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Exploring the Interconnection Between Diet, Microbiome, and Human Health: A Systematic Review

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ABSTRACT

Recent research increasingly highlights the connection between diet, the gut microbiome, and overall human health. It has been established that the gut microbiome functions as an independent "organ" and its metabolic activity influences the overall metabolism of the body. This paper emphasizes the key roles of the gut microbiome, its composition, and its importance in maintaining the body's health, as well as the changes that occur under pathological conditions. Our study includes recent in vivo and in vitro findings that demonstrate a direct link between microbiome imbalances and various diseases. Changes in microbiome composition have been observed in conditions such as Alzheimer's disease, gastrointestinal disorders, and skin diseases. This paper provides an overview of the fundamental concepts and relationships between the health of the gut microbiota and the health of the human body.

Keywords: Bacteria, Microbiome, Health, Disease

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Introduction

The gut microbiome, a vast community of microorganisms located throughout the small intestine, plays a critical role in maintaining the normal functioning of the human body. Numerous studies have established a clear link between the health of the intestinal microbiome and the overall health of the host, with lifestyle factors, especially diet, having a significant influence on this relationship [1-3].

It has been shown that modifications in lifestyle, particularly dietary changes, lead to shifts in the composition of the gut microbiome. In essence, improving one's diet and lifestyle can enhance the microbiome, which in turn promotes better health and may even prevent the onset of certain diseases [1].

To better understand these effects, it is important to examine the complex interactions between food intake and gut bacteria. Many studies indicate that changes in the gut microbiome composition can result in either positive or negative health outcomes [4, 5]. Factors such as temperature, pH levels, the presence of bacteriophages, nutrient availability, and anaerobic conditions are all key elements that influence the diversity and function of the gut microbiome [6, 7].

Given the extensive activity of gut microorganisms, the microbiome is now often referred to as a "functional organ" within the human body, due to its significant impact on overall health [8]. The composition of the microbiome can reflect the individual's lifestyle and behaviors, influencing biomarkers in the bloodstream [9]. Recent advancements in research suggest that tailored nutritional approaches, guided by the gut microbiome, could lead to more effective and precise methods for disease prevention [10].

The purpose of this paper is to explore recent research on the interplay between the microbiome's health and the host's health, with a focus on how diet and nutrition can help prevent or treat various diseases.

Results and Discussion

The human colon and fermentation

The colon is home to a vast number of bacteria, estimated to be in the trillions, all of which are involved in food digestion, absorption, and metabolism. The first step in this process involves fermentation [11-13]. Complex carbohydrates, which are often resistant to digestion by human enzymes, such as pectin, cellulose, and gums, are fermented by the microbiota, producing short-chain fatty acids (SCFAs) like propionate, acetate, and butyrate, as well as gases [14-17].

Besides these SCFAs, the fermentation of proteins and carbohydrates produces byproducts like branched-chain fatty acids (BCFAs), lactic acid, and amines. These products play a significant role in maintaining metabolic balance in the host and can also contribute to boosting the immune system [18, 19].

Protein fermentation, however, occurs only after carbohydrates have been fermented and typically happens in the distal colon [20-22]. While protein fermentation can sometimes have harmful effects, such as its role in the development of colorectal cancer, it can also be beneficial by helping regulate nitrogen balance in the body through the release of ammonia, which is absorbed by cells [23, 24].

The microbiome's role in lipid metabolism is more complicated, as it produces various fatty acids that, in excessive amounts, can negatively affect host health. For instance, the microbiome's metabolism of linolenic acid is linked to Roseburia bacteria, which can promote health by producing vaccenic acid, a precursor to conjugated linoleic acid [18].

A study conducted in vivo indicates that the presence of bacteria like *Lactobacillus* sp. can affect the metabolism of unsaturated fatty acids. The levels of intermediates in the reactions, particularly hydroxylated compounds, show that these levels vary based on the microbial flora composition. Essentially, the state of the gut microbiota can influence the lipid profile of the host [18, 25, 26].

The main bacteria involved in fermentation processes are from the genera *Bifidobacterium*, *Lactobacillus*, *Ruminococcus*, and *Clostridium*. Other important species include *Eubacterium rectale*, *Roseburia* spp., and *Faecalibacterium prausnitzii* [8, 20, 27, 28].

The role of the microbiome in disease development

Numerous studies have investigated the impact of the microbiome on overall health and its direct relationship with various diseases. **Table 1** offers a summary of the intestinal bacterial species and genera that are frequently affected by dietary factors.

Table 1. Overview of intestinal bacterial genera and species commonly affected by diet

Bacteria	Characteristics	Associated physiological changes	Associated disease states	Reference
Bifidobacterium spp.	- Gram-positive	- Low SCFA production	- Low obesity levels	[29, 30]
	- Branched-chain anaerobic	- Improves intestinal mucosa barrier		
		- Reduces intestinal LPS levels		
Lactobacillus spp.	- Facultative anaerobic	- Regulates SCFA production	- Low levels in IBD	[31]
	- Rod-shaped	- Anti-inflammatory activity		
	- Gram-positive	- Anti-cancer activity		
Alistipes spp.	- Gram-negative	-	- Found in acute appendicitis, perirectal and cerebral abscesses	[32]
	- Rod-shaped anaerobic	- Resistant to bile acids and pigments		
Bilophila spp.	- Gram-negative	- Promotes TH1 pro-inflammatory immunity	- Observed in colitis, perforated appendicitis, gangrene, liver and soft tissue abscesses, cholecystitis	[33, 34]
	- Anaerobic	-		

	- Resistant to bile acids and pigments			
Eubacterium spp.	- Gram-positive	- Involved in SCFA production	- Low levels in IBD	[35, 36]
	- Rod-shaped aerobic	- Forms beneficial phenolic acids		
Escherichia coli	- Gram-negative	-	- Increased in gastroenteritis, IBD, and meningitis	[37, 38]
	- Rod-shaped anaerobic	-		
Akkermansia muciniphila	- Gram-negative	- Anti-inflammatory effects	- Low levels in IBD, obesity, and psoriasis	[39]
	- Anaerobic	- Oval shape		

Alzheimer's disease

Alzheimer's disease (AD) is a progressive neurodegenerative disorder with no known cure or preventive treatment [40]. AD is typically characterized by the accumulation of peptides outside cells and the formation of hyperphosphorylated protein deposits within cells [41, 42]. Recent studies suggest a strong link between the gut microbiome and cognitive health, often described as the gut-brain axis, involving immune, endocrine, and neural signaling pathways. In patients with mild cognitive impairment or dementia, an imbalance in gut microbiota has been associated with increased pro-inflammatory lipopolysaccharides at the neuronal level [43-46]. The ketogenic and low-calorie diets are considered beneficial for these patients, offering neuroprotective effects and preventing the accumulation of extracellular peptides in neurons. Additionally, such diets help regulate the bacterial species in the gut positively [17, 47].

Inflammatory Bowel Disease (IBD)

Genetic factors and lifestyle play significant roles in the development of inflammatory bowel disease (IBD) [48]. The imbalance of the gut microbiome contributes heavily to these disorders, as microbial imbalances produce pro-inflammatory components during fermentation, which contribute to the pathogenesis of conditions like Crohn's disease (CD) and ulcerative colitis [38, 49].

CD primarily affects the mucosal and submucosal layers of the intestines, leading to regional ileitis. Studies show that microbial changes in CD patients include increased populations of *Enterobacteriaceae* species such as *Escherichia coli*, *Fusobacterium*, *Serratia marcescens*, and *Candida tropicalis*, which are not present in healthy individuals [50]. This microbial imbalance causes oxidative stress, reducing the production of beneficial intermediates like short-chain fatty acids (SCFAs), which play a crucial role in maintaining metabolic health [51-53].

In ulcerative colitis, the primary feature is an imbalance with increased populations of *Enterobacteriaceae* and *Bacteroides fragilis* [3, 54, 55].

Inflammatory skin diseases

Atopic dermatitis (AD) affects 15%–20% of children and 1%–3% of adults worldwide [56]. In this condition, the gut microbiome is often disrupted. Research indicates that probiotics can help manage inflammatory skin diseases, supporting the idea of a gut-skin axis. Thus, future treatments may focus on rebalancing the gut microbiome, followed by topical therapies for these conditions [56-60].

Type 2 diabetes and obesity

High-fat and high-sugar diets are linked to changes in the gut microbiome, suggesting that gut bacteria might act as environmental factors influencing energy production and contributing to obesity [61, 62].

Obesity is associated with alterations in the diversity and composition of gut microbiota, with an increase in Firmicutes and a decrease in Bacteroidetes, two dominant groups of gut bacteria. Studies have shown that a high-fat diet leads to a reduction in bacteria like Eubacterium rectale and Blautia coccoides and a decrease in bifidobacteria [17, 63].

Obesity and type 2 diabetes are linked to an increased Firmicutes/Bacteroidetes ratio [30, 64-66]. Additionally, Bifidobacterium levels are lower in overweight, obese, or type 2 diabetic individuals compared to healthy ones. Faecalibacterium prausnitzii, another bacterium associated with anti-inflammatory effects, is also found at lower levels in type 2 diabetes patients. Studies have suggested that microbial composition in childhood may predict future weight gain [30]. In one study, higher levels of Staphylococcus aureus and lower levels of bifidobacteria were found in the feces of children who became overweight. Interestingly, recent research demonstrated that transferring healthy gut microbiota temporarily improved insulin sensitivity in individuals with metabolic syndrome [2, 67, 68].

Conclusion

Clinical, epidemiological, and immunological evidence suggests that alterations in the gut microbiota could play a crucial role in the development of various inflammatory disorders. The recent discovery of beneficial bacteria with strong anti-inflammatory effects, and their absence in certain diseases, points to the significant influence the microbiota may have on human health. This highlights the importance of maintaining a healthy gut microbiome for overall well-being. Reassessing the role of microbial flora in medical and social contexts could lead to significant improvements in health, potentially benefiting future generations. Understanding the complexities of the gut microbiome and how its composition can influence the onset of different disorders is essential, as these imbalances can have both immediate and long-lasting effects on health.

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