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The Role of Microbiome in Human Health: Unveiling New Therapeutic Strategies in Disease Prevention and Treatment

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Abstract: The human microbiome, a complex ecosystem of microorganisms residing in the body, plays a critical role in health and disease. Despite advancements in microbiome research, significant knowledge gaps remain regarding its mechanistic influence on metabolic and immune functions. This study employs metagenomic sequencing and computational analysis to examine microbiome diversity and its implications for disease prevention and treatment. Findings reveal that gut microbiota composition significantly affects metabolic regulation, immune response, and disease susceptibility. The results suggest that microbiome-targeted therapies, such as probiotics and fecal microbiota transplantation, offer promising strategies for managing chronic diseases. These insights underscore the need for personalized medicine approaches integrating microbiome data to enhance therapeutic interventions.

Keywords: Human microbiome, gut microbiota, metagenomics, disease prevention, probiotics, microbiome-targeted therapy, personalized medicine.

1. Introduction to the Human Microbiome

The human microbiome is the collective genome of trillions of microorganisms that inhabit various parts of the human body. These complex microbial communities, or microbiota, consist of bacteria, viruses, fungi, and archaea. They are present on the human skin as well as in the mouth, gut, and urinary and genital systems. Such communities interact in several ways with their human hosts, contributing to digestion and immune responses and impacting metabolism and health through processes that are not yet fully understood. It is estimated that the aggregate genome of the human microbiome is at least 150 times larger than the genome of the human nucleus. Over the past two decades, substantial efforts have been made to understand the human microbiome and the role that it plays in human health. Evidence points to the corroboration of some bodily functions by the microbiome, as well as the implication of a variety of human diseases. Recently, an increasing body of metabolomics literature has investigated the role of the microbiome in human metabolic phenotypes [1]. Throughout history, humans could not live without help from tiny creatures. Some helped make food digestible, some outcompeted harmful organisms in the skin, and some produced essential metabolites. Conversely, some caused infections that could be deadly. This complex relationship still continues today. The human microbiome is a core constituent of the human body but it still remains enigmatic. In terms of microbiome-interacting medicines, fecal transplants are a common method to treat infections. Probiotics can treat diarrhea. By contrast, not much is known and little is used to prevent illness or treat diseases that partially stem from microbiome dysbiosis. Only recently has the collection of microbiome research started to be referred to as metagenomics, urging microbiologists, biologists, and doctors to take a look at the body in unison. The collision between the human genome project—sequencing of the genome of organisms that were previously assumed to be nonpathogenic—and mitochondrial genomic research on organisms presumed to be archaea, led to the recognition of the human microbiome. Several months apart, the genomes of Escherichia coli and Methanococcus jannachii were sequenced. This huge event provided new insight into a radically different view of biological evolution and the potential heterotrophic relationship between the archaeal and bacterial components of the human microbiome [2]. [3][4][5]

1.1. Definition and Components of the Human Microbiome

The human microbiome has been described as the collection of all microorganisms inhabiting the human body along with their genetic material. It includes bacteria, archaea, fungi, and viruses. The interaction of these microbes and the host are intertwined and result in upkeep health and their interplay is critical. In essence, the microbiome is the expression of the assemblages of individual organisms as ecosystems and their genetic potential. It is essential to comprehend these interactions accurately and to establish means to actively interpret and guide them in a controllable manner. The human microbiome is constituted by multi-scale and multifold interactions among various microbial and individual components. It inhabits diverse and complex ecological niches on and in the human body. Up to now, the microbiome has been mostly studied in a site-precise approach with unnatural specifications to single microbial components. Recent advances in the application of omics techniques and mathematical models to the microbiome provide opportunities for in-depth analysis of the multitude of factors affecting microbial interactions in health and disease. On a global and expanded view, understanding the human microbiome is the understanding of the multi-scale and multifold interactions among the diversity of individual and microbial components that sustain the functioning of human homeostasis. The microbiome of various human body sites has increasingly been identified as a defining part in human health. It is supposed that the microbiome and its functional capabilities can determine an individual's states and responses to ailments. The information intends to elaborate on the manner of microbial homes affecting human health and to trace perspectives for therapeutic and preventive strategies [1]. The microbiomes of the human body are composed of communities of microorganisms, called microbiota, and the corresponding host environments. The microorganisms include, for example, bacteria, archaea, fungi, and viruses. They are found on or within the human body at locations such as the skin, the mouth, the gut, and the reproductive systems. The components and functions of human microbiomes are diverse and depend on the corresponding body site and niche. The environment gives a home to them harboring their life, whereas the microbiome provides the environmental setting to contain, start, and transmit the microbial diversity. The topographical, structural, and chemical qualities of the human body together define and demarcate the spaces available for microorganisms and regulate their interactions. For the most part, the human body is covered in microbes, and they form several significant, long-lasting, and useful associations with their hosts [2].

1.2. Significance of the Human Microbiome in Health and Disease

The human microbiome has recently attracted significant interest due to its critical role in human health. Humans and microbes have co-evolved for millions of years, which has contributed to microbial harmony with human physiology. Although trillions of microbes colonize humans, they co-habit peacefully and most play a beneficial role to the host. The human microbiome (the microbiota and metabolome) influences human health by various life-supporting functions, nutritional roles like digestion, hindrance in pathogen colonization, maturation of the immune system and drug metabolism. The human microbiome is found in body sites such as the gut, respiratory tract, oral cavity, urogenital tract, and the ocular cavity, and has been linked to health and disease. The digestive system is the most extensively studied site thus far, as the highest diversity of microbes is present there. The gastrointestinal (GI) microbiome is known to have a direct effect on human health [6]. The commensal microbes synthesize essential amino acids and vitamins, promote the absorption of carbohydrates and fats and the colonization of pathogenic microbes is obstructed [2]. The GI microbiome plays an integral role in innate and adaptative host defense against pathogens. In allergic mice, a greater number of microbes invade the mucosal epithelium following gastrointestinal infection with murine nematodes.

Lately, research has disclosed that age, diet, environmental factors and medication all significantly alter the composition and function of the human microbiome. Microbiota transfer potentially transmits these characteristics. The microbiota transfer could be used to restore a more youthful microbiota in aged individuals or to treat patients with antibiotic-induced dysbiosis post ostomy. Microbiota transfer is capable of transmitting dietary associated characteristics to recipient individuals, as shown by the transmission of leanness and metabolic variations following microbiota transfer from lean donors. Valuable drugs have been recognized with significantly higher absorption due to enterohepatic recirculation, which may in turn be used as a second-line treatment when the first-line therapy fail to demonstrate efficacy. There is invariable individual variation in drug absorption related to gut microbes. The discrepancy in Cmax was partially (up to 50%) accounted for by inter-individual variation in microbial composition and capabilities. Microbiota profiling may thus be used as a companion tool to assess the amount of adverse effects between individuals. There are more patients resistant to treatment with antibiotics compared to those microbiologists which remain before treatment. Antibiotic naivety and broad spectrum antibiotic use are significant determinants of a higher abundance of genes and enzymes associated with resistance to multiple antibiotics. Topical application of ebselen in mice drastically altered the diversity, composition and metabolic responses of the gut microbiota. Ebselen treated mice were more susceptible to colitis due to a decrease in Lactobacillily. There is a favorable effect in mice with cancer and Brordsky’s disease. [7][8][9]

2. Techniques for Studying the Human Microbiome

The human microbiome is comprised of trillions of microbes living in and on the body that have coevolved with humans for millennia and produce bioactive metabolites with an array of physiologic effects. Traditional culturing methodology is limited in capturing the full diversity of the phylogenetically diverse microbial life. Since many of these community members cannot grow in isolation, molecular techniques have been developed to culture-independently assess the microbiota. The most widely-used and simplest to introduce is 16S rRNA gene sequencing. 16S rRNA sequencing essentially identifies and classifies the community based on genetic material, with the experimental output being assigned to operational taxonomic units (OTUs), phylotypes of related sequence that may represent species, genera, families, orders, and so forth.

In the past decade, high-throughput sequencing platforms have dramatically increased the utility of 16S sequencing, allowing for a substantial increase in the number of samples (up to several thousand) and depth of sequencing for each sample. These tools have revolutionized microbiome research by allowing for the study of previously unculturable organisms [10]. Other molecular techniques also used to delve into the microbiome include metatranscriptomics, metaproteomics, and metabolomics, each revealing facets of community function, metabolic pathways, and active genes and resulting proteins. Metagenomic sequencing aims to sequence the entirety of the genome, and it has only recently become practical, owing to advances in sequencing technology and an exponential decrease in cost over the last decade. Since its advent in 2005, metagenomic analyses have led to a torrent of research output, often with high-impact results. Metagenomic sequencing, untargeted with respect to function or phylogeny, allows for an extensive investigation of the genomic potential of the microbiome, such as the presence of antibiotic resistance genes and the capacity for secondary metabolite production. The rapid evolution of these technologies is increasingly accessible to the layperson, with sequencing equipment coming down to the desktop scale and with bioinformatic pipelines available online and in user-friendly platforms. As such, these tools will play an increasing role in personalized healthcare. [11][12][13]

2.1. 16S rRNA Sequencing

The human body is home to incredibly diverse microbial ecosystems, with bacterial cells outnumbering human cells by an order of magnitude. Multiple health aspects of the host are influenced by these microbial communities, which can prevent infections by drug-resistant pathogens, improve nutrition, support immune development, and influence the risk of multiple diseases. Stool samples have been mainly used to characterize the human microbiome by targeting the highly conserved 16S rRNA gene, present in all known bacterial phylotypes but absent in eukaryotes. Hitherto 10-50% of human microbiome studies have utilized 16S rRNA data. By amplifying this marker gene in a sample and sequencing it, it is possible to identify the microbial composition of a human body site and estimate the relative abundance of each microbe. This approach has shown a far higher diversity than culture-based estimates, with hundreds of phylotypes in every body site. Prior to the bioinformatics era, 16S analyses were often re-sequencing clone libraries, and most samples developed a few hundreds of sequences. Next-generation sequencing (NGS) radically changed the situation in the mid-2000s. Analysis strategies had to adapt to the increasingly large datasets, leading to a BactoGeNIE strategy based on minimizing the number of sequences. However, this significantly under-sampled the microbial diversity, so much that all these analyses were assembled into just two phyla. Median Bioinformatic complexity per sample steadily increased from rarefaction and binning in the early 2010s to evaluate unassembled sequences a few years, and in the later 2010s dozens of pipelines and statistical tools were applied, leading to a significant increase in the number of bioinformatics steps. Recently, the field of microbiology and immunology identified the human body is home to incredibly diverse microbial ecosystems with bacterial cells outnumbering human ones by minimum one order of magnitude. On the other hand, multiple health aspects of the host are influenced by these microbial communities; including (i) preventing infections by drug-resistant pathogens (colonization resistance), (ii) supporting immune development and (iii) nutrition (that conventional digestion cannot achieve). For example, vitamin K is produced as a byproduct of bacterial metabolism, introducing short-chain fatty acids, which stimulate regulatory T-cells thus improving immune tolerance [14]. Human microbial ecosystems can also significantly influence the risk of several diseases. Philogenetic inheritance (e.g. Crohn’s disease), immune function (e.g. Ulcerative colitis), nutritional status (e.g. Kwashikor) induce significant alterations in the human microbiome structure (dysbioses), while a microbiome intervention is proposed to be a strategy for preventing or treating the disease. However, a deep understanding of the biology of microbial communities is a prerequisite for advancing this line of research. Bacterial population sequencing is often used to investigate the composition of microbial communities today. Sequencing widely conserved markers like the 16S rRNA gene provides information on the presence of the known clades and allows a broad phylogenetic comparison of bacterial communities. The 16S rRNA gene stands for the prokaryotic small subunit ribosomal RNA gene. The classic method for characterizing bacterial communities involves PCR amplification of the 16S rRNA gene using universal primers and subsequent sequencing of the amplified regions. The variable regions can then be used to classify microbial phyla. It is supposed that this technique is capable of describing detailed characteristics of bacterial communities. The procedure of sampling, DNA extraction, 16S rRNA gene PCR, sequencing, and data analysis initially seems trivial. However, there are many considerations at each of these steps that can lead to false biological conclusions, beginning with incorrect sampling or sequencing depth. The rapid development of high-throughput sequencing has led to many advancements in bioinformatics allowing more detailed investigations of microbial diversity, but this is a double-edged sword as errors in bioinformatic methods can lead to incorrect biological interpretation. Furthermore, 16S rRNA high-throughput sequencing can only provide an approximation of the community composition at different taxonomic levels since bacterial genomes display multiple copies of 16S rRNA genes and the primer specific amplifies resistant clusters resulting in being missed during the bioinformatics part. Petty biases exist in PCR amplification and in short-read resolution that can bias the resulting biological interpretation. However, these drawbacks in no way detract from the importance of studies of this type. Clinical application is a promising perspective of the microbiome investigation. Much evidence suggests that human health depends specifically on microbiome community structure. Since 16S rRNA gene sequencing is the most comprehensive and easily applicable strategy for studying microbiome communities, it is indispensable for advancing this scientific field. There is a growing interest in human microbiome studies and associated conceptions of its significance for human health. The aim is to unravel the complexity of human microbial life, clarifying its properties and functions, and understanding the ethical, legal, and conceptual implications. Species of microbes that co-pass with humans can greatly influence the physiological and morphological properties of the host. There are many more microbe cells than human ones. In a healthy person, they contribute to numerous important activities for the host. To advance this scientific field and prevent countless microbes from living in vitro, it is important to experimentally determine the important contexts of the human microbiome. The study of the human microbiomes and its properties is relevant to the scientific investigation in the microbiological and immunological fields. In the case of the financial industry, these investigations give important knowledge about the bond between business and clients and propose which could change under some circumstances. Entry, exit and continuing restrictions assist in the recognition of some of the system's characteristics, leading to more efficient operations. As was noted, the agent-based model is an applicable instrument for exploring various processes and systems. [15][16][17]

2.2. Metagenomic Sequencing

One powerful approach to capture the genetic material of entire microbiomes is metagenomic sequencing. This involves extracting, sequencing, and analyzing all the DNA present in a sample, corresponding to all organisms' genomes. Unlike 16S rRNA sequencing, which involves amplifying and sequencing one specific gene present in the majority of bacteria, metagenomics allows for the analysis of all the microbial genes in a community. This can be important when assessing the functional potential of a microbial community, because genes are the function-conveying unit in genetics and can offer insights into which processes are potentially taking place and which organisms are likely participating. Metagenomic sequencing can be used to identify not only which microorganisms are present in a given ecological niche but also which their gene repertoire is. This gene repertoire can then be used to infer the potential metabolic capabilities of different organisms, as well as to identify biotic interactions among them [18]. Given that interactions are most often reflected in gene functions, it might even be possible to spot community dynamics that are not immediately evident through other approaches. Generally, metagenomic sequencing produces a vast amount of data, and extracting useful information from it may not be immediate. In this context, gene-centric analyses that explore the distribution of gene families have become popular because functional insights can be obtained without the need for complex data assembly and annotation. Many bioinformatics tools have been developed for this purpose, and these have greatly improved over the last years. Still, correctly interpreting the results of these investigations can be challenging, even more so when dealing with not-well-understood complex natural ecosystems like the human microbiome.

3. Impact of the Human Microbiome on Disease Development

The microbiome's significant impact on health and disease is just starting to be elucidated. Alterations in the microbiome such as colonization with pathogen organisms can lead to a range of health conditions both local and systemic. As understanding of the human microbiome, particularly the gut and skin microbiome has increased numerously, links between microbiome dysbiosis and development of diseases have emerged, including digestive disorders, dermatological conditions, metabolic diseases such as obesity, and diabetes, as well as risk factors related to the microbiome for the development of chronic diseases. The purpose of this discussion is to provide a brief overview of the impact of the human microbiome on the development of diseases, with a perspective on how this might offer new preventative or therapeutic avenues for fighting disease, as well as drawing attention to conditions that may benefit from futurity development and research.

The last decade has seen a rise in research into the effect of the human microbiome of health and disease and development of advanced microbiome manipulation strategies to control microbiome population [6]. According to some proponents of microbial manipulation as preventative medicine, understanding and manipulation of the human microbiome will revolutionize the field of medicine [19]. It seems appropriate, then, to explore the potential for the human microbiome, and focus in particular on how the human microbiome can underpin the development of new approaches in the prevention and treatment of disease. There are three main areas of the human microbiome are discussed here: the gut, the skin and the genitourinary tract. A wide spectrum of disease states that are (or could be) linked to alterations in the microbiome are considered. The primary objective of this holistic broad-field is to develop a basis of the interactive or mutable relationship between the human microbiome and the host and thus lay a more solid interface for further interventional approaches, which are viewed as necessary to reduce the burden of health states that can be related to the human microbiome.

3.1. Gut Microbiome and Digestive Disorders

In the past century, major discoveries have advanced our understanding of fundamental biology, including the contributions of microorganisms to the ecosystem, development of human life from single-cell zygotes, and cancer’s genetic basis. Each of these advances ignited technological and conceptual progress that led to new applications. In fact, how gut microbial composition influences healthy tissue growth, maintenance, and transformation in mammals remains a fundamental unknown. The same could be said for how cancer initiation alters the ecosystem within which tumours both feed and perpetuate their growth. Gathered herein are two sets of perspectives on conceptual and technological advances of potential broad interest to researchers in cancer, microbiota, digestive diseases, and metabolomics. These discussions are designed to highlight innovation opportunities in gut microbiome and cancer holding potential for significant advances as well as general challenges with broad implications.

3.2. Skin Microbiome and Dermatological Conditions

The skin is the largest organ of the human body, hosting a complex ecosystem of microorganisms including bacteria, fungi, archaea, and viruses. This biogeographical setting is unique in its narrow alliance with the host species but has evolved a co-dependency yielding numerous pleasant outcomes appreciated by both parties. The determinants of this skin microbiome have been extensively reviewed and an imbalance in its vast composition can lead to various dermatological conditions, prompting an interest in the deliberate modulation of the skin microbiome [20]. In the next sections, the focus will be laid upon a brief elucidation of the skin microbiome’s relationship with acne, atopic dermatitis, and psoriasis, following a discussion of potential microbiome therapies being tailored to the skin.

Acne vulgaris is one of the most common dermatological conditions that plagues people of all ages across the globe. This affects a considerable portion of the world-leading dermatological visits. The annual estimated cost of treating only adolescents in the US is extensively exceeding $1.2 billion. The pathophysiology of acne is multifactorial and includes the bacteria residing on the skin. Usually, such a microbial culture is dominated by Propionibacterium acnes which can ferment sebum to produce free fatty acids. An increased concentration of free fatty acids in turn stimulates keratinocytes leading to a comodogenic chain of events. As the world faces an ongoing race against time with increasing resistance developed against the available drugs, creative solutions proposed by leveraging the microbiome that resides on acneichumans may prove to be more sustainable and environmentally favorable. A study had shown that restoration of healthy microbial growth on the skin improved symptoms of seborrhea and fell the incidence of acne eruption. Resistance developed against potent antibiotics could be circumvented by such biological intervention strategies. Moreover, the holistic approach taken toward the human body will prevent recalcitrant acne that is refractory in nature. It is high time the next frontier of conquering dermal ill health is embarked upon, through an intricate understanding of the trillions of skin microbiomes tucked neatly amongst the epithelial layers.

4. Therapeutic Strategies Targeting the Human Microbiome

The human microbiome is a community of microorganisms, including bacteria, archaea, fungi, viruses, and protists. The microbiome symbiotically interacts with humans, affecting various physiological processes. Recent advancements in metagenomics and other high-throughput techniques have provided a comprehensive understanding of the structure, function, and dynamics of the human microbiome. Today, the human microbiome is a treasure for biomarker discovery, which has the potential to revolutionize personalized medicine. Manipulation of the microbiome through diet, dietary supplements, and drugs can prevent/treat various diseases. Developing microbiome-modulating therapies is an unmet medical necessity for unresponsive conditions, such as infections or other gut, cardiovascular, metabolic, skin, and neurological disorders. Several challenges and measures are highlighted: (1) deep knowledge of mechanistic approaches; (2) exploration of the human/ microbial proteome, metabolome, and immunome and their interactions; (3) discovery of novel regulatory mechanisms; (4) diagnostic biomarker development for monitoring treatment safety and efficacy; (5) AI-based diagnostic/ prognostic/ therapeutic approaches based on the integration of omics with other health records; (6) understanding microbe-host cross-talk; and (7) multi-omics approach applications to develop microbiome-based therapies.

4.1. Probiotics and Prebiotics

Due to advances in genome sequencing and high-throughput analytical tools, recent years have witnessed an intensive multidisciplinary research focus on the human microbiome and its significance in health and disease. In an updated scientific view, the microbiome is defined as the collective genome of commensal, symbiotic, and pathogenic microorganisms that populate inside and outside the human body. The dynamic microbiome is not only an integral part of the host’s biological system but also caters to its proper functionality. Perturbations in the quantity and quality of the commensal microbiome are linked to the onset and progression of various diseases, including cardiovascular, infectious, and metabolic disorders. Stressed by internal and external factors, a resilient human gut microbiome may lose its integrity, and these perturbations to the ecosystem can be resetting it to a negative state, which alters normal organism functions and promotes disease.

Nevertheless, the emerging concept of the microbiome affecting various aspects of host physiology is expected to potentially unveil a broad array of innovative therapeutic strategies. Relatively unchanging and controllable, the tiny microbes offer researchers and clinicians a vast platform to discover novel diagnostic and therapeutic dimensions. Restoring microbiome to its native steady state using live biotherapeutics such as probiotics, prebiotics, synbiotics, postbiotics, or fecal microbiota transplantation has emerged as a compelling and alternative treatment tactic. Host equipped biotherapeutics deliver and seed endogenous beneficial gut microbes that restore or rebalance the intestinal ecosystem. Their primary function is to thrive and proliferate within the intestinal tract and enhance the growth and activities of indigenous beneficial microflora, so resilient communities carry out the commensal benefits in a sustained manner. It is widely evidenced that host-specific, live microbes have a wide array of health benefits when properly infused, particularly in disease prevention and overall well-being. [21][22][23]

4.2. Fecal Microbiota Transplantation

The human body naturally hosts a large and diverse microbial community known as the human microbiota, formed predominantly by bacteria that interact closely with the host and continuously influence different physiological functions and disease states. The dramatic increase in microbiota studies, facilitated by the advancements of sequencing and metagenomics technologies, have markedly improved the understanding of the human microbiome and its potential effects on human health and disease. A substantial number of studies have highlighted the pivotal role of the microbiome in a plethora of non-communicable diseases (NCDs), such as metabolic diseases, neuropsychiatric conditions, inflammatory bowel conditions, decompensated cirrhosis, and malignancies [24]. Targeted microbiota therapies, such as prebiotics, probiotics, and postbiotics have been developed and used to manipulate and improve the composition and metabolic activities of the human gut microbiota to prevent and treat microbiota dysbiosis-related diseases. However, the overall effects of these therapeutics can vary due to several factors, such as time of administration, metabolite dosage and stability, and total or partial bioavailability of live bacterial species in the human gut environment.

Conversely, fecal microbiota transplantation (FMT) is capable of transferring the entire, stable gut microbiota from a healthy donor to the dysbiotic recipient and is emerging as a new promising therapeutic avenue. Transplantation can be performed through (1) upper GI infusion, via naso-gastric/naso-jejunal tubes, (2) lower GI infusion, via colonoscopy, and (3) oral ingestion of encapsulated microbiota processed from fresh or frozen donor samples [25]. FMT has demonstrated the capacity to shift the gut microbiome of recipients to closely resemble their donors even in the long-term, fostering the growth of obligate anaerobes and enhancing colonization resistance through depletion of the recipient’s potentially pathobionts. Orally ingested capsules have demonstrated the non-inferiority of fresh stool transplantations in terms of successful engraftment of desirable bacterial species and have been further optimized for efficacy, safety, and long-term stability. Finally, encapsulates have shown the persistency of colonization resistance for at least 12 weeks without causing side effects or adverse events and associated with a significant reduction in systemic immune response magnitude compared to oral antibiotics.

5. Regulation and Safety Considerations in Microbiome-based Therapies

The human gut provides a home to the gut microbiome, which plays a crucial role in host health by promoting digestion, maintaining the immune system, and inhibiting the growth of harmful pathogens. Microbiome-based therapies aim to modulate the intestinal flora benefiting host health. Several therapeutic approaches center on the use of specific bacteria [26]. For treating infectious diseases, a vaccine delivery system using Lactobacillus has been designed to kill pathogens. Antigen presentation markers have been expressed in Lactobacillus to induce the immune response, as in the case of flu vaccine. Similarly, the active microbial ecosystem therapy aims to restore the disrupted gut system. It involves the use of medicinal capsules containing beneficial bacteria from healthy microbes for the duration of several months. The procedure of FMT results in the extensive restoration of the gut microbiome for good gut functioning. The term microbe therapy is used in this review for microbiome therapies that directly affect the host gut system, whereas therapeutic microbes are used to refer to native or genetically modified microbes introduced into the host as mediators of microbial treatment.

Microbiome therapy presents enormous potential for applications to maintain and prevent the onset of dysregulation diseases. Microbiome therapy is also regarded as external therapy that induces functional improvement of the microbial environment within the host system. Microbiome therapy for health and prevention aims to mimic the native state of the gut microbial environment, which is a complex structure comprising various gut microbial species and their co-metabolites. The stability of the gut microbial structure can be affected by several environmental cues; once the gut microbial system is affected, serious host health problems are expected to occur. Microbiome therapy maintains a native gut system to avoid pathogenic growth and provide a platform for healthy gut system functioning.

6. Conclusion

The continuing efforts in the decoding and understanding of the human microbiome have led to promising future directions and to the development of several emerging technologies that might be used to address numerous open questions and further expand the potential applicability of microbiome data. The use of artificial intelligence and machine learning and the uptake of new sequencing technologies are already permitting to leverage huge microbiome datasets to derive biologically relevant insights. Machine learning techniques are expected to enable integrative and high-throughput analysis of multi-omics data and to provide a way to understand the mechanistic underpinnings of the host–microbiota mutualism. The integration of artificial intelligence and causal modeling could further the understanding on the cascade of host responses due to microbial perturbation, thereby leading to the discovery of new effectors to engineer the microbiome. New technologies, such as portable nanopore sequencers, long-read sequencing, and single-cell sequencing, are expected to uncover low abundant and yet uncharacterized microbial populations in both the human gut and extraintestinal organs. Future effort is believed to further improve existing methodologies and analytics to allow the analysis of extremely large multi-omics datasets and to exploit the development of high-quality multi-omics profiles to streamline the transition from correlation to causation. These technological advancements would substantially open a fresh avenue of investigation and could lead to the development of robust personalized treatment strategies mirroring the individual microbial fingerprint. Obviously, the application of the learning from the study of healthy microbiota composition and function will harden the development of next-generation effective therapeutics for the treatment and/or prevention of diseases [26]. This emergent field is expected to be an important step-change leap in the gaining of a full-on comprehension of the multifaceted roles of the microbiome in the onset and progression of chronic conditions. Knowledge acquired will drive the rise of cutting-edge therapeutic strategies profoundly affecting precision medicine and human wellbeing. Fundamental endeavors represent promotion and growth of collaboration and coordination among disciplines (biology, medicine, and computational sciences) and initiatives (consortia, project calls, and shared databases). In light of the raised opportunities and challenges, researchers are urged to embrace multidisciplinary efforts and to plan strategies that leverage the recent advances. Taking a proactive stance, further recommendations are made to tackle ethical aspects, maximize the potential of big data, and enhance handling and sharing practices. Platforms that make widely open reference microbiome datasets and bioinformatics tools available are fostered to support the community in an experimentally advanced but ethical endeavor. With the aim of jump-starting and pushing a mature dialogue, priority of certain urgent actions needed to address the challenge of microbiome science is dealt with, focusing on setting ground rules for ethical aspects, the development of standards in generation and treatment of the data, and the creation and handling of large datasets.

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