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MICROBIOME-HOST INTERACTION AND THEIR IMPACT ON HUMAN HEALTH

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ABSTRACT

Through metabolic, immune, and neurological interactions, the human microbiome, particularly the gut microbiota, plays a crucial role in maintaining host physiology. These microorganisms have a significant impact on overall health because they help regulate the immune system, digest food, and absorb nutrients. The composition and diversity of the gut microbiome vary across individuals due to genetic, dietary, and environmental factors. Dysbiosis, a disturbance in the microbial balance, has been linked to a variety of diseases, including metabolic disorders, inflammatory conditions, and neurological problems. Understanding microbiome-host interactions is essential for developing targeted therapeutic interventions. The human gut microbiome's composition and diversity, as well as the mechanisms by which it affects host physiology and changes in health and disease, are the subjects of this review. A chemist's perspective on the identification and characterization of microbial metabolites and their potential therapeutic applications will also be presented.

Keywords: Microbiome, Gut microbiota, Health, Therapy, Disease

INTRODUCTION

Through interactions with the immune system, metabolism, and nervous system, the human microbiome—and especially the gut microbiota—plays a critical role in preserving host physiology. These microbes have a major impact on general health by aiding in digestion, nutrition absorption, and immunological control (Andoh, 2016).

Individual differences in gut microbiota diversity and composition can be attributed to dietary, environmental, and genetic variables. Dysbiosis, or disturbances in the balance of microorganisms, has been linked to a number of illnesses, such as neurological dysfunctions, inflammatory diseases, and metabolic problems. Developing focused treatment approaches requires an understanding of the interactions between the microbiota and the host (Thursby and Juge, 2017; Gomma, 2020).

This review looks at the human gut microbiome's diversity and composition, how it affects host physiology, and how it changes in health and illness. Furthermore, a chemist's viewpoint will be presented, emphasizing the detection and description of microbial metabolites as well as their possible medical uses.

Composition and Diversity

Trillions of microorganisms, including bacteria, viruses, fungus, and archaea, make up the human gut microbiome. The phyla Firmicutes and Bacteroidetes comprise the majority of gut bacteria, with Actinobacteria, Proteobacteria, and Verrucomicrobia following closely behind. Although each person's microbiome is different, they all share a common structure that is impacted by their lifestyle, environment, food, and genetics (Jones, 2016).

Factors Influencing Gut Microbiome Diversity

Geographical and Cultural Differences: The gut microbiome's makeup varies by region; for example, plant-based diets in rural communities enhance the predominance of Bacteroidetes, while Western diets result in higher levels of Firmicutes (Mondot, 2013). Age and Development: The microbiome changes from birth, and breastfeeding and the method of delivery (vaginal vs. C-section) affect early colonization. Microbial diversity stabilizes by adulthood, but as people age, more changes occur (Krishnan et al., 2015). Antibiotics and processed meals decrease microbial diversity, whereas plant-based, high-fiber diets increase it. Host Genetics: A genetic relationship between the host and microbiome is demonstrated by the higher prevalence of specific bacterial strains in genetically related individuals (Afzaal et al., 2022).

Role of Gut Microbiome Diversity in Health

Improved immunity, disease resistance, and metabolic health are all associated with a more diverse microbiome. Obesity, diabetes, autoimmune illnesses, and inflammatory bowel diseases (IBD) have all been linked to a decline in microbial diversity (Greenhalgh et al., 2016).

Evolution of the Gut Microbiome

Over millions of years, the gut microbiota has changed with people, adjusting to environmental influences and dietary modifications. Microbial diversity has decreased as a result of industrialization and the use of processed foods, according to studies comparing ancient and modern microbiomes (from preserved fecal samples). Compared to contemporary high-fat, low-fiber diets, research suggests that early human diets high in fiber supported a more diversified microbiome (Dapa et al., 2023).

Mechanisms of Microbiome-Mediated Effects on Host Physiology

Numerous physiological processes, such as metabolism, immunology, and neurological processes, are significantly influenced by the human gut microbiota. The creation of metabolites by microorganisms, immune system modulation, and gut-brain axis connections are just a few of the intricate processes via which the microbiome affects human physiology. To provide a thorough grasp of these mechanisms, this section aggregates research paper findings with supplementary information (Chen and Garud, 2022).

The synthesis of metabolites such as neurotransmitters, bile acids, and short-chain fatty acids (SCFAs) is one of the main ways the microbiome influences host health. Microbial fermentation of dietary fibers produces SCFAs such acetate, propionate, and butyrate, which are essential for maintaining gut barrier integrity, energy balance, and anti-inflammatory reactions (Sajjad et al., 2024). Bile acids, modified by gut bacteria, regulate lipid metabolism and influence host immune responses (Noor et al., 2024).

The immune system's development and regulation depend on the gut flora. Polysaccharide A, which is produced by some bacterial species, including Bacteroides fragilis, has been demonstrated to encourage the development of regulatory T cells (Treg), resulting in immunological tolerance (Round & Mazmanian, 2010). Furthermore, pattern recognition receptors such as Toll-like receptors (TLRs) are influenced by gut microorganisms, which sets off signaling cascades that influence inflammatory regulation and immune responses (Sattar et al., 2024).

There is growing evidence that the gut-brain axis—a term that encompasses neurological, endocrine, and immunological pathways—is how gut microorganisms interact with the central nervous system. Serotonin and gamma-aminobutyric acid (GABA), two neurotransmitters generated from microorganisms, have an impact on mood and cognitive processes (Shahin et al., 2024). Furthermore, SCFAs have been linked to altering the integrity of the blood-brain barrier. and neuroinflammation, potentially affecting neurological diseases such as Parkinson’s and Alzheimer’s (Bilal, 2021).

Through controlling the extraction of energy from meals and influencing adipogenesis, the gut microbiota has a major impact on host metabolism. Research has indicated that obesity is linked to a changed microbiome makeup, namely a higher Firmicutes-to-Bacteroidetes ratio

(Bilal et al., 2025). Immunity, metabolism, and digestion are all significantly impacted by the human microbiome, especially the gut bacteria. Diseases ranging from neurological illnesses to metabolic disorders are increasingly associated with dysbiosis, which is an imbalance in the makeup of microorganisms (Wang et al., 2022).

A complex biochemical ecosystem, the human microbiome—and especially the gut microbiota—has a significant impact on immunity, metabolism, and overall health. The chemical compounds, enzymatic processes, and metabolic networks that control homeostasis or disease control the chemistry that underlies microbial interactions with host systems. Understanding these chemical processes provides profounder insights into microbiome purposes and healing plans. The gut microbiota comprises diverse bacterial phyla, including Bacteroidetes, Firmicutes, Actinobacteria, and Proteobacteria. These microbes involve in biochemical changes that effect metabolic flux and physiological consequences (Yadav et al., 2021).

Key chemical aspects

Acetate, propionate, butyrate, and other short-chain fatty acids (SCFAs) are produced when anaerobic bacteria degrade food fibers. They operate as energy sources, alter pH, and control gene expression by inhibiting histone deacetylase. Complex carbohydrate breakdown is facilitated by glycoside hydrolases and polysaccharide lyases, which provide nutrients that are accessible. The metabolism of tryptophan through microbial routes affects the synthesis of neurotransmitters, such as serotonin and derivatives of kynurenine, which in turn affects neurological processes. Chemical changes and metabolite interactions determine how the microbiome affects human physiology (Wu et al., 2022).

Through deconjugation and 7α-dehydroxylation, gut bacteria chemically alter bile acids, which affects lipid absorption and metabolic signaling via FXR and TGR5 receptors. Redox Chemistry and Oxidative Stress: Reactive oxygen species (ROS) levels are regulated by microbial redox processes, which affect cellular homeostasis and inflammatory pathways. Chemistry of Proteins and Peptides: Microbial proteases convert dietary proteins into bioactive peptides that alter gut permeability and immunological responses. Microbial imbalance, or dysbiosis, modifies biochemical homeostasis and is linked to neurological, inflammatory, and metabolic problems. Obesity and Metabolic Syndrome: Insulin sensitivity and fat storage are impacted by alterations in microbial metabolite synthesis, namely branched-chain amino acids (BCAAs) and short-chain fatty acids (SCFAs) (Barreto and Gordo, 2023).

Modified microbial synthesis of polyamines and hydrogen sulfide affects immunological regulation and epithelial integrity. Neurological Disorders: Microbial activity is linked to neurodegenerative and mental disorders through the influence of gut-derived metabolites like GABA, dopamine precursors, and SCFAs on the gut-brain axis (Huang et al., 2021).

The Organic Chemistry of Microbiome Therapeutics

Targeted modification of microbial enzymatic pathways and metabolite production is necessary to use microbiome chemistry for therapeutic intervention. Both prebiotics and probiotics use: The production of SCFA is increased and pathogenic colonization is decreased through the selective promotion of beneficial microbial species. In diseases like recurrent Clostridium difficile infection, fecal microbiota transplantation (FMT) restores the metabolic processes and microbial composition. Bacterial genomes can be precisely modified using CRISPR-Cas and metabolic engineering to increase the synthesis of advantageous metabolites. Microbial enzymes, such as beta-glucuronidases in the metabolism of irinotecan, alter medications, affecting their toxicity and effectiveness. The metabolism of lignan and flavonoids by gut microbes regulates their anti-inflammatory and antioxidant properties. Microbiota-produced nitric oxide (NO) and hydrogen sulfide (H_2S) control immunological signaling and vascular tone (Ghosh and Pramanik, 2021).

Microbial Metabolites and Their Signaling Functions

Microorganisms create these tiny molecules as part of their metabolic processes. These metabolites are essential to the biology of the microbes as well as to how they interact with other living things, such as humans, animals, and plants. Since microbial metabolites are essential to many biological processes and ecological interactions, their signaling roles have drawn a lot of interest recently. This paper explores the types, nature, and signaling roles of microbial metabolites, emphasizing their significance for agriculture, environmental sustainability, and human health (Lau et al., 2021).

Primary and secondary metabolites are two major categories into which microbial metabolites can be divided. The development and reproduction of microorganisms depend on primary metabolites. They consist of organic acids, nucleotides, and amino acids, all of which have a direct role in metabolic processes. Secondary metabolites, on the other hand, have different ecological roles but are not necessary for microbial growth. These include signaling chemicals, pigments, and medicines that help bacteria and their hosts communicate with one another as well as within microbial communities (Shine and Crawford, 2021).

Antibiotics, which are produced by some bacteria and fungi to prevent the growth of competing microorganisms, are among the most well-known types of microbial metabolites. For instance, the fungus Penicillium yielded the antibiotic penicillin, which transformed medicine by effectively treating bacterial infections. However, because the presence of other microbes can affect the formation of these molecules, antibiotics can contribute to microbial signaling by establishing a chemical environment that controls community dynamics (Dillon et al., 2021).

Bacteria use quorum sensing molecules, another important class of microbial metabolites, to communicate with each other. By releasing and detecting signaling molecules known as autoinducers, bacteria can use a process known as quorum sensing to determine the density of their population. When the concentration of these chemicals hits a particular threshold, coordinated activities including bioluminescence, virulence factor synthesis, and biofilm formation are triggered. Bacterial populations can operate collectively through signaling mechanisms, which improves their adaptability and survival (Dahiya and Nigma, 2023).

Microbial metabolites have a significant impact on the host organisms in addition to their functions in microbial communication. For example, it has been demonstrated that the gut microbiota's production of short-chain fatty acids (SCFAs) during the fermentation of dietary fibers affects host metabolism and immunological responses. SCFAs, such as acetate, propionate, and butyrate, are essential for gut health maintenance and provide colonocytes with energy. Additionally, they have the ability to regulate inflammatory reactions and may be used as a treatment for diseases including inflammatory bowel disease and obesity (Luger et al., 2021).

Microbial metabolites have signaling roles outside of the gut microbiome. For example, metabolites produced by specific bacteria associated with plants have an impact on the growth and development of plants. By acting as phytohormones, these compounds can enhance nutrient intake and encourage root growth. Furthermore, by triggering systemic acquired resistance (SAR) or encouraging the synthesis of antimicrobial chemicals, certain microbial metabolites might increase a plant's resistance to infections (Flaig et al., 2023).

Microbial metabolites' signaling properties can be used in agricultural settings to increase crop yields and sustainability. Inoculating crops with beneficial microbial strains that produce plant growth-promoting metabolites can enhance plant health and resilience against environmental stressors. Furthermore, understanding the interactions between microbial metabolites and plant signaling pathways can lead to the development of novel biopesticides and biofertilizers, reducing the reliance on chemical inputs in agriculture (Tan, 2023).

Microbial metabolites also play a vital role in shaping the interactions within the soil microbiome. The complex web of microbial life in the soil is influenced by the production of metabolites that affect nutrient cycling, soil structure, and plant-microbe interactions. For example, exudates from plant roots can stimulate the growth of beneficial soil microbes, which, in turn, produce metabolites that enhance nutrient availability to plants. This mutualistic relationship is essential for maintaining healthy ecosystems and promoting soil fertility (Ganesan et al., 2022).

Furthermore, microbial metabolites' signaling roles can contribute to pathogenicity in addition to positive interactions. Virulence factors, such as metabolites that interfere with host cell signaling pathways or elude immune responses, are frequently produced by pathogenic bacteria. Gaining knowledge of these processes can help develop fresh approaches to treating infectious disorders (Bargiel et al., 2021).

With the recent development of sophisticated analytical methods like mass spectrometry and genomics, scientists can now more thoroughly investigate the intricate web of microbial metabolites and their signaling functions. Biotechnological applications in environmental research, agriculture, and medicine have been made possible by these technologies, which have made it easier to identify new metabolites and clarify their biosynthesis routes (Raja et al., 2021).

There are still a number of obstacles to overcome in spite of the advancements in our knowledge of microbial metabolites and their signaling roles. Interpreting the ecological roles of microbial communities can be challenging due to their complexity and the wide variety of metabolites they produce. To completely comprehend the dynamics of microbial signaling, more research is also needed to determine how environmental elements like temperature, pH, and nutrient availability affect the generation of metabolites (Sumida et al., 2021).

Therapeutic Potential

A complex community of billions of bacteria living in and on the human body, the human microbiome is essential to preserving homeostasis and health. Numerous physiological functions, including as digestion, metabolism, immunological response, and even mental health, are influenced by the microbiome. The therapeutic potential of microbiome modulation—methods intended to change the makeup and function of microbial communities to improve health outcomes—has been brought to light by recent developments in research. The mechanics of microbiome regulation, its consequences for different medical disorders, and the prospects for microbiome-based treatments are all examined in this essay (Wahid et al., 2022).

Numerous strategies, such as dietary changes, probiotics, prebiotics, synbiotics, and fecal microbiota transplantation (FMT), can be used to modify the microbiome. Each of these tactics seeks to improve or restore the microbiome's advantageous processes, particularly when those processes have been disturbed by environmental stresses, poor diet, or antibiotic usage (Bilal et al., 2024).

The microbiota is fundamentally affected by dietary interventions. The diversity and makeup of gut microbial communities can be greatly influenced by the foods we eat. For example, fiber-rich diets encourage the development of good bacteria that convert fiber into short-chain fatty acids (SCFAs), which improve gut health and have anti-inflammatory qualities. On the other hand, diets heavy in fat and sugar can encourage the growth of pathogenic microbes, which can lead to dysbiosis, a microbial imbalance linked to a number of health problems. People can improve the health and functionality of their microbiome by eating a diet high in whole foods, fruits, vegetables, and fermented goods (Bilal et al., 2024).

As a way to modify the microbiome, probiotics—live bacteria that provide health advantages when taken in sufficient quantities—have become more and more popular. Following disruptions like antibiotic treatment, common probiotic strains like Lactobacillus and Bifidobacterium can help restore the equilibrium of gut bacteria. According to clinical research, probiotics can enhance gut barrier function, lessen the frequency of antibiotic-associated diarrhea, and relieve the symptoms of irritable bowel syndrome (IBS). The necessity for individualized methods to probiotic therapy is highlighted by the fact that probiotic benefits might be strain-specific and that individual efficacy can differ (Afzal et al., 2024).

Another important factor in microbiome modulation is prebiotics, which are indigestible food ingredients that specifically promote the growth and activity of advantageous microbes. Inulin and fructo-oligosaccharides, which are present in foods like bananas, onions, and garlic, are examples of common prebiotics. Prebiotics can improve the synthesis of SCFAs and promote general gut health by giving good bacteria a substrate. According to research, prebiotics may potentially affect immune system performance, metabolic health, and even mood modulation on a systemic level (Ali et al., 2021).

A synergistic approach to microbiome modification is represented by synbiotics, which are a blend of probiotics and prebiotics. Synbiotics can improve the effectiveness of probiotic therapies by providing live beneficial microorganisms along with the nutrients they need to flourish. According to preliminary studies, synbiotics may be especially useful in treating gastrointestinal conditions like ulcerative colitis and inflammatory bowel disease (IBD) (Saghir et al., 2024).

Another cutting-edge method of microbiome modification is fecal microbiota transplantation (FMT), which involves transferring fecal material from a healthy donor to a recipient who has dysbiosis. With cure rates above 90%, FMT has demonstrated exceptional efficacy in treating recurring Clostridium difficile infections. The process efficiently outcompetes the harmful bacteria by reestablishing a varied and healthy microbial community in the recipient's gut. Although FMT shows promise for additional illnesses like metabolic syndrome and IBD, more research is required to fully understand its safety and long-term effects (Simon et al., 2021).

Modification of the microbiota has effects that go beyond gastrointestinal health. According to new research, the microbiota may have an impact on a number of systemic diseases, such as type 2 diabetes, obesity, allergies, and even mental health issues. For instance, gut microorganisms can influence how specific foods are metabolized and how insulin sensitivity is controlled, establishing a connection between the health of the microbiome and metabolic outcomes (Fatima et al., 2024). Furthermore, research has turned its attention to the gut-brain axis, a network of bidirectional communication between the gut and the brain. Studies have indicated that gut microbiota may be involved in mood regulation and the pathophysiology of disorders like depression and anxiety (Chandra et al., 2022).

The potential for microbiome manipulation in clinical practice grows along with our understanding of the microbiome. More successful interventions may result from personalized medical strategies that take into account each person's distinct microbiome composition, genetic background, and lifestyle factors. Depending on a person's microbiome makeup, this may entail personalized prebiotic formulations, certain probiotic strains, or dietary recommendations (Wang et al., 2021).

Nonetheless, there are still a number of obstacles in the field of microbiome therapy and study. The intricacy and individual differences in microbiota is a major obstacle. It is challenging to provide general principles for microbiome regulation because of the variability of microbial communities, which is influenced by factors like age, genetics, nutrition, and environmental exposures. Furthermore, the regulatory environment surrounding probiotics and microbiome-based treatments is still developing, necessitating thorough clinical trials to guarantee their efficacy and safety (Ke et al., 2021).

Challenges and Considerations

Trillions of bacteria make up the human microbiome, which is essential for promoting health and preventing illness. Our knowledge of the microbiome's complexity has grown as a result of the expansion of this field's study, which has shown its complicated connections to human physiology, immunity, and metabolism (Bilal et al., 2021). To properly advance the area, microbiome research must overcome a number of obstacles and constraints, notwithstanding the encouraging discoveries and possible medicinal uses. The main barriers to microbiome research are examined in this essay, including methodological difficulties, moral dilemmas, and the requirement for interdisciplinary cooperation (Shanahan et al., 2021).

The intricacy of microbial communities is one of the main obstacles to microbiome study. Individual differences in microbiome composition and function can be attributed to a variety of factors, including genetics, diet, age, lifestyle, and environment. Because of this heterogeneity, it is more difficult to draw generalizations or inferences about the roles of microbes and health consequences (Rasheed et al., 2024). For instance, what may be deemed a beneficial microbial species in one individual could be neutral or even dangerous in another due to changes in host genetics or environmental interactions. Adopting personalized techniques in microbiome research is crucial because researchers must carefully account individual variability when developing studies and analyzing results (Singh and Rastogi, 2024).

Methods for studying the microbiota present another important methodological problem. Since many microbes cannot be grown in a lab, traditional culture-based techniques for separating and describing microorganisms sometimes fall short of capturing the complete variety of the microbiome. Instead, metagenomics and molecular methods like 16S ribosomal RNA gene sequencing are now widely used to profile microbial populations. These techniques provide a more thorough understanding of microbial diversity, but they also make data interpretation and analysis more difficult. Researchers must work with data scientists and bioinformaticians to extract valuable insights from microbiome databases since the vast volumes of data collected require advanced bioinformatics techniques and skills to interpret (Khan et al., 2022).

Confounding variables might further complicate the interpretation of microbiome data. It is challenging to determine the causal relationships between the microbiome and health outcomes because variables including diet, medication, and lifestyle can all affect the makeup and function of microorganisms. For example, a study may reveal a correlation between a specific microbial profile and a disease state, but this relationship may be impacted by other factors, such as the patients' dietary habits or genetic predispositions. Researchers must use rigorous study methods, such as controlled experiments and longitudinal studies, to overcome this difficulty in order to limit the impact of confounding variables and establish causal linkages (Ejtahed et al., 2023).

Research on the microbiome must also take ethics very seriously, especially when human participants are involved. Potential therapeutic uses of microbiome manipulation were investigated; however, concerns about the effectiveness and safety of such therapies were raised (Ejtahed et al., 2023). Fecal microbiota transplantation (FMT), for example, has demonstrated promise in the treatment of some gastrointestinal illnesses; nonetheless, there are still worries regarding the potential for pathogen transfer or unforeseen repercussions. Ethical frameworks must be constructed to ensure that microbiome-based medicines are safe, effective, and ethically sound. Strong informed consent procedures that properly explain the possible dangers and advantages of taking part in microbiome research are also necessary (Ahmed and Hens, 2022).

The industrialization of microbiome research raises further ethical concerns. As the popularity of probiotics, prebiotics, and products based on the microbiome has grown, so too have commercial claims, some of which could have been deceptive or without scientific backing. Products that purport to affect the microbiota must pass stringent safety and effectiveness testing, according to regulatory agencies. Disclosure in research and product development is vital to safeguard consumers and sustain the confidence of the public in microbiome science (Bharti and Grimm, 2021).

Furthermore, the methods used in microbiome research need to be standardized. Results from different studies may differ due to variations in gathering samples, processing, and analysis. Standardized procedures can facilitate researcher cooperation and data exchange by ensuring that results are similar and reproducible. The reliability of results and the general caliber of the field can be improved by initiatives to establish efficient methods for microbiome research (Dada et al., 2021).

In microbiome research, public involvement and awareness are also essential considerations. It is crucial to provide research results to the public in an approachable and clear way as the area develops. Research might be misunderstood and confused by false information about the microbiome and its effects on health. Public engagement initiatives can support healthy lifestyle choices, increase participation in scientific studies, and increase knowledge of the significance of the microbiome. Furthermore, integrating microbiome-based therapeutics into clinical practice can be made easier by teaching medical professionals about the function of the microbiome in health and disease (McGuire et al., 2008).

CONCLUSION AND SUGGESTIONS

Human health and illness outcomes are determined by the complex chemical lexicon of microbiota-host interactions. The importance of chemistry in microbiome research is highlighted by developments in organic chemistry, metabolomics, and synthetic biology, which are opening up new avenues for therapeutic microbiome manipulation.

Microbial metabolites play an important role in the complex web of life by acting as molecules of communication that let bacteria and their hosts communicate with one another. The roles and purposes of metabolites produced by bacteria are numerous and varied, ranging from their responsibilities in the manufacture of antibiotics to their participation in immunological regulation and plant growth. The potential uses of these metabolites in agriculture, health, and environmental sustainability present intriguing opportunities for the future as research into their intricacies continues. Gaining insight into and using the potential of microbial metabolites may help develop novel answers to some of the most important problems confronting humanity today.

Although research on the microbiome has the potential to revolutionize our knowledge of health and illness, a number of obstacles and factors need to be taken into account in order to fully realize its therapeutic potential. The development of microbiome research will be greatly influenced by the intricacy of microbe populations, methodological difficulties, ethical issues, and the requirement for interdisciplinary cooperation. We can unleash the entire potential of the microbiome and open the door to novel therapeutic approaches that enhance human health and well-being by addressing these issues and creating a cooperative, moral research environment. Opportunities to capitalize on the microbiome's advantages in medicine and other fields will grow as our knowledge of it does.

Modification of the microbiome has a wide range of possible applications. We may restore and improve the health of our microbiomes and improve health outcomes for a variety of illnesses by utilizing the power of dietary treatments, probiotics, prebiotics, synbiotics, and FMT. As the intricacies of the microbiome are further understood, tailored methods to microbiome regulation have the potential to transform healthcare and open the door to novel and potent treatments that target the underlying causes of illnesses rather than just their symptoms. The future of medicine may very well lie in understanding and manipulating the intricate relationships between our bodies and the microorganisms that inhabit them.

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