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"Microbiome and its impact on Health: A Detailed Review"

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Abstract
The human microbiome, including bacteria, archaea, viruses, and eukaryotes, impacts human physiology and health by enhancing or impairing metabolic and immune functions. These organisms colonize various sites in the body, adapting to specific niches. The microbial community's diversity accounts for specific metabolic activities and functions. Understanding the microbial composition and activities of the human microbiome is crucial for understanding its impact on health and disease. Recent research has revealed the microbiome's influence on various diseases, including cardio-metabolic diseases, allergies, obesities, and life-threatening ones like cancer. Recent studies have uncovered the impact of microbiome on both human cognition and physical well-being, as well as its involvement in several disease transitions, including cardio-metabolic disorders, allergies, obesity, and even life-threatening conditions like cancer. Although the precise mechanisms of many diseases remain unclear, research has shown that metabolites, nutrients, and microorganisms play a crucial role in certain physiological conditions. The primary objective of this chapter is to elucidate the correlation between the microbiome and human health, whether it be through a cooperative or conflicting method.

Keyword: Microbiome, Diseases, microorganisms, human health

Introduction

The human microbiota refers to a collection of organisms that reside in and interact with the human body [1]. The interactions can be classified as communalistic, mutualistic, or pathogenic. The human microbiome is defined as the complete set of genetic material of microorganisms (microbiota) residing in a certain location within the human body. Microorganisms inhabit several anatomical body areas including the skin, mucosa, gastrointestinal system, respiratory tract, urogenital tract, and mammary gland. The ecosystem they create is intricate and distinct, according to the specific environmental circumstances of each niche [2]. The symbiotic relationship between the human body and its indigenous microbiota commences at birth. These connections have significant functions in preserving overall health and well-being. Through the process of coevolution, organisms

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form the microbiota. They actively adapt to their individual environments and occupy their respective niches within the human body [3–5]. These organisms are recognized as integral components of the body due to their biological functions, resulting in a range of alterations from conception to death. The human microbiome undergoes continuous changes in response to various host circumstances. Age, nutrition, lifestyle, hormonal fluctuations, inherited genes, and underlying disease are significant factors that determine the composition of the human microbiome at any particular moment. Nevertheless, a change in the composition of the human microbiota (known as dysbiosis) can result in severe and even fatal diseases [2]. An equilibrium in the microbiota has demonstrated a significant function in maintaining good health [2]. The gut contains the highest density of the human microbiome. These creatures perform a crucial role in preserving and supporting human health.

Systemic Microbiome: Its Distribution and Diversification

It is believed that there are more than 100 trillion microorganisms living within and on the skin of humans. These bacteria have a genome that is around 150 times larger than the whole human genome (6). Microbes, including bacteria, fungi, archaea, and viruses, have over eight million distinct protein-coding genes. In comparison, the human genome contains only about 22,000 protein-coding genes (7). The variety and characteristics of the organism are determined by the specific anatomical site of the body, which in turn is influenced by their specific growth requirements. Other factors contributing to this growth include the coevolution of microorganisms, their extensive interactions with each other and with the human host, variations in population composition and function, human lifespan and variations in body sites, ecological conditions, differences in oxygen levels, airway temperature, mechanisms of muco-ciliary clearance, sex, genetics, and socio-economic status. Therefore, the idea of interdependence has emerged to describe the interconnectedness of several physiological, immunological, and metabolic processes that eventually shape the composition of the microbiome community in a specific location inside the human body.

Different microbiome

- **The gut microbiome:** which consists of the genetic material of microbes in the gut, holds a crucial and unique role within the broader human systemic microbiome. They have a significant impact on several physiological systems such as metabolism, immune system development, and nutrient provision. The genetics and immune system of the host have been demonstrated to play a role in the formation of gut microbiota (8). The human immune system and the microbiome engage in a reciprocal communication, known as crosstalk, in response to environmental stimuli such as nutrition, infections, and xenobiotic chemicals. An example of crosstalk occurs between the myeloid cells, epithelial layer, and innate lymphoid cells, which are all part of the immune system, and the gut microbiota. This interaction has significant effects on the composition of the microbiome, host physiology, and susceptibility to disease. These consequences arise from the feedback loops and interactions between these components. In addition to the bacterial community, which includes species such as Firmicutes and Bacteroidetes, these interactions are also influenced by other microorganisms such as fungus (9), archaea, and viruses (10). The primary components of the gut microbiota are the bacteriome, virome, and mycobiome. These components have a significant dependency that is crucial for

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maintaining the functionality of the gut microbiota. However, if this balance is disrupted, it can also have varied effects on other systems. From the moment a person is born, their sterile gut is exposed to the microorganisms present in their mother's vagina during a vaginal delivery or to the microorganisms in the hospital environment during a caesarean section. These microorganisms can include species that are resistant to multiple drugs. Over time, these microorganisms colonize the gut and by the age of 3-5 years, the gut microbiota of an individual begins to resemble that of an adult in terms of both structure and function (11). The distribution of gut microbiota in adults is heterogeneous along the whole gastrointestinal tract. In contrast to the small intestine, which is abundant in species belonging to the phylum Firmicutes, the colon contains members of the phylum Bacteroidetes. The microbiome present in the lumen and the microbiome adhered to the epithelial lining exhibit distinct variations. The stool sample contained *Bacteroides, Streptococcus, Ruminococcus, Lactobacillus, Enterococcus, Bifidobacterium, and Clostridium* in the lumen community. On the mucous layer, Enterococcus, Lactobacillus, and Clostridium were detected (12).

Diseases related: The intimate connection between the gut microbiota and cardiovascular disease (CVD) is indicated by the metabolic source of classical CVD risk factors, such as obesity, dyslipidaemia, and insulin resistance. Recent research have indicated that the gut microbiota is strongly linked to atherosclerosis, with a significant quantity of data supporting this association. According to a hypothesis, metabolites produced by the bacteria in the gut cause an inflammatory response by moving into the bloodstream and contribute to the development of atherosclerosis. The presence of oral bacteria responsible for dental cavities has also been detected in atherosclerotic plaque (39). Heart failure is commonly regarded as the final step in numerous cardiovascular diseases, characterized by a heightened incidence of illness and death (40). Reduced cardiac output and blood redistribution have been attributed to low intestinal perfusion and disturbance of the intestinal barrier. Microbiota and endotoxins entering the bloodstream cause a heightened systemic inflammation, which might potentially result in an elevated risk of heart failure (41).

- **The Microbiome of the Lungs:** At the commencement of HMP, the investigation excluded the airways and lungs due to the belief that these regions had sterility (13). This fact has always been acknowledged because to the adverse outcomes observed in the several conventional microbiological culture tests conducted on healthy individuals (14). The examination of the lower tract posed a hurdle due to the complexity of evaluating it without invasive methods like bronchoscopy. Consequently, the systemic microbiome assay was postponed until the publication of the first study that demonstrated the similarity in bacterial density between this particular area and the upper small bowel of the human body (15). The ability to achieve this has been facilitated by the progress in molecular approaches that are not reliant on culture practices (14). The human respiratory system is anatomically split into the upper respiratory tract (URT) and the lower respiratory tract (LRT). The LRT contains alveoli, which have a surface area of around 70 square meters (15). The

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entire tract is inhabited by a specialized microbiota, with a greater concentration residing in the upper respiratory tract (URT).

The microbiota has been hypothesized to influence the morphological development of this system (15). Within the initial hours of a healthy new-born, non-specific microorganisms, believed to originate from the mother, have been identified. The presence of a large number of Staphylococcus spp. in the upper respiratory tract (URT) during the first week is attributed to niche specialization. Subsequently, the URT is colonized by Corynebacterium spp., with Dolosigranulum spp. being the dominant species. The Moraxella species has its highest prevalence throughout the age range of 4–6 months. Individuals harbouring such microbiota have been observed to exhibit a stable microbiome community, which is associated with improved airway health (16-17). The optimal growth and progress of this development can be disrupted by various factors, including the use of antibiotics, changes in oxygen levels, temperature and pH, the presence of other siblings, seasonal changes, vaccines, exposure to smoking, and the genetic makeup of the host.

- **Urogenital Microbiome:** Previously, it was believed that the human urinary tract, as well as urine, was devoid of any microorganisms. However, recent scientific research has established the existence of microbes in this system, particularly in persons who are in good condition. The utilization of advanced methods like 16 s rRNA sequencing has greatly facilitated the identification of the typical microbiota present in the human body system. Upon urine examination, the predominant genera observed are Lactobacillus (more prevalent in women) and Streptococcus (more prevalent in men). These genera, along with a few other groups, play a crucial protective role in the urinary system by defending against various infections. However, several genera such as *Saccharofermentans, Proteiniphilum, Parvimonas*, and *Jonquetella* were only found in individuals over the age of 70. The diversity of the urine microbiome, which is influenced by age and sex, can be attributed to disparities in voiding habits, cleanliness practices, urinary metabolites, anatomical structures, hormone fluctuations, and histology. The vaginal microbiome demonstrates fluctuation during the premenstrual phase, reproductive age, and post-menopausal phase (18).
- **The microbiome of the Nervous system:** The central nervous system is regarded as highly immunological privileged due to its enclosed compartmentalization. The brain is physically separated from the vascular system by barriers such as the blood-brain barrier and blood-cerebrospinal fluid barrier (19-20). Therefore, the reason for the isolated and protected status of the central nervous system from the microbiota can be attributed to the absence of lymphatic outflow, the presence of major histocompatibility complex in the parenchymal cells, and the anti-inflammatory environment (21).

  The human body contains a bidirectional communication system between the brain and the gut, which involves hormonal, immunological, and neurological signalling pathways. This system is accessed by the microbial flora of the intestine and specific metabolites, and is sometimes referred to as the gut-brain axis. Approximately 90% of serotonin (5-HT), a type of neurotransmitter, is believed to be produced in the intestine due to the influence of gut microbiota. The activation of serotonin receptors

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in the enteric nervous system is responsible for the protection of nerve cells and the generation of new nerve cells in adult mice (22).

- **Microbiome of the skin:** The skin is the biggest organ that serves as the external interface between the human body and the environment. An average human body is covered by around 1.5–2.0 square meters of skin, which has a depth of 2–3 millimetres. The skin is composed of three distinct tissue layers: the epidermis, dermis, and hypodermis. The epidermis is inhabited by a multitude of microorganisms, including bacteria, fungus, arthropods, and even viruses. The body's physical, anatomical, and immunological barrier protects against many infections. However, if this barrier is compromised or there is an imbalance between beneficial and harmful organisms, it can lead to skin or systemic disorders. Their low pH level, ongoing shedding of outer skin cells, water-repellent properties, saltiness, and interaction with antimicrobial substances contribute to their effectiveness as a barrier (23). Despite the aforementioned qualities, bacteria can still be found on the skin, with a population ranging from one million to around one billion per square centimetre. Human skin is inhabited by a variety of microorganisms, with the most typically encountered bacterial phyla being Proteobacteria, Corynebacteria, Propionibacteria, Bacteroidetes, Firmicutes, and Staphylococcus spp. The most often encountered fungi include *Malassezia spp., Cryptococcus spp., Epiciccum spp., Aspergillus spp.,* and *Rhodotorula spp*. The incidence and dominance of communities on the skin are influenced by various parameters, including biological sex, skin depth, skin location (such as thickness, folds, and hair density), age, health, geographical location, ethnicity, usage of lotions, soaps, cosmetics, antibiotics, and hygiene practices.

Diseases

Cancer: The gut microbiota exerts a substantial influence on the overall health of its host [24]. Research on the interaction between microbial communities and their host indicates that these organisms engage in biochemical processes that impact the development of cancer, tumour formation, and the effectiveness of immune therapy. Based on a comprehensive model examining factors that could contribute to an imbalance of gut bacteria, it is suggested that persistent infections within the abdomen, the use of antimicrobial medications, or a combination of both, could potentially raise the likelihood of developing colorectal cancer. Also, end products generated by the gut bacteria influence the intestinal cell coverage, favouring carcinogenesis or preventing tumorigenesis [25]. In addition to colorectal cancer, the microbiota of the intestinal tract has been found to contribute to extraintestinal cancer, such as hepatocellular carcinoma, by spreading these organisms systematically to other areas of the body[26]. Furthermore, H. pylori significantly increases the susceptibility of individuals to developing stomach cancer. Recent research has discovered a connection between the human microbiome and cancer, namely gastric cancer. It has been observed that Fusobacterium and Clostridium are more prevalent in persons with gastric cancer [27]. Environmental and host variables exert a direct influence on the progression of breast cancer. Nevertheless, bacterial communities have the potential to trigger breast cancer. persons with breast cancer have been more likely to have Bacillus, members of the Enterobacteriaceae, and Staphylococcus in their breast tissue as compared to healthy persons. In addition, Escherichia coli and Staphylococcus epidermidis obtained from cancer patients induced a double-stranded

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DNA break in HeLa cells. The presence of Lactobacillus spp., which is associated with various health advantages, was not detected in the breast tissue of women diagnosed with breast cancer. *Bacteroides massiliensis* has been linked to a greater incidence of prostate cancer. The modification of the human microbiota has played a role in the intricate relationship between cancer and the human microbiota.

Inflammatory Bowel Disease (IBD): The proliferation of pathogenic microorganisms elicits an aberrant immune reaction targeting the body's tissues. Indeed, this phenomenon has a role in the development of autoimmune disorders, inflammatory bowel disease, and other potentially fatal problems [25]. The human microbiota and the immune system engage in a coevolutionary process, resulting in a harmonious and methodical interplay throughout time. Nevertheless, any modification in the host-microbiota has an impact on this interaction, causing a decline in the immune response, perhaps leading to the development of inflammatory disorders [24]. Sunil et al. [26] explain the correlation between the gut microbiome and a weakening of the gastrointestinal barrier in inflammatory bowel disease (IBD). The tight junction surrounding epithelial cells acts as a barrier, effectively separating the tissue space and regulating the transport of solutes across the epithelium. The integrity of the intestinal barrier can be compromised by a disrupted mucus layer, resulting in impaired cell adhesion [25]. A decrease in gut Firmicutes results in elevated levels of proinflammatory cytokines (IL12, IFN-γ) and decreased levels of anti-inflammatory cytokine (IL-10) [14]. Helminth infections have been linked to the presence of anti-inflammatory organisms that protect against the development of inflammatory bowel disease in animals that are sensitive to IBD [22].

Cardiovascular Diseases: The gut microbiota's production of metabolites has systemic effects in addition to its impact on the gut. The synthesis of trimethylamine N-oxide (TMAO) metabolites by specific gastrointestinal microorganisms may be associated with cardiovascular disease [16]. The gut microbiota metabolizes trimethylamine from diets that are high in l-carnitine, choline, and phosphatidylcholine into trimethylamine N-oxide (TMAO) using hepatic flavins containing monooxygenase. TMAO impacts lipid transit in the body and also causes the production of precursors which increase foam cell development and hardening of the arteries in animal models [27]. Intestinal dysbiosis has been found to be linked to cardiovascular disorders. Kho and Lal conducted a clinical investigation on two cohorts: individuals with a low risk of cardiovascular disease and individuals with a high risk of cardiovascular disease. According to their research, persons with an imbalanced gut microbiota have an increased susceptibility to cardiovascular disease [28-29]. The presence of certain organisms in excessive amounts has been identified as a contributing factor to cardiovascular disorders. Transferring faecal matter from hypertensive individuals who had elevated levels of *Prevotella* and *Klebsiella* bacteria resulted in an elevation in blood pressure in germ-free mice used as animal models. In addition, the stool of hypertensive mice exhibited a notable elevation in the ratio of Firmicutes to Bacteroidetes in their faecal microbiota [30].

Chronic Kidney Disease (CKD): Intestinal dysbiosis commonly coincides with impaired intestinal barrier function, leading to the generation of bacterial by-products that are quickly absorbed and remain in the intestinal lumen. When there is an increase in the absorption of these substances and a decrease in their removal by the kidneys, the levels of toxins

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originating from the gut increase in the bloodstream. This can lead to the development of vascular calcification, atherosclerosis, and negative cardiovascular effects, which are clinical conditions observed in the later stages of chronic kidney disease (CKD). Multiple epidemiological studies have established a correlation between vascular toxins originating from the stomach and cardiovascular events in patients with chronic kidney disease (CKD) (42).

The Human Microbiome in Health Sustenance

Maintenance of Homeostasis: The human microbiome fulfils crucial functions in the preservation and advancement of the human body. These organisms have a crucial role in initiating the immune system, influencing the balance of inflammation and immunological control in new-borns and early children. In a study conducted in 2015, Melli found that infants who acquire allergies later in life have a larger occurrence of *Bacteroidaceae* and anaerobic bacteria, along with a reduced number of *Bifidobacterium adolescentis*, *Bifidobacterium bifidum*, and *Lactobacillus* spp. [31-32]. Further investigations on microbiome have revealed that these organisms engage in interactions with and break down external pollutants, including heavy metals, polycyclic aromatic hydrocarbons, herbicides, ochratoxins, plastic monomers, and organic chemicals [33]. After the kidneys filter the blood, the toxins are deposited in the bladder. The bladder supplies the necessary ingredients and habitat for the urinary tract microbiota to neutralize these harmful compounds [34]. The interactions between these organisms play a crucial role in determining the fate of an infection. The female vaginal tract relies on its indigenous microbial flora to activate a protective process that triggers innate immunity. This includes the release of cytokines, antimicrobial peptides, and inhibitory chemicals.

Development of Host Immune System: The immune system develops and strengthens immune responses through the coevolution of indigenous microbiota and the ability to distinguish between hazardous pathogens and commensal organisms that need to be preserved [35]. The microbiota in the gut has a significant impact on the development of the adaptive immune system. As a result, the human microbiota plays a role in shaping the mammalian immune system, which is responsible for regulating microorganisms. Recent research on the human microbiome have demonstrated that the absence or early disruption of commensal microbes might lead to heightened type II immunity and allergies due to aberrant immune functioning. Changes in the microbiota of children, caused by factors including caesarean deliveries, a more inactive lifestyle, pollution, and Western-style meals, have been associated with a rise in incidence of childhood allergic rhinitis [36]. Probiotics, breastfeeding, lifestyle modifications such as encouraging children to play outdoors in the morning sunlight (to enhance vitamin D synthesis), and allergen-specific immunotherapy have been suggested as factors that facilitate the maturation of the immune system and the prevention of atopy in children. The gut microbiota is responsible for stimulating the activation of proinflammatory Th17 cells and regulatory T-cells (Tregs) in the colon. Furthermore, the human microbiome exerts a substantial impact on innate immunity. Neutrophil ageing is an instance where the proinflammatory properties in the body are diminished. These organisms accelerate the aging process of neutrophils by activating Toll-like receptor (TLR) and MyD88-mediated signalling pathways. The modification of microorganisms causes a decrease in the movement of old neutrophils, which in turn leads to

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harm to organs connected to inflammation in models of sickle cell disease or septic shock generated by endotoxins. Thus, these organisms actively regulate disease-promoting neutrophils, which are essential for inflammatory disorders [30]. Moreover, the intestinal microbiota plays a crucial role in protecting against harmful pathogens. Their function is to enhance resistance to colonization and produce antimicrobial chemicals to combat invading infections. A well-balanced gut microbiome may have a role in controlling the activity of antibodies (specifically CD8-T cells and CD4 cells) that respond to the invasion of the influenza virus in the respiratory tract. Additionally, the intestinal microbiota plays a crucial role in enhancing and sustaining gastrointestinal functioning. The intestinal immune system has a challenge due to the large number of organisms present in the gut. It must strike a balance between accepting beneficial microorganisms and food antigens, while yet being able to eliminate harmful infections. The activation of regulatory T-cells (Tregs) in the colon is crucial for the establishment of immunological homeostasis. There exist two categories of Tregs: thymus-derived Tregs and peripherally derived Tregs (pTregs). The distinction of these two immunological responses is intricate, yet they play a crucial role in immune control. However, the peripheral regulatory T cells (pTregs), specifically, rely on the presence of microbiota for their activation in the colon.

Host Nutrition: The microbial community of the colon plays a crucial role in meeting the nutritional needs of the organism it inhabits [37]. These organisms enzymatically degrade complicated dietary elements, such as complex polysaccharides, within the intestinal cells, hence facilitating the absorption and assimilation of complex food materials. The primary by-products of carbohydrates and amino acids in the digestive system are short-chain fatty acids (SCFAs), including acetic, propionic, and butyric acids [38]. Upon being absorbed by the colonic mucosa, these three dietary components act as sources of energy and building blocks for the production of mucosal lipids. Additionally, they promote the proliferation of epithelial cells, which helps maintain the integrity of the gut. The colonic microbiota safeguards the large bowel against cancer by generating butyrate through the fermentation of intricate food components. The microbial activity in the colon play a crucial role in providing vital nutrients that are necessary for maintaining the health of the colon. African women and new-borns have been shown to have elevated levels of Bacteroidetes and SCFAs in their faces, in contrast to European infants whose moms follow Western diets that are low in SCFAs. Research has indicated that the intake of conventional and fermentable carbohydrates may have played a role in the widespread presence of a healthy gut microbiome. Another crucial role of the intestinal microbiota is to supply essential vitamins required for the growth and development of the host. The production of vitamins is attributed to intestinal bacteria, specifically Bifidobacterium spp., Bacteroides spp., and enterobacteria. Vitamin K is a crucial coenzyme that plays a role in the production of several clotting components, such as prothrombin. Insufficient levels of this vitamin can result in delayed blood clotting and excessive bleeding. Furthermore, folic acid plays a crucial role as a precursor in the production of DNA and RNA. Ultimately, they participate in the production of erythrocytes and leukocytes. Currently, probiotics that contain lactobacillus or Bifidobacterium are employed in the treatment of allergic disorders. Research on the use of probiotics as therapy alternatives has shown that they can strengthen the immune system by lowering or blocking the activation of T-cells that are responsible for triggering immune responses to antigens.

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Additionally, probiotics can reduce the activity of a cell signalling protein called tumour necrosis factor (TNF), which is involved in causing inflammation throughout the body.

Effects of Antibiotic Abuse on Microbiota

In 2015, the United States and Europe had approximately 50,000 deaths due to the emergence of antibiotic resistance in disease-causing microorganisms. It is estimated that by 2050, the global mortality toll might reach roughly ten million per year (43).

Furthermore, the utilization of antibiotics has been documented to disturb the ecology of the human microbiome, in addition to fostering the emergence of resistance. A dysbiotic microbiome is characterized by the loss of its capacity to carry out essential duties such as providing nutrients, producing vitamins, and protecting against infections. This ultimately results in the deterioration of the host's metabolic, immunological, and developmental systems. Drug-induced alteration of the gut microflora can impact a specific population of Foxp3+Treg cells that regulate demyelination in experimental autoimmune encephalomyelitis (EAE) (44). A separate study demonstrates that the antigens generated by Bacteroides fragilis, specifically the capsule polysaccharide, have the ability to provide protection against CNS demyelination, known as EAE, and perhaps against multiple sclerosis in humans.

Probiotics

Probiotics are defined as living bacteria that are not naturally found in the human microbiome, but provide a health benefit to the host when given in adequate amounts. In recent years, there has been substantial research on probiotics due to their ability to provide numerous health benefits through the metabolites they create. These benefits include relieving certain intestinal problems and regulating EAE. Probiotics have been shown in clinical trials to effectively control some cardio metabolic disorders (CMD) including type 2 diabetic mellitus (T2D), dyslipidaemia, arterial hypertension, and chronic kidney diseases (CKD) (45). Saccharomyces boulardii has demonstrated anti-inflammatory properties that aid in regulating inflammation associated with dysbiosis in the lumen (46).

Prebiotics and synbiotics

Prebiotics are indigestible food components that can be selectively digested by probiotics, serving as a dietary fiber for them. Recent research has shown that the utilization of prebiotics can improve the ecological function of the gut microbiota, leading to the development of a more advantageous community (47). This suggests that the human microbiota can be improved, stabilized, and altered by consuming certain prebiotics, such as carbs. Nevertheless, the characterization of the connection between the prebiotic and probiotic remains a challenging task. When the concept of synbiotic was initially introduced, two configurations were suggested: firstly, a setup where the prebiotic and probiotic components were separate, each responsible for a specific effect or health benefit, and secondly, a symbiotic component, where the probiotic was specifically designed with a prebiotic substrate that would synergistically enhance the potency, survival, or metabolic activity of a related probiotic strain in the gastrointestinal system's ecology (48).Recently, two new approaches have been suggested for developing synergistic synbiotics, both based on their ecological role and well-being. The in vivo approach involves identifying and isolating a probiotic strain that will multiply when a certain prebiotic component is given to a particular group of individuals (49). Another approach, known as multi-taxon insertion, involves sequencing and identifying genes to assess the effectiveness of a probiotic strain in

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connection to the specific prebiotic used. This is done by analysing libraries of transposon mutants (50).

Faecal Microbiota Transplantation

In many cases, antibiotics alone may not be enough to treat certain infections and instead, immediate alternatives are needed to effectively manage the severity of the clinical condition. As a result, the transplantation of the faecal microbiota has been introduced. The procedure entails extracting and transferring the microbial community found in the feces of a healthy donor to the gastrointestinal tract of the recipient patient. This approach facilitates an effective treatment by restoring the natural composition of the microbiota. Recent studies have elucidated the mechanism underlying faecal microbiota transplantation (FMT), a treatment for Clostridium difficile infection (CDI) that aims to restore the gut microbiome. FMT works by indirectly inhibiting *Clostridium difficile* through competition for nutrients. The faecal microbiota prevents the colonization of unwanted microorganisms through the activation of the immune system and the release of specific antimicrobial components and metabolites. These substances inhibit the growth of disease-causing organisms in both their vegetative and sporulated forms (51).

Immunomodulators

Methods that involve antibiotics, probiotics, prebiotics, synbiotics, faecal microbiota transplantation, and nutritional modulators directly affect the immune system of an individual, specifically targeting the innate immunity. Consequently, the alteration in immunological state is impacting the human microbiome in a beneficial manner. Currently, there is insufficient information available regarding this strategy. However, the use of steroids for treating inflammatory illnesses is widely available. The regulation of gut microbiota is accomplished by a variety of processes, including intestinal innate and acquired immunity, as well as systemic acquired immunity. Several factors contribute to the proper functioning of the gut microbiome, such as alterations in barrier function, leptin expression, molecule β, human leukocyte antigen (HLA) class I and class II loci, toll-like receptor activation, natural killer cells, CD4+ cells, Foxp3+ cells, and the production of antimicrobial peptides and α-defensins (52).

Phage therapy

Phage therapy entails the deliberate administration of specific bacteriophages that selectively target a particular microbe, hence inducing a favourable shift in the microbiome. Nevertheless, a drawback of this approach is the concurrent resistance exhibited by the microorganism under consideration, which has not yet been substantiated. As of now, none of the methods used for phage therapy have been officially recognized as a medicine approved by the FDA. Lately, scientists have been diligently researching the use of phages to eliminate microorganisms, however the process is very intricate. CRISPR, which stands for clustered regularly interspaced short palindromic repeats, is a method used to overcome the restrictions (53). This technology is derived from the prokaryotic immune system and is capable of studying and modifying organisms with ease and efficiency. The mechanism facilitates the alteration of the gut genome of gut bacteria and bacteriophages. The modified CRISPR-Cas system has the ability to regulate gene expression and manipulate the synthesis of metabolites and proteins. This presents a novel method for creating medications that can specifically target the microbiome.

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Conclusion

The study of the human microbiome provides a comprehensive understanding of the relationship between humans and their indigenous microbiota, which can be used to combat life-threatening diseases. However, the continuous use of antibiotics can disrupt the microbiota, leading to an imbalance. Probiotic therapy should be encouraged for treating infectious diseases, and further research should focus on the effects of the microbiome on mental health and the impact of mycobiome and virome community on indigenous microbiota. Advancements in this field are challenging, but future research is crucial for understanding the human microbiome's influence on health.

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