International Journal of Scientific Research in Biological Sciences
Vol.**12**, Issue.**1**, pp.**36-43**, February **2025**
E-ISSN: 2347-7520
Available online at: www.isroset.org

Review Article

The Universe of Microbiome and how it Influences our Health Outcomes

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Received: 06/Dec/2024; **Accepted**: 08/Jan/2025; **Published**: 28/Feb/2025 | https://doi.org/10.26438/ijsrbs.v12i1.668

Abstract— The human microbiome consists of bacteria, archaea, viruses, and eukaryotes that inhabit both our internal and external environments. These microorganisms influence human physiology, affecting our health status, and can enhance or impair our metabolic and immune functions. Microbes can be found in many different places in the human body and have adapted to each location. For example, certain types of microbes are more common in the gastrointestinal tract, while others inhabit the respiratory tract, nasal cavity, and skin surface. The microbes that naturally live in the human body have become well-suited to interacting with the immune system over time. Changes in the microbial community in the intestines play a significant role in human health and the development of diseases. These changes can be due to lifestyle or the presence of an underlying disease. Imbalance in the microbiota can make the body more susceptible to infections, with the likelihood of infection depending on which part of the body is affected. The various kinds of microbes found in the human body have different metabolic activities and functions depending on their location. It is crucial to understand the composition and activities of the human microbiome in order to understand the impact on human health and disease.

Keywords— Microbiome, Human health, Immune functions, Gastrointestinal tract, Respiratory tract, Nasal cavity, and skin surface.

1. Introduction

The word microbiome refers to the complex community of microorganisms that inhabit the bodies of all multicellular organisms and various environments, collectively comprising a microecosystem. This review predominantly focuses on the human microbiome. One of the most characterized and studied microbiome components is the human microbiome that inhabits a broad and diverse range of habitats, including but not limited to the gut, oral cavity, skin, and various other niches. The human body is colonized by an extremely diverse and abundant internal microbiota, comprising bacteria, eukaryotes, and viruses, with increasing evidence indicating interplay with antibiotics and micro plasma. Human microbiomes share their essential genetics and have an impact on biological features, encompassing a broad range of systemic functions such as metabolism, immunity, and cognitive brain function.

It has been increasingly recognized that microbiome composition and functionality may show geographical and/or individual variations over diverse environments. At the phyla level, the human gut microbiome is highly dominated by Firmicutes and Bacteroidetes. However, the relative abundances of these two phyla are known to vary across populations and individuals depending on factors such as diet, age, and the use of antibiotics. Microbiome phyla variations have been linked to several health conditions and diseases. In the gut, there is a complex dynamic link between the microbiota and host phenotype. The oral microbiome plays a direct role in local oral disorders and is also relevant to systemic diseases, including type 2 diabetes. A change in skin microbiota can be closely related to various skin diseases, such as atopic dermatitis. This is based on the well-documented evidence of various microbiome correlates with different environmental factors, interindividual variation, and seasonality. In health science, one size fits all does not always get it right.

The exploration of the human microbiome has emerged as a significant area of research, particularly in understanding its profound impact on health outcomes. The literature reveals a complex interplay between the microbiome and various physiological processes, with a focus on the gut microbiota, which is home to a diverse array of microorganisms that contribute to host health in multifaceted ways. In the

foundational work by Singh et al. (K. Singh *et al.*, 2017), the authors elucidate the extensive composition of the gut microbiome, emphasizing the predominance of gram-positive Firmicutes and gram-negative Bacteroidetes. This article highlights the essential roles these microorganisms play in synthesizing vitamins and amino acids, as well as producing short-chain fatty acids (SCFAs) that serve as energy sources for intestinal epithelial cells. The findings indicate that dietary changes can rapidly alter microbial composition, reflecting the dynamic nature of the microbiome and its susceptibility to external influences. Furthermore, the association of gut microbiota with various diseases, such as inflammatory bowel diseases and metabolic disorders, underscores the critical need for understanding microbial interactions within the gastrointestinal tract. Building upon this foundation, Malla et al. (Ahmad Malla *et al.*, 2019) delve into the implications of next-generation sequencing technologies in microbiome research. They emphasize the evolutionary relationship between humans and their microbiota, suggesting that a deeper understanding of microbial diversity can illuminate its role in health and disease. The authors discuss the potential of therapeutic interventions, such as fecal transplantation and dietary modifications, to restore microbial balance and mitigate health issues. Their research highlights the importance of microbial communities in immune modulation and the pathogenesis of various diseases, including anxiety and chronic fatigue syndrome, thus reinforcing the significance of maintaining a healthy microbiome.

In a more recent study, Chaudhary *et al*. (2024) examined the concept of gut-organ cross-talk and the role of symbiotic formulations in enhancing gut health. They address the influence of lifestyle factors on microbial composition, noting that stress and sleep disturbances can disrupt gut microbiota and lead to systemic inflammation. The authors also advocate for a better understanding of microbiome-host interactions to overcome challenges in implementing microbiome-modulating interventions. Their work emphasizes the need for ongoing research to develop effective strategies for harnessing the microbiome's potential in promoting health and preventing disease. Together, these articles illuminate the intricate relationship between the microbiome and health outcomes, highlighting the need for continued investigation into the mechanisms that govern microbial interactions and their implications for human health. The evolving understanding of the microbiome's role in various health conditions paves the way for innovative diagnostic and therapeutic approaches aimed at optimizing health through microbiome modulation.

1.1. Definition and Importance

The human body is inhabited by a complex and diverse assemblage of microorganisms, including those surrounding us as well as some residing in or on humans. The human microbiome consists of all the microbes and their genetic elements. It is estimated that the body hosts a unique microbiome with a distinct, functionally structured community of bacteria, archaea, eukaryotic microbes, yeasts, and viruses. Commensal microorganisms express various dynamic and intricate relationships with the human body, significantly contributing to host metabolism by metabolizing complex indigestible polysaccharides. Human intestinal bacteria ferment these to produce the short-chain fatty acid butyrate, which is important for colon health. They also convert primary bile salts to secondary bile acids in the colon, and they synthesize vitamins, including vitamin K, which is important for blood coagulation. Moreover, the microbiome has been shown to play multiple other roles in immune function and host defense, such as by activating gut-associated lymphoid tissue.

The role of microorganisms in human well-being and health has recently caught scientific and public attention. The influence of a high and diverse microbial load on the body on worsened health outcomes has been continually observed in patients with end-stage cancer. On the other hand, it is well established that sterile environments in high-income countries account for the observed increase in death rates from reactive airway disease in populations aged 5–34, considered one of the top ten leading causes of the burden of chronic diseases worldwide. Hence, keen scientific interest in spotlighting the underpinning of the human microbiome has been on the rise, as well as unveiling how it relates to various other congenital and acquired factors. Dysbiosis, which describes a bacterial imbalance that promotes deleterious changes in the composition and/or function of the microbiota, is said to play a role in different diseases. Ever since the term microbiome was coined as an attempt to describe the ecological community of commensals and pathogens that literally share our body space, researchers have shown strong interest in retrieving clinical information by taking functional measurements of the microbiome. This will aid greater understanding of acute conditions, such as allergies, obesity, cancer, and chronic diseases with autoimmunity, such as type 1 diabetes and Crohn's disease, before it is too late. Researchers began to comprehend how diet and lifestyle, including poor nutrition, alcohol, and pollution, influence these systemic genes. It is this interest that has caused a growing body of reports deeply describing the biological activities of the human microbiome. Personalizing medicine for better outcomes would provide data pertaining to an individual's microbiome metabolic and systematic functional libraries. With the view of the specific health of the individual, all functional data and genes pertaining to various organs relating to diet and immune mechanisms should be read, regulated, and rectified for proper functional support in relation to health outcomes. The microbiome plays a central role in human health and disease. The evidence is growing that it is entwined with many human chronic and acute diseases, including type 1 and 2 diabetes, obesity, autoimmune disorders, asthma, and allergic disorders.

1.2 Related work

The article titled "Influence of diet on the gut microbiome and implications for human health" by Singh et al. (K. Singh *et al.*, 2017) provides a comprehensive overview of the intricate relationship between dietary patterns and the gut microbiome, emphasizing its significant implications for human health. The authors effectively outline the composition of the human gut microbiome, which includes an extensive array of microorganisms, predominantly gram-positive Firmicutes and

gram-negative Bacteroidetes. This foundational understanding sets the stage for exploring how dietary choices can dynamically influence microbial composition and functionality. A critical insight from the article is the identification of distinct enterotypes within the gut microbiome, which are characterized by specific bacterial genera yet exhibit functional uniformity across various host demographics, including age, sex, and body mass index. This suggests that while individual microbiomes may differ, their functional roles in health and disease are remarkably consistent, underscoring the potential for targeted dietary interventions to modify gut microbiota in a beneficial manner (K. Singh *et al.,* 2017). The authors delve into the metabolic contributions of the gut microbiome, particularly the production of short-chain fatty acids (SCFAs) such as butyrate, propionate, and acetate. These metabolites are not merely byproducts of microbial fermentation but serve as critical energy sources for intestinal epithelial cells and play a vital role in maintaining the integrity of the mucosal barrier. This connection highlights the importance of a balanced diet in supporting gut health and preventing disorders linked to microbiome dysbiosis. Moreover, the article presents compelling evidence from studies using germ-free mice, illustrating that the microbiota enhances local and systemic immunity. The modulation of immune responses through various mechanisms, including the expression of toll-like receptors and the activation of T cells, points to the gut microbiome's role as a key player in immune regulation. This aspect of the research is particularly relevant given the rising prevalence of autoimmune and inflammatory diseases, which have been associated with alterations in gut microbiota composition (K. Singh *et al.,* 2017). The rapid adaptability of the gut microbiome to dietary changes is another critical finding. The authors report that significant shifts in microbial composition can occur within 24 hours of dietary modification, with a return to baseline within 48 hours of diet cessation. This rapid response underscores the potential for dietary strategies to be employed as therapeutic interventions for various health conditions. Additionally, the article discusses how high-fat or high-sugar diets can disrupt circadian rhythms in the microbiome, further linking dietary habits to broader aspects of health and metabolic regulation.

Finally, the article highlights the associations between gut microbiota and several diseases, including inflammatory bowel diseases, autoimmune disorders, obesity, and atherosclerosis. These connections reinforce the notion that the gut microbiome serves not only as a mediator of dietary effects but also as a determinant of health outcomes, warranting further investigation into microbiome-targeted therapies. The article "Exploring the Human Microbiome: The Potential Future Role of Next-Generation Sequencing in Disease Diagnosis and Treatment" by Muneer Ahmad Malla et al. (Ahmad Malla *et al.,* 2019) provides a comprehensive overview of the human microbiome and its significant implications for health outcomes. The authors emphasize the intricate relationship between humans and their microbiota, highlighting that the microbial community within the human body outnumbers human cells. This symbiotic relationship has evolved over millions of years, underscoring the microbiome's critical role in maintaining human health. A central theme of the article is the diversity of the microbiome, particularly within the gastrointestinal tract. The authors detail how this diversity varies among individuals and how it is essential for normal physiological functions. The microbiome contributes to digestion, bolsters the immune system, and acts as a barrier against pathogenic invasions. The article effectively illustrates the concept of dysbiosis, where an imbalance in the microbial community is linked to various health issues, including chronic fatigue syndrome, cancer, and mental health disorders like anxiety and depression. The authors also discuss the potential of next-generation sequencing technologies in advancing microbiome research. By deciphering the composition and functional properties of the microbiome, researchers can gain deeper insights into its role in health and disease. The article suggests that understanding these microbial communities could lead to innovative diagnostic and therapeutic strategies, such as fecal transplantation and dietary interventions, which have shown promise in modulating the microbiome and addressing health-related problems.

Furthermore, the article highlights the microbiome's influence on immune responses, particularly through the modulation of Treg cells. This aspect is crucial, as it suggests that gut microbiota not only aids in digestion but also plays a pivotal role in immune tolerance, indicating a complex interplay between the microbiome and the host's immune system. The article titled "Does 'all disease begin in the gut'? The gut-organ cross talk in the microbiome" by Chaudhary, Kaur, and Myles presents a comprehensive exploration of the intricate relationship between the gut microbiome and overall health outcomes. The authors emphasize the significance of synbiotic formulations, which integrate prebiotics and probiotics, in fostering gut health. This dual approach not only supplies essential substrates for microbial fermentation but also introduces live beneficial bacteria that can enhance microbial diversity and functionality. A critical aspect of the article is its discussion on lifestyle factors, such as stress management, regular exercise, and sufficient sleep, which are highlighted as pivotal in maintaining gut health. The authors present a compelling argument that chronic stress and sleep disturbances can lead to dysbiosis—an imbalance in the gut microbiome—resulting in gastrointestinal symptoms and systemic inflammation. This connection underscores the necessity of a holistic approach to health that considers both microbial and lifestyle factors. Chaudhary et al., (2024) also addresses the impact of aging on the microbiome, noting that elderly individuals often exhibit significant alterations in microbial composition. These age-related shifts can influence not only gut health but also the health of other microbiome sites throughout the body, illustrating the interconnectedness of the microbiome ecosystem. However, the article does not shy away from discussing the challenges associated with developing interventions aimed at modulating the microbiome. The authors highlight the complexity and diversity of the human microbiome, which complicates the creation of universally applicable treatments. The lack of standardized protocols regarding dosage, duration, and administration methods further complicates the

implementation of effective interventions. Additionally, the limited understanding of microbiome-host interactions raises safety concerns about potential adverse effects, which could hinder public acceptance and adoption of microbiome-based therapies.

The article effectively calls for ongoing research to deepen understanding of the microbiome and to develop safe, effective, and accessible interventions. It emphasizes the importance of recognizing the bidirectional communication between the gut and other microbiomes, which influences physiological processes, immune responses, and susceptibility to diseases. This perspective is pivotal in unraveling the complexities of human health and disease, suggesting that a thorough understanding of these microbial communities is essential for advancing health outcomes.

2. Microbiome Diversity

Any microbial community inhabiting a specific environment is called a microbiome. For example, humans harbor microbiomes that are quite different from each other, prescribed by the body parts inhabited by them (e.g., the skin, genital tract, and gut microbiomes are different), as well as by external factors such as geographical location, lifestyle, diet, and so forth. Various microbiomes also inhabit different environmental ecosystems, like the soil, air, and water, and can include archaea, bacteria, fungi, parasites, and viruses together with their phages (Sharon *et al.,* 2022) (Manos, 2022) (Sepich-Poore *et al.*, 2021). One of the most salient features of microbial communities is their incredible diversity, i.e., the numbers of different species—estimated to be between 10 to 100 million—divided into more than 1000 different bacterial phyla that make up the many habitats and environments on Earth (Hoshino *et al*., 2020) (Rubin *et al*., 2022) (Dueholm *et al.,* 2022). This diversity is also found in humans, as revealed by the human microbiome projects. Indeed, the makeup and composition of an individual's microbiome differ within one group to another and vary among nations.

Microbial diversity, especially in the human gut, is thought to positively impact health. For instance, a diverse microbiome helps in the easy access to a cumulative gene pool responsible for metabolism, respiration, and colonization, meaning the mixture and variation of many genes can give a wide variety of metabolic pathways by which resources are adapted. Preserving diversity, for example, can help maintain a population whose members have varied features, thus enabling some individuals to respond adaptively to future change. Microbial diversity allows for the competition by diverse beneficial bacteria against pathogens and parasitic bacteria, with pathogens failing to establish and then becoming transitory members of a larger, stable community rather than taking over and crowding out beneficial bacteria (Gomaa, 2020). Conversely, disease is correlated with a decrease in diversity, with the composition of the gut microbiome being skewed and the beneficial bacteria replaced by enormous numbers of pathogens and other dysbiosis. This could be associated with various disorders, such as colitis and irritable bowel syndrome, metabolic diseases, autoimmune diseases, and neurological mental health dysfunctions (Fousekis *et al.* 2021) (El-Hakim *et al.,* 2022). For this, the determination of educational microbiome diversity and whether additional resources can be recruited to diversify the organ should be used to improve therapies in the future. Metagenomics and sequencing technologies assist large-scale genomic studies to reveal which microorganisms are primarily present in the different human microbiomes.

The gut microbiome is believed to establish after birth and is influenced by genetics, diet, and antibiotics. It primarily consists of two major bacterial gut microbiomes, namely Bacteroides and Firmicutes, thus showing both functional redundancy and novelty (Konstantinidis *et al.,* 2020) (Fishbein *et al.,* 2023). It was also found that different body parts, for example, were inhabited by different microbial residents than the gut microbiome. While in the oral cavity, the microbial residents were derived from the intake of food, in the vagina, they were primarily derived from the fluid secreted in the tract that builds up to form an umbilical cord for the baby. Host and lifestyle factors like the use of medication or the frequency of inserting tampons that smooth the passage of microorganisms from the external environment into the body could influence microbiome composition in the different body habitats or parts, e.g., the gut and vagina, or the skin, oral, and urethral mucosa. In addition, illnesses like cancer appear to drive changes within certain human microbiomes.

2.1. Factors Influencing Diversity

Diversity in the microbiome is influenced by a myriad of factors. Some of these are intrinsic to a particular environment, defined by the host that they inhabit, while others are extrinsic within that environment. At a broad level, factors such as genetics that make a person individual and vary from person to person play a crucial role in providing the initial instruction for the colonization and evolution of unique microbial communities within and on our bodies. Each host's immune system that responds to microbiota also evolves to take on the features of its surroundings, and by way of such adaptations, it indirectly influences the richness and structure of the local microbiota. Of the extrinsic factors, variations in host diet, lifestyle, antibiotic use, and hygiene are those that are most notable in research studies.

Early life exposures can provide a blueprint for the development of host physiology and the likelihood of developing chronic diseases later in life. The mode of birth affects microbial diversity for the first few years of life, impacting the ability of the infant to become a healthy adult. Birth via cesarean delivery is the first exposure to life and has been associated with numerous adverse health outcomes including allergy, asthma, and obesity. Intuitively, a child born via cesarean is exposed to fewer microbes than a child born vaginally, as the birthing canal is essentially a canal filled with bacteria providing the neonate with an antibody-rich environmental bath. Similarly, breastfeeding provides valuable compounds that further develop the nascent immune system. The Westernized lifestyle with limited birth

techniques may have deficits in health if that infant does not acquire a healthy, functioning microbiome. Emerging evidence has shown that diversity may have an important role in protecting our bodies from developing disease states.

3. Microbiome-Health Connection

Healthy humans host a diverse community of microorganisms in various anatomical sites of the body, such as the gut, the respiratory tract, the reproductive organs, and the skin. The total number of microorganisms collectively referred to as the microbiome outnumbers human cells by at least one order of magnitude. Despite minor quantitative differences among individuals, there is a hierarchical core of microorganisms that mainly contribute to the composition of the human microbiome. Acquisitions of these microbial communities begin shortly after birth and continue throughout an individual's entire life. Importantly, the microbiome interacts with the host at different biological levels, such as the molecular, cellular, and organ systems, which, in turn, influence various physiological functions of the latter. Different pathways are responsible for this communication, such as the production of microbial compounds, the immune response, and the nervous system, and several of these functions are being intensively studied. Importantly, several studies associating the microbiome with alterations of the immune system, adipocyte metabolism, and gut homeostasis considerably enriched our view of the involvement of these microorganisms in the mechanisms underpinning several health outcomes, including overweight, obesity, diabetes, allergies, and autoimmune diseases.

The immune system is one of the most complex subjects studied in connection with the human microbiome. Several lines of evidence show a strict relation between the composition and abundance of particular microbial communities and the function of the immune system. Indeed, the microbiome is now considered an integral player in the ontogenesis of the immune system, and dysbiosis has been supposed to be one of the main causes of various diseases, such as type 2 diabetes, metabolic diseases, allergies of all types, asthma, degenerative and malignant pathologies, and neurodegenerative diseases. Moreover, the immune system is largely responsible for homeostasis and the maintenance of a "healthy status" of the host. Of interest, the immune system does not operate solely as the final line of defense of higher anatomical and physiological levels but is also able to communicate with more central pathways, such as those related to neurotransmission and hormonal systems. The microbiome is strictly involved in both of these aspects. Indeed, the first contact the newly developed immune system has been with these microorganisms, which will help proper maturation of lymphocyte lineages according to final immune-differentiation status or may even suppress immune maturity, thus mirroring the immune-escape pathway followed by various microorganisms.

3.1. Impact on Immune System

The impact of microbiota on the immune system is massive and can be divided into two major outcomes: immune tolerance and immune responses. In recent decades, a large number of research studies have shown that a diverse microbiome is beneficial for immune system development and function, including immune tolerance, gut immune responses, the gut-brain axis, immune system surveillance, and resistance to tumor development. It is very interesting that numerous research studies have demonstrated that exposure to different types of microorganisms plays a critical role in the programming, recruitment, and lifespan of different subsets of innate and adaptive immune effector cells. The interaction between different types of bacteria, especially gram-negative and gram-positive bacteria, and pathogen-associated molecular patterns or vaccine antigens occurs via different signaling pathways in a direct way or through the molecules.

In early life, commensal microorganisms have been shown to promote immune tolerance to food and airborne antigens by stimulating the development of different Tregs through increasing the secretion of Th2 cytokines, type 1 interferons, the alarmin IL-33, retinoic acid, or the differentiation of IL-10-secreting regulatory B cells. Dysbiosis, or a decreased diversity or richness of commensal microorganisms or a decreased abundance of probiotics in the gut, might lead to immune-related disorders, including allergies, autoimmune diseases, and inflammatory chronic diseases. Different types of prokaryotes have been shown to modulate immune functions directly by either promoting the secretion of pro-inflammatory cytokines or reducing the secretion of pro-inflammatory cytokines. Rescue of dysbiosis has been shown to decrease T cell dysfunction and eliminate the anti-tumor effect. Immune-related disorders have been shown to be reversible after fecal microbiota transfer therapy. Probiotics or prebiotics play a beneficial role in modulating immune responses through treatment.

4. Microbiome Modulation

The microbiome can be influenced by various strategies that interact through different mechanisms to alter the composition and activity of the microbial communities with the goal of improving health outcomes. The microbiome has emerged as a compelling interdisciplinary subject with substantial translational potential. Alimentary interventions remain one of the most effective management strategies for the modulation of the microbiota, largely due to their direct interaction with the gut. Regular or moderate consumption of some fermented foods has been related to positive health outcomes, while individuals who consume food with added fibers have been shown to have a higher gut microbiota diversity.

Probiotics are live microorganisms that, when administered in adequate amounts, confer a health improvement on the host. Probiotics exhibit health advantages such as boosting microbial populations that have been linked to various health outcomes, modulating immune function, possibly causing pathogen inhibition, and overall contributing to the maintenance of the balanced enteric ecosystem. A prebiotic, on the other hand, is a selectively fermentable ingredient that

enables the greater abundance of beneficial or commensal microorganisms. One of the most well-studied prebiotics is beta-glucans, which have been shown to both enhance gut barrier permeability and modulate immunity. In health management and therapeutics, it is necessary to include, as well as avoid, practices that impact the microbiota. Over time, numerous disorders may develop from changing the composition and function of the gut microbiome in a non-intentional manner. Unnecessary interventions, antibiotics, and food contaminants are examples of aspects to be avoided. Cutting-edge technology and constant evolution in new treatment options have brought about the emergence of potential optimal therapeutic interventions. Although this idea remains in the experimental stage, the cure of specific conditions, particularly those linked to the microbiome, will be a huge structural change moving forward. In the near future, transplanting the gut microbiota is anticipated to be the focus of off-the-shelf terminologies and business development.

4.1. Dietary Interventions

A key method to modulate the composition of the gut microbiome is diet. There is strong evidence to show a direct relationship between diet and microbiome composition. Different dietary patterns are associated with positive effects on microbiome composition, such as promoting microbial diversity, increasing the abundance of beneficial bacteria including Bifidobacterium and Lactobacillus species, and improving health outcomes (Bolte *et al*., 2021) (Beam *et al.*, 2021) (Dahl *et al.*, 2020). Many plant-based dietary approaches rich in fruits, vegetables, fiber-containing food sources, and whole grains are beneficial. These food groups are high in prebiotics, indigestible fiber that can be fermented by the gut microbiota to produce short-chain fatty acids, which provide a range of physiological benefits. In contrast, the typical Western diet, high in processed and ultra-processed foods often containing high sugar content and high glycemic load, shows a negative impact on the gut microbiota (Sidhu *et al.,* 2023) (Miao *et al.*2022) (Toribio-Mateas *et al.,* 2021). Some further evidence has suggested that a beneficial effect of a low-carbohydrate diet may be short-lived, with concerns raised that long-term consumption of a ketogenic diet could have a detrimental effect on microbes that have been shown to either promote health or have no defined impact.

These interactions can be specific and varied based on an individual's experience, environment, and health status, thus highlighting the rise of personalized nutrition and recommendations based on the richness and diversity of an individual's microbiota. Recent studies exploring the impact of different diet types found a response to either plant-based, Mediterranean-style, or ketogenic diets, in that Bacteroidetes were increased in abundance after ketogenic and Mediterranean diet interventions, and Actinobacteria, Bifidobacterium spp., and Lactobacillus spp. numbers were all increased (Mancin *et al.,* 2022) (Deledda *et al.,* 2022) (Güzey *et al.,* 2024). A further review classified a positive, neutral, or negative response to dietary interventions and resulted in the same conclusion, suggesting the need for personalized approaches and the poor availability of robust data linking dietary strategies with microbiome profiles. Given the link between diet and gut health, the potential benefits of personalized dietary plans could be extended beyond gut health and targeted at diseases that may be mediated by the gut, such as through an impact on the gut microbiota (Wolter *et al*., 2021) (Yeşilyurt *et al.,* 2022) (Fitzpatrick *et al.,* 2022).

5. Conclusion

The exploration of the human microbiome has revealed its significant impact on health outcomes, particularly through the intricate relationship between the gut microbiota and various physiological processes. The foundational work by Singh et al. (K. Singh *et al.,* 2017) elucidates the composition of the gut microbiome, emphasizing the predominance of gram-positive Firmicutes and gram-negative Bacteroidetes. These microorganisms are crucial in synthesizing vitamins, amino acids, and short-chain fatty acids (SCFAs), which serve as energy sources for intestinal epithelial cells. The rapid adaptability of the gut microbiome to dietary changes highlights its susceptibility to external influences and its role in health and disease. Malla et al. (Ahmad Malla *et al.,* 2019) build upon this foundation by discussing next-generation sequencing technologies, which enhance our understanding of microbial diversity and its implications for health. They highlight the potential for therapeutic interventions, such as fecal transplantation and dietary modifications, to restore microbial balance and address health issues. The authors emphasize the importance of microbial communities in immune modulation and disease pathogenesis, further reinforcing the significance of maintaining a healthy microbiome. Chaudhary *et al.* (2024) examined gut-organ cross-talk and the role of symbiotic formulations in promoting gut health. They note that lifestyle factors, including stress and sleep disturbances, can disrupt gut microbiota and lead to systemic inflammation. The authors advocate for a comprehensive understanding of microbiome-host interactions to develop effective strategies for harnessing microbiome potential in health promotion and disease prevention. Collectively, these articles underscore the intricate and complex interplay that exists between the microbiome and various health outcomes. Highlighting the necessity for continued and thorough research into the diverse microbial interactions and their profound implications for human health. This understanding paves the way for innovative diagnostic and therapeutic approaches that are specifically aimed at optimizing health through thoughtful microbiome modulation and manipulation, which can ultimately enhance well-being. By integrating advanced genomic technologies and personalized medicine, we can harness the potential of the microbiome to not only prevent disease but also foster a more resilient and healthier population. This approach not only enhances our understanding of individual health profiles but also promotes the development of targeted therapies that can optimize health outcomes based on unique microbiome compositions. Ultimately, by acknowledging the intricate relationship between the microbiome and our overall health, we can take

significant strides towards personalized medicine and preventative health strategies. This understanding paves the way for innovative treatments that are tailored to individual microbiome profiles, ultimately enhancing our ability to combat diseases and improve health outcomes.

6. Future Directions in Microbiome Research

In order to understand the functional features of the microbiome in the context of human health, considerably larger and longer-running hypo- and normative studies must be carried out across all life stages and different populations with deep additional omics and phenotyping. The speeding up of this area of research will be driven by exploiting the state of the art in high throughput meta sequencing technologies, use of multi-omics and bioinformatics platforms, and integration of online national and international datasets. It is equally vital that translational programs are run to test some of the theories and hypotheses that are coming up from bioinformatics and sequencing analyses in the laboratory and, hopefully, introduce population-based controlled studies. Typically, the therapeutic approaches enunciated here lean towards modulation of the microbiome potentially via drugs with improved delivery systems or exploitation of the systemic effects of microbiome metabolites, broad-spectrum vs. tailored probiotics, and dietary intervention. Hence, interdisciplinary thinking linking physical and mental health with environmental, social, and cultural factors must prevail. It is hoped that a 7Ps approach, as expounded before, with participation, prevention, population studies, personalization, prediction of ill health and its progression to drive cost-effective precision-based prevention and treatment could be a foremost aim. The compilation of this special issue, reflecting just some of the many areas where microbiome-brain state and functioning interact, should provide the data needed to set up clinical investigative studies.

Data availability statement: Data sharing is not applicable to this article, as no new data were created or analyzed in this study.

Conflict of Interest: The authors have declared that no competing interests exist.

Funding source: NA

Author's contribution: Conceptualization by JN. And original draft preparation by JN, review and editing AG and PK. All authors have read and agreed to the published version of the manuscript.

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