CODEN [USA]: IAJPBB ISSN : 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES
SJIF Impact Factor: 7.187
https://doi.org/10.5281/zenodo.19766301

Available online at: http://www.iajps.com A Comprehensive Review

HUMAN MICROBIOME AND ITS ROLE IN HEALTH AND DISEASE: A COMPREHENSIVE REVIEW

Ms. Sakshi D. Zore, Ms. Sakshi G. Jaybhaye, Ms. Sakshi D. Ghuge, Ms. Sadashiv P. Mundhe, Mr. Nivrutti D. Pandit, Dr. Prafulla R. Tathe
Samarth College of Pharmacy, Deulgaon Raja.

Abstract:
The human microbiome represents a complex and dynamic ecosystem composed of trillions of microorganisms, including bacteria, viruses, fungi, and archaea, residing in and on the human body. These microbial communities play a fundamental role in maintaining physiological homeostasis and influencing various aspects of human health. Advances in high-throughput sequencing technologies and metagenomic analysis have significantly expanded our understanding of microbiome composition, diversity, and functionality. This review paper explores the structure, diversity, and functions of the human microbiome, emphasizing its critical role in health and disease. The gut microbiome, in particular, has been extensively studied for its involvement in metabolic processes, immune modulation, and protection against pathogens. Dysbiosis, or imbalance in microbial communities, has been linked to numerous diseases, including gastrointestinal disorders, metabolic syndromes, autoimmune conditions, neurological disorders, and cancers. The review further discusses recent findings on microbiome-host interactions, microbial metabolites, and therapeutic interventions such as probiotics, prebiotics, and fecal microbiota transplantation. Understanding the human microbiome offers promising opportunities for personalized medicine and disease prevention strategies. This paper synthesizes current literature to provide a comprehensive overview and highlights future research directions in this rapidly evolving field.

Keywords: *Human microbiome, gut microbiota, dysbiosis, probiotics, host-microbe interaction, metagenomics, immune system, metabolic disorders, personalized medicine*

Corresponding author:
Sakshi D. Zore,
Samarth College of Pharmacy, Deulgaon Raja

QR CODE

Please cite this article in press Sakshi D. Zore et al Human Microbiome And Its Role In Health And Disease: A Comprehensive Review, Indo Am. J. P. Sci, 2026; 13(04).

1. INTRODUCTION:

The human body is not a solitary biological entity but rather a complex "superorganism" composed of both human cells and a vast community of microorganisms collectively known as the human microbiome. These microorganisms inhabit various niches of the body, including the skin, oral cavity, respiratory tract, gastrointestinal tract, and urogenital system. Among these, the gastrointestinal tract hosts the largest and most diverse microbial population, with an estimated 10^{14} microbial cells, outnumbering human cells by approximately tenfold (Turnbaugh et al., 2007).

The concept of the microbiome has evolved significantly over the past few decades. Traditionally, microbes were primarily associated with infectious diseases; however, recent research has revealed their indispensable role in maintaining health. The human microbiome contributes to digestion, nutrient absorption, vitamin synthesis, immune system development, and protection against pathogenic organisms. It also plays a crucial role in regulating metabolic pathways and influencing host physiology.

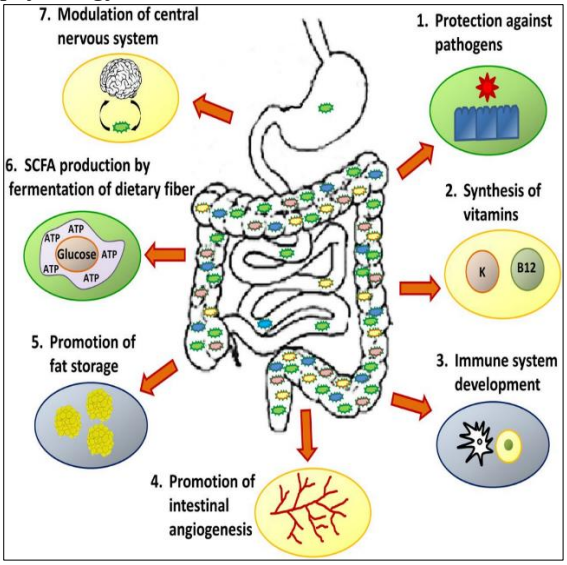

Figure No 01: Human microbiome and its role in health

The advent of next-generation sequencing (NGS) technologies, such as 16S rRNA gene sequencing and whole-genome shotgun sequencing, has revolutionized microbiome research. These techniques allow for comprehensive analysis of microbial diversity and function without the need for culturing, which was previously a major limitation in microbiology. Large-scale initiatives like the Human Microbiome Project (HMP) and the MetaHIT project have provided valuable insights into the composition and functional potential of microbial communities in healthy and diseased individuals (Human Microbiome Project Consortium, 2012).

The human microbiome is highly dynamic and influenced by multiple factors, including genetics, diet, age, environment, lifestyle, and antibiotic use. From birth, microbial colonization begins and continues to evolve throughout life. The mode of delivery (vaginal birth vs. cesarean section), breastfeeding, and early-life exposures significantly shape the initial microbiome composition. Disruptions in microbial balance, known as dysbiosis, can lead to adverse health outcomes and have been implicated in a wide range of diseases.

One of the most extensively studied aspects of the microbiome is its role in the gut-brain axis—a bidirectional communication network linking the gastrointestinal tract and the central nervous system. Emerging evidence suggests that gut microbiota can influence mood, behavior, and cognitive functions through neural, endocrine, and immune pathways. This has opened new avenues for understanding neuropsychiatric disorders such as depression, anxiety, and autism spectrum disorders.

Additionally, the microbiome plays a significant role in immune system modulation. It helps in the development and maturation of immune cells and maintains immune tolerance. Alterations in microbial composition can lead to immune dysregulation, contributing to autoimmune diseases such as rheumatoid arthritis, inflammatory bowel disease (IBD), and multiple sclerosis.

The metabolic functions of the microbiome are equally important. Microbial fermentation of dietary fibers produces short-chain fatty acids (SCFAs), such as acetate, propionate, and butyrate, which serve as energy sources and have anti-inflammatory properties. Dysregulation of these metabolic processes has been linked to obesity, diabetes, and cardiovascular diseases.

Given its profound impact on human health, the microbiome has become a promising target for therapeutic interventions. Strategies such as probiotics, prebiotics, synbiotics, and fecal microbiota transplantation (FMT) are being explored to restore microbial balance and treat diseases.

This review aims to provide a comprehensive understanding of the human microbiome, its composition, functions, and its role in health and disease. It also highlights recent advances and future perspectives in microbiome research.

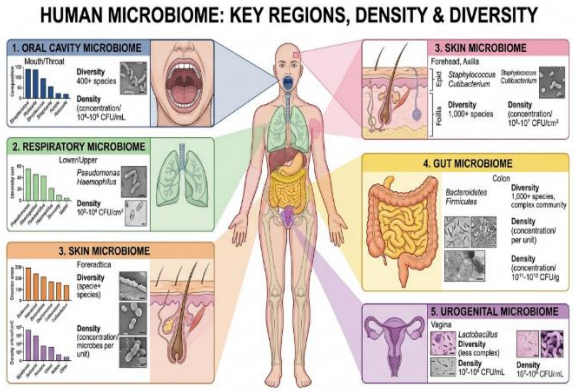

Figure No. 02 : Human Microbiome Distribution Across Body Sites

2. LITERATURE REVIEW:

The human microbiome represents a highly diverse and dynamic consortium of microorganisms distributed across various anatomical sites, each characterized by unique ecological conditions that shape distinct microbial communities. These microbial populations include bacteria, archaea, viruses, and fungi, with bacteria being the most extensively studied due to their abundance and functional relevance. Different body sites harbor specialized microbiota; for instance, the skin microbiome is predominantly composed of genera such as *Staphylococcus* and *Corynebacterium*, whereas the gut microbiome is largely dominated by the phyla *Firmicutes* and *Bacteroidetes* (Ley et al., 2008). Among all body habitats, the gastrointestinal tract contains the highest microbial density and diversity, making it a focal point of microbiome research. It is estimated that the human gut hosts over 1000 bacterial species, collectively forming a vast genetic reservoir known as the microbiome genome or metagenome, which significantly expands the metabolic capabilities of the host beyond what is encoded in the human genome (Turnbaugh et al., 2007).

The composition of the microbiome is not static but is continuously shaped by multiple environmental and host-related factors, including diet, antibiotic exposure, infections, age, genetics, and lifestyle. Dietary patterns, in particular, play a crucial role in modulating microbial composition; diets rich in dietary fiber promote the proliferation of beneficial bacteria that produce short-chain fatty acids (SCFAs), whereas high-fat and low-fiber diets are often associated with microbial imbalance or dysbiosis (Rinninella et al., 2019). Such environmental influences highlight the adaptability of the microbiome and its responsiveness to external stimuli, which can have profound implications for health and disease.

Microbial colonization begins at birth and undergoes significant changes during early life. The initial establishment of the microbiome is influenced by the mode of delivery, with vaginally delivered infants acquiring microbes from the maternal vaginal and intestinal microbiota, while cesarean-delivered infants are primarily colonized by skin-associated microbes (Dominguez-Bello et al., 2010). Breastfeeding further contributes to microbiome development by supplying beneficial microorganisms and prebiotic compounds such as human milk oligosaccharides (HMOs), which selectively promote the growth of beneficial bacteria like *Bifidobacterium*. During the first few years of life, the microbiome undergoes rapid diversification and gradually stabilizes into an adult-like composition by approximately three years of age. This developmental period is critical for immune system maturation, and disruptions during this window may predispose individuals to various diseases later in life.

The human microbiome performs a wide range of essential functions that are vital for maintaining physiological homeostasis. One of its primary roles is metabolic, as gut microbes facilitate the digestion of complex carbohydrates and dietary fibers that are otherwise indigestible by human enzymes. Through fermentation processes, these microbes produce SCFAs such as acetate, propionate, and butyrate, which serve as important energy sources and play key roles in regulating metabolic pathways and maintaining intestinal health (Lynch & Pedersen, 2016). In addition to metabolic functions, the microbiome provides protective benefits by acting as a barrier against pathogenic microorganisms. This is achieved through competitive exclusion for nutrients and adhesion sites, as well as the production of antimicrobial compounds that inhibit pathogen growth.

Structurally, the microbiome contributes to the integrity of the intestinal barrier by promoting mucus secretion and enhancing the expression of tight junction proteins, thereby preventing the translocation of harmful substances into the systemic circulation. Furthermore, the microbiome plays a critical role in immunological processes by influencing the development and regulation of the host immune system. It aids in distinguishing between harmful and harmless antigens, thereby preventing inappropriate immune activation and maintaining immune tolerance. Microbial interactions with host immune cells occur through pattern recognition receptors, which detect microbial-associated molecular patterns and initiate appropriate immune responses (Shreiner et al., 2015).

Disruptions in the normal composition of the microbiome, commonly referred to as dysbiosis, have been associated with a wide range of diseases.

Dysbiosis can result from factors such as antibiotic overuse, poor dietary habits, infections, and environmental stressors. This imbalance often leads to reduced microbial diversity and an overrepresentation of pathogenic species. One of the key consequences of dysbiosis is increased intestinal permeability, often termed "leaky gut," which allows toxins and microbial components such as lipopolysaccharides (LPS) to enter the bloodstream and trigger systemic inflammation (Kho & Lal, 2018). Such inflammatory responses have been implicated in the pathogenesis of numerous conditions, including inflammatory bowel disease (IBD), obesity, type 2 diabetes, allergies, asthma, and neurological disorders.

The role of the microbiome in gastrointestinal diseases has been extensively studied, with strong evidence linking altered microbial composition to conditions such as irritable bowel syndrome (IBS), Crohn's disease, and ulcerative colitis. These conditions are often characterized by reduced microbial diversity and a decrease in beneficial bacterial populations, along with an increase in pro-inflammatory microbes. Such alterations can disrupt gut homeostasis, leading to chronic inflammation and impaired intestinal function (Lynch & Pedersen, 2016).

Beyond gastrointestinal health, the microbiome has been shown to influence neurological function through the gut-brain axis, a complex bidirectional communication network connecting the gastrointestinal tract and the central nervous system. This communication occurs via neural, endocrine, and immune pathways, with the vagus nerve playing a central role in transmitting signals between the gut and the brain. Gut microbes produce a variety of neuroactive compounds, including gamma-aminobutyric acid (GABA), serotonin, and dopamine, which can influence brain function and behavior (Cryan & Dinan, 2012). Notably, a significant proportion of the body's serotonin is synthesized in the gut, underscoring the importance of the microbiome in regulating mood and emotional health.

Alterations in gut microbiota composition have been associated with several neurological and psychiatric disorders, including depression, anxiety, autism spectrum disorders, and Parkinson's disease. Reduced microbial diversity and specific compositional changes have been observed in individuals with these conditions. Experimental studies using germ-free animal models have demonstrated that the absence of microbiota leads to altered stress responses and behavioral abnormalities, which can be reversed through microbial colonization, further supporting the role of the microbiome in brain function.

The microbiome also plays a critical role in metabolic health, influencing processes such as energy balance, glucose metabolism, and lipid regulation. Dysbiosis has been strongly linked to metabolic disorders, including obesity and type 2 diabetes mellitus. Certain microbial communities have an enhanced capacity to extract energy from the diet, contributing to increased fat deposition. For example, an elevated ratio of *Firmicutes* to *Bacteroidetes* has been associated with obesity (Turnbaugh et al., 2006). Additionally, microbial metabolites such as SCFAs regulate metabolic pathways by influencing insulin sensitivity, appetite, and inflammatory responses.

Chronic low-grade inflammation, a hallmark of metabolic disorders, is often associated with increased intestinal permeability and the translocation of LPS into the bloodstream, a condition known as metabolic endotoxemia. Furthermore, the microbiome influences bile acid metabolism, which plays a crucial role in lipid digestion and cholesterol homeostasis. Alterations in bile acid profiles can disrupt metabolic signaling pathways and contribute to disease development.

In addition to metabolic and neurological functions, the microbiome is deeply involved in immune system modulation. It plays a fundamental role in the development of both innate and adaptive immunity and is essential for maintaining immune homeostasis. Microbial exposure during early life is critical for proper immune maturation, and insufficient exposure has been linked to an increased risk of allergic and autoimmune diseases, as described by the hygiene hypothesis. Dysbiosis can lead to immune dysregulation, contributing to conditions such as rheumatoid arthritis, systemic lupus erythematosus, and inflammatory bowel disease. Microbial metabolites, particularly SCFAs, are known to promote the differentiation of regulatory T cells, which help suppress excessive inflammatory responses and maintain immune tolerance.

Emerging research has also highlighted the role of the microbiome in cancer development and progression. Certain microbial species have been implicated in carcinogenesis through mechanisms such as chronic inflammation, production of genotoxic metabolites, and modulation of host immune responses. For instance, *Helicobacter pylori* infection is a well-established risk factor for gastric cancer, while *Fusobacterium nucleatum* has been associated with colorectal cancer. These microorganisms can promote tumor growth by inducing inflammatory pathways and suppressing anti-tumor immunity.

Furthermore, the microbiome has been shown to influence the efficacy of cancer therapies, including chemotherapy and immunotherapy. The presence of specific microbial taxa can enhance the response to immune checkpoint inhibitors, whereas antibiotic-induced disruption of the microbiome may reduce treatment effectiveness. Microbial enzymes can also metabolize chemotherapeutic agents, affecting their bioavailability and toxicity, thereby highlighting the importance of microbiome-drug interactions in clinical outcomes.

3. Aim and Objectives

3.1 Aim

The primary aim of this review is to comprehensively analyze the structure, composition, and functional roles of the human microbiome and to evaluate its impact on human health and disease.

3.2 Objectives

1. To examine the diversity and distribution of the human microbiome across different body sites.
2. To analyze the functional roles of microbiota in metabolism, immunity, and protection against pathogens.
3. To investigate the association between microbiome dysbiosis and various diseases, including gastrointestinal, metabolic, neurological, and immune disorders.
4. To explore the mechanisms underlying microbiome-host interactions.
5. To evaluate current and emerging microbiome-based therapeutic strategies.
6. To identify future research directions in microbiome science.

4. Main Content

4.1 Microbiome Composition and Diversity

The human microbiome is composed of trillions of microorganisms belonging to different domains, including bacteria, archaea, viruses, and fungi. Among these, bacteria are the most extensively studied due to their abundance and functional significance.

The gut microbiome is dominated by four major phyla:

- *Firmicutes*
- *Bacteroidetes*
- *Actinobacteria*
- *Proteobacteria*

The relative abundance of these microbial groups varies among individuals and is influenced by factors such as diet, genetics, environment, and lifestyle. A diverse microbiome is generally considered a marker of good health, as it enhances resilience against environmental perturbations.

Alpha diversity (within-sample diversity) and beta diversity (between-sample diversity) are commonly used metrics to assess microbial diversity. Reduced diversity is often associated with disease states.

4.2 Mechanisms of Microbiome-Host Interaction

The interaction between the microbiome and the host occurs through multiple mechanisms:

4.2.1 Microbial Metabolites

Microbes produce a wide range of metabolites, including SCFAs, vitamins (e.g., vitamin K, B vitamins), and secondary bile acids. These metabolites influence host physiology by regulating gene expression, immune responses, and metabolic pathways.

4.2.2 Immune Signaling

Microbial components interact with immune receptors, leading to the activation of signaling pathways that regulate inflammation and immune responses.

4.2.3 Barrier Function

The microbiome helps maintain the integrity of the intestinal barrier by promoting mucus production and tight junction protein expression.

4.2.4 Epigenetic Modulation

Microbial metabolites can influence epigenetic modifications, such as DNA methylation and histone acetylation, thereby affecting gene expression.

4.3 Microbial Metabolites and Their Functions

Microbial metabolites are key mediators of microbiome-host interactions. Some of the most important metabolites include:

- **Short-Chain Fatty Acids (SCFAs):** Regulate inflammation, energy metabolism, and gut health.
- **Bile Acids:** Influence lipid metabolism and signaling pathways.
- **Tryptophan Metabolites:** Affect immune responses and neurological functions.
- **Lipopolysaccharides (LPS):** Trigger inflammatory responses when present in high levels.

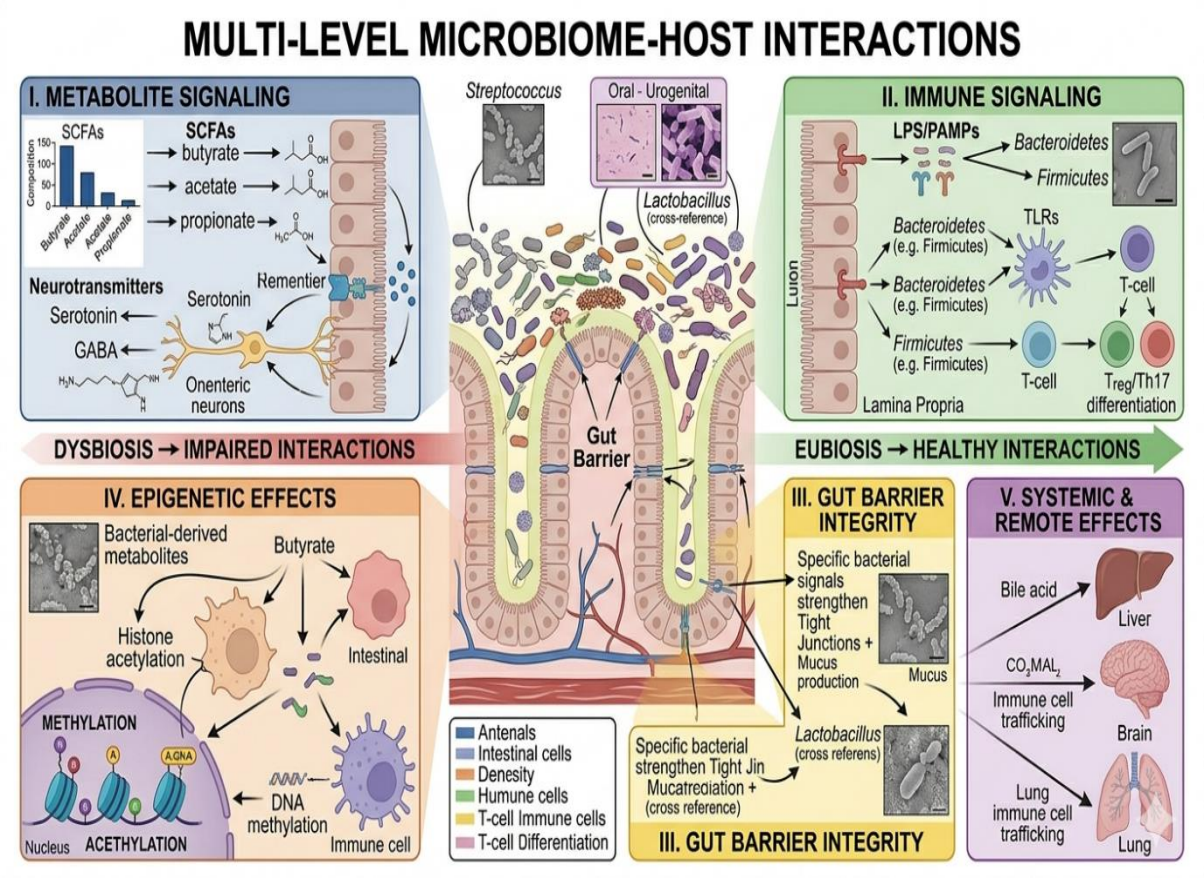

Figure No. 04: Microbiome-Host Interaction Mechanisms

4.4 Therapeutic Applications of the Microbiome

With growing evidence of the microbiome's role in disease, targeted therapeutic strategies have emerged to restore microbial balance and improve health outcomes.

4.4.1 Probiotics

Probiotics are live microorganisms that confer health benefits when administered in adequate amounts. Common probiotic strains include *Lactobacillus* and *Bifidobacterium*. These beneficial microbes help restore gut microbial balance, enhance intestinal barrier function, and modulate immune responses.

Clinical studies have demonstrated the efficacy of probiotics in managing conditions such as diarrhea, irritable bowel syndrome (IBS), and inflammatory bowel disease (IBD). Probiotics also play a role in reducing antibiotic-associated diarrhea and improving lactose intolerance.

However, the effectiveness of probiotics varies depending on the strain, dosage, and host-specific factors. Therefore, personalized probiotic therapy is an emerging area of research.

4.4.2 Prebiotics

Prebiotics are non-digestible food components that selectively stimulate the growth and activity of beneficial microorganisms. Examples include inulin, fructooligosaccharides (FOS), and galactooligosaccharides (GOS).

Prebiotics enhance the production of SCFAs, improve gut health, and support immune function. They are commonly found in foods such as bananas, onions, garlic, and whole grains.

4.4.3 Synbiotics

Synbiotics are combinations of probiotics and prebiotics that work synergistically to improve microbial balance. These formulations enhance the survival and colonization of beneficial microbes in the gut.

4.4.4 Fecal Microbiota Transplantation (FMT)

Fecal microbiota transplantation involves the transfer of stool from a healthy donor to a recipient to restore microbial diversity. It has shown remarkable success in treating recurrent *Clostridioides difficile* infections, with cure rates exceeding 90%.

FMT is also being investigated for other conditions, including IBD, obesity, and neurological disorders. Despite its potential, concerns regarding safety, standardization, and long-term effects remain.

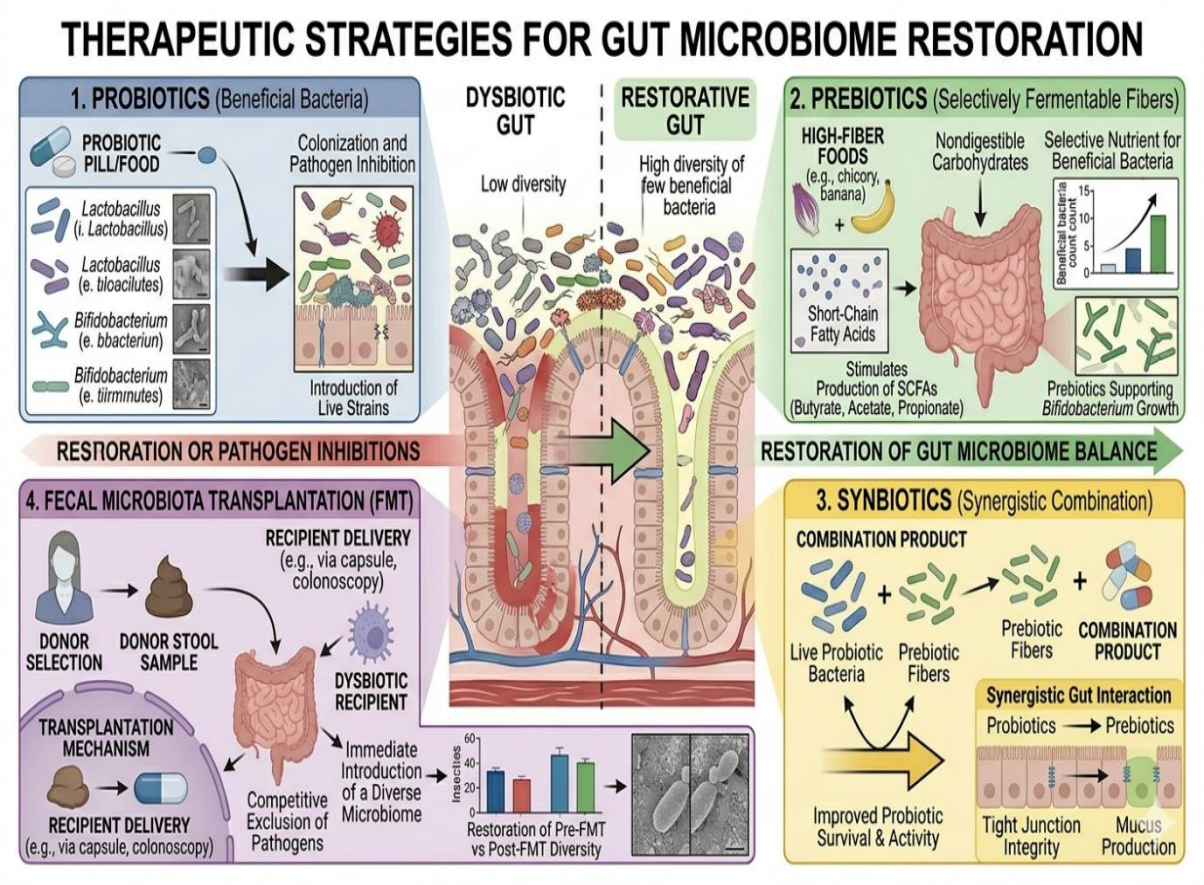

Figure No. 03: Microbiome-Based Therapeutic Strategies

4.5 Personalized Medicine and the Microbiome

The variability in microbiome composition among individuals has led to the concept of **personalized medicine**, where treatments are tailored based on an individual's microbial profile.

Microbiome-based diagnostics are being developed to predict disease risk, treatment response, and drug metabolism. For example, specific microbial signatures can indicate susceptibility to diseases such as diabetes or colorectal cancer.

Pharmacomicrobiomics is an emerging field that studies how microbiota influence drug metabolism and efficacy. Microbes can activate, inactivate, or modify drugs, affecting therapeutic outcomes.

Advances in artificial intelligence and machine learning are further enhancing the ability to analyze complex microbiome data and develop personalized treatment strategies.

4.6 Future Perspectives in Microbiome Research

Microbiome research is rapidly evolving, and several promising directions are emerging:

- **Next-Generation Sequencing (NGS):** Continued advancements will improve accuracy and reduce costs.
- **Multi-omics Approaches:** Integration of genomics, proteomics, metabolomics, and transcriptomics will provide a holistic understanding of microbiome function.
- **Microbiome Engineering:** Genetic modification of microbes to deliver therapeutic compounds.
- **Microbiota-Targeted Drugs:** Development of drugs that specifically modulate microbial composition.
- **Precision Nutrition:** Diet-based interventions tailored to individual microbiomes.

Despite these advancements, several challenges remain, including standardization of methodologies, data interpretation, and ethical considerations.

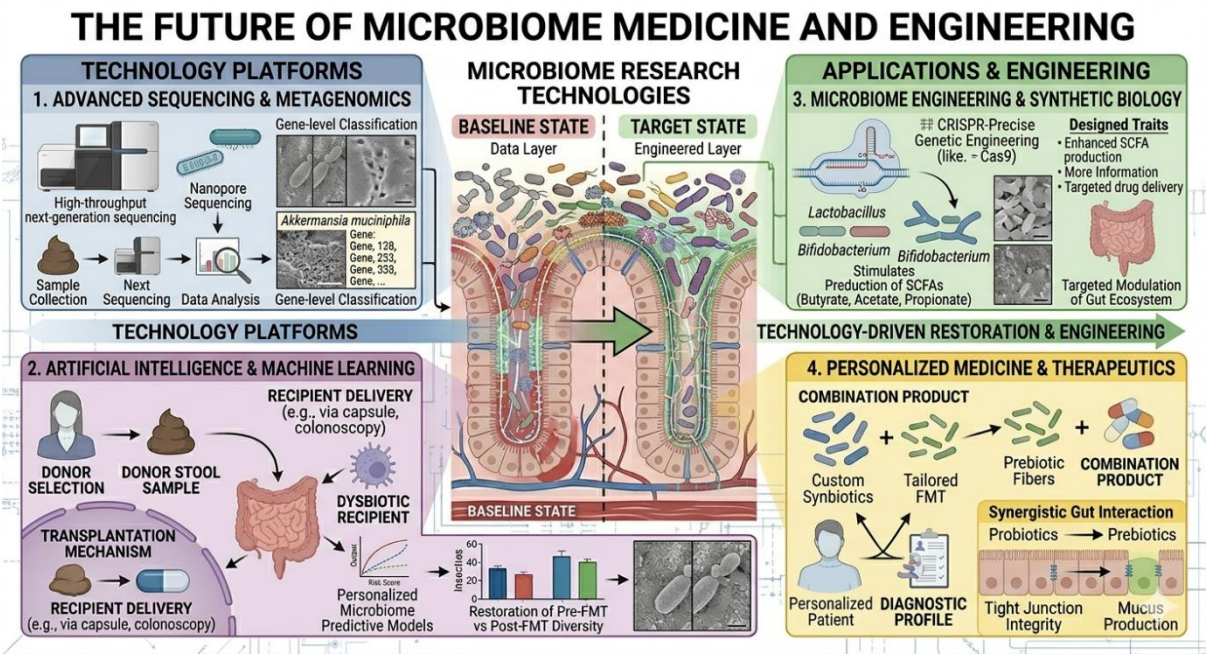

Figure No. 05: Future Directions in Microbiome Research

5. CONCLUSION:

The human microbiome is a complex and dynamic ecosystem that plays a crucial role in maintaining health and influencing disease development. Advances in sequencing technologies and computational tools have significantly enhanced our understanding of microbial diversity and function.

This review highlights the essential roles of the microbiome in metabolism, immune regulation, neurological function, and disease pathogenesis. Dysbiosis has been identified as a key factor in various diseases, including gastrointestinal disorders, metabolic syndromes, autoimmune diseases, neurological conditions, and cancer.

Therapeutic strategies such as probiotics, prebiotics, synbiotics, and fecal microbiota transplantation offer promising approaches for restoring microbial balance and improving health outcomes. Furthermore, the integration of microbiome research into personalized medicine has the potential to revolutionize healthcare by enabling targeted and individualized treatments.

Future research should focus on elucidating the complex interactions between the microbiome and the host, identifying disease-specific microbial signatures, and developing safe and effective microbiome-based therapies. Addressing current challenges will be essential for translating microbiome research into clinical practice.

In conclusion, the human microbiome represents a frontier in biomedical research with vast potential to transform our understanding of health and disease.

6. REFERENCES:

1. Cryan, J. F., & Dinan, T. G. (2012). Mind-altering microorganisms: The impact of the gut microbiota on brain and behaviour. *Nature Reviews Neuroscience, 13*(10), 701–712. https://doi.org/10.1038/nrn3346
2. Dominguez-Bello, M. G., Costello, E. K., Contreras, M., Magris, M., Hidalgo, G., Fierer, N., & Knight, R. (2010). Delivery mode shapes the acquisition and structure of the initial microbiota across multiple body habitats in newborns. *Proceedings of the National Academy of Sciences, 107*(26), 11971–11975. https://doi.org/10.1073/pnas.1002601107
3. Fan, Y., & Pedersen, O. (2021). Gut microbiota in human metabolic health and disease. *Nature Reviews Microbiology, 19*(1), 55–71. https://doi.org/10.1038/s41579-020-0433-9
4. Flint, H. J., Scott, K. P., Louis, P., & Duncan, S. H. (2012). The role of the gut microbiota in nutrition and health. *Nature Reviews Gastroenterology & Hepatology, 9*(10), 577–589.
5. Gilbert, J. A., Blaser, M. J., Caporaso, J. G., Jansson, J. K., Lynch, S. V., & Knight, R. (2018). Current understanding of the human microbiome. *Nature Medicine, 24*(4), 392–400. https://doi.org/10.1038/nm.4517
6. Human Microbiome Project Consortium. (2012). Structure, function and diversity of the healthy human microbiome. *Nature, 486*(7402), 207–214. https://doi.org/10.1038/nature11234
7. Kho, Z. Y., & Lal, S. K. (2018). The human gut microbiome—A potential controller of wellness and disease. *Frontiers in*

Microbiology, *9*, 1835. https://doi.org/10.3389/fmicb.2018.01835

8. Koneru, S., Thiruvadi, V., & Ramesh, M. (2023). Gut microbiome and its clinical implications: Exploring key players in human health. *Current Opinion in Clinical Nutrition & Metabolic Care*, *36*(5), 353–359.
9. Ley, R. E., Peterson, D. A., & Gordon, J. I. (2006). Ecological and evolutionary forces shaping microbial diversity in the human intestine. *Cell*, *124*(4), 837–848.
10. Ley, R. E., Hamady, M., Lozupone, C., Turnbaugh, P. J., Ramey, R. R., Bircher, J. S., Schlegel, M. L., Tucker, T. A., Schrenzel, M. D., Knight, R., & Gordon, J. I. (2008). Evolution of mammals and their gut microbes. *Science*, *320*(5883), 1647–1651.
11. Lynch, S. V., & Pedersen, O. (2016). The human intestinal microbiome in health and disease. *New England Journal of Medicine*, *375*(24), 2369–2379. https://doi.org/10.1056/NEJMra1600266
12. Marchesi, J. R., Adams, D. H., Fava, F., Hermes, G. D. A., Hirschfield, G. M., Hold, G., Quraishi, M. N., Kinross, J., Smidt, H., Tuohy, K. M., Thomas, L. V., Zoetendal, E. G., & Hart, A. (2016). The gut microbiota and host health: A new clinical frontier. *Gut*, *65*(2), 330–339.
13. Rinninella, E., Raoul, P., Cintoni, M., Franceschi, F., Miggiano, G. A. D., Gasbarrini, A., & Mele, M. C. (2019). What is the healthy gut microbiota composition? *Microorganisms*, *7*(1), 14. https://doi.org/10.3390/microorganisms7010014
14. Shreiner, A. B., Kao, J. Y., & Young, V. B. (2015). The gut microbiome in health and in disease. *Current Opinion in Gastroenterology*, *31*(1), 69–75.
15. Sommer, F., & Bäckhed, F. (2013). The gut microbiota—Masters of host development and physiology. *Nature Reviews Microbiology*, *11*(4), 227–238.
16. Tilg, H., & Moschen, A. R. (2014). Microbiota and diabetes: An evolving relationship. *Gut*, *63*(9), 1513–1521.
17. Turnbaugh, P. J., Ley, R. E., Mahowald, M. A., Magrini, V., Mardis, E. R., & Gordon, J. I. (2006). An obesity-associated gut microbiome. *Nature*, *444*(7122), 1027–1031. https://doi.org/10.1038/nature05414
18. Turnbaugh, P. J., Hamady, M., Yatsunenko, T., Cantarel, B. L., Duncan, A., Ley, R. E., Sogin, M. L., Jones, W. J., Roe, B. A., Affourtit, J. P., Egholm, M., Henrissat, B., Heath, A. C., Knight, R., & Gordon, J. I. (2007). A core gut microbiome in obese and lean twins. *Nature*, *457*(7228), 480–484. https://doi.org/10.1038/nature07540
19. Valdes, A. M., Walter, J., Segal, E., & Spector, T. D. (2018). Role of the gut microbiota in nutrition and health. *BMJ*, *361*, k2179. https://doi.org/10.1136/bmj.k2179
20. Zmora, N., Suez, J., & Elinav, E. (2019). You are what you eat: Diet, health and the gut microbiota. *Nature Reviews Gastroenterology & Hepatology*, *16*(1), 35–56. https://doi.org/10.1038/s41575-018-0061-2
21. Collado, M. C., Devkota, S., & Ghosh, T. S. (2024). Gut microbiome: A biomedical revolution. *Nature Reviews Gastroenterology & Hepatology*, *21*, 830–833. https://doi.org/10.1038/s41575-024-01001-3
22. Sangiuolo, K., Cheng, E., Terala, A., Dubrosa, F., & Milanaik, R. L. (2022). The gut microbiome: Trends and risks in pediatric populations. *Current Opinion in Pediatrics*, *34*(6), 634–642.
23. Gulliver, E. L., Young, R. B., Chonwerawong, M., et al. (2022). The future of microbiome-based therapeutics. *Alimentary Pharmacology & Therapeutics*, *56*(2), 192–208.
24. Pal, P., & Shastry, R. P. (2023). Role of gut microbiome in colon cancer and precision medicine. *Folia Microbiologica*, *68*, 691–701.
25. Journal of Advanced Research. (2025). Targeting the human gut microbiome: Probiotics, prebiotics, synbiotics, and postbiotics. *Journal of Advanced Research*.