research is essential to elucidate the complex relationships between the gut microbiome, host genetics, and

environmental factors. By targeting the gut microbiome, we may unlock novel treatments for chronic diseases, improving the lives of millions worldwide and revolutionizing the future of healthcare.

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