The Microbiome Revolution: Understanding Gut Health

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Abstract

The gut microbiome, a highly diverse community of trillions of microorganisms residing in the human gastrointestinal tract, plays a fundamental role in preserving health and preventing disease. Emerging research underscores its critical involvement in various physiological functions, such as nutrient digestion, immune system modulation, and metabolic balance maintenance. This growing body of research, often referred to as the "microbiome revolution," emphasizes the complex interplay between the host and its microbial inhabitants. Imbalances in microbial composition, known as dysbiosis, have been associated with the onset of a range of chronic diseases, such as inflammatory bowel disease, obesity, diabetes, and neurodegenerative conditions. Advances in sequencing technologies and bioinformatics have propelled our understanding of the microbiome's functional dynamics, revealing how dietary patterns, antibiotics, and environmental factors shape microbial communities. Emerging strategies, such as the use of beneficial microorganisms, dietary fibers that support gut bacteria, and stool microbiota transfer, present promising therapeutic approaches for the restoration of gut health. This chapter explores the revolutionary discoveries in microbiome science, underscoring the potential for personalized medicine based on gut microbial profiles. As the microbiome revolution continues to evolve, understanding its implications offers transformative possibilities for medicine, nutrition, and overall well-being.

Keywords: Microbiome, Dysbiosis, Bioinformatics, Nutrition, Gut Health, Antibiotics

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Introduction

The human body is home to many microorganisms, such as bacteria, archaea, fungi, and viruses, which comprise the microbiome. While the concept of microorganisms influencing human health has existed since Pasteur's germ theory, recognizing their essential role in maintaining homeostasis and preventing disease is relatively recent. Initiated in 2007, the Human Microbiome Project (HMP) transformed our knowledge of the gut microbiome, highlighting its intricate nature and dynamic relationship with human physiology (Turnbaugh et al., 2007).

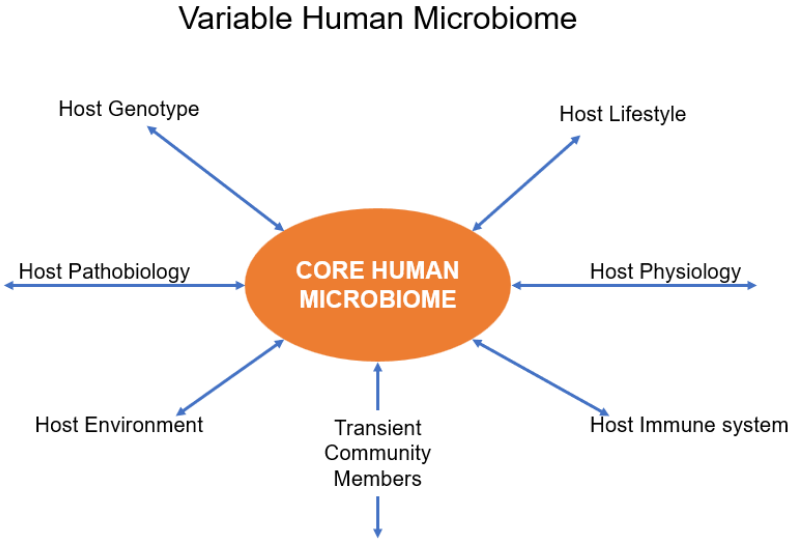

Fig. 1: The idea of a basic set of microbes found in all humans

The gut microbiome, in particular, is central to systemic health, influencing metabolic functions, immune responses, and mental health via the gut-brain axis shown in Figure 2 (Lu et al., 2024). The human microbiome, often referred to as a "hidden organ," consists of trillions of microorganisms whose collective genome significantly surpasses that of the host. These microbes inhabit various body regions, including the gastrointestinal tract (GIT), skin, saliva, oral mucosa, and conjunctiva, primarily colonizing external and internal surfaces. The colon harbors the majority of commensal bacteria, previously estimated to number approximately 10^{14}, while the skin is thought to contain around 10^{12} bacteria. Other body regions collectively accommodate fewer than 10^{12} microorganisms (Saheb et al., 2021). Within the alimentary canal, the bacterial population is minimal in the stomach and small intestine but reaches its peak in the colon, which serves as the primary reservoir for gut microbiota (Sender et al., 2016).

The gut microbiota is essential for breaking down non-digestible substrates, such as dietary fibers, facilitating the growth of specialized microorganisms that produce short-chain fatty acids (SCFAs). Among the SCFAs produced, acetate, propionate, and butyrate are particularly important for maintaining human health (Deleu et al., 2021). Prebiotics, defined as substrates selectively metabolized by beneficial host microorganisms, contribute to health by fostering SCFA production through microbial fermentation in the gut. Prebiotics are known to impact human health by shaping the composition and functional activity of the gut microbiota (Yoo et al., 2024)

2. Development of the Gut Microbiome

2.1 From Birth to Adulthood

The establishment of the gut microbiome commences at birth. Infants delivered through the vaginal birth canal typically acquire a microbiota composition that closely mirrors their mother's vaginal microbial flora (Heczko et al., 2024). In contrast, those born through cesarean section are primarily colonized by microorganisms commonly found on the skin, resulting in a distinctly different microbial community. This variation in early colonization can have long-term implications for the development of the infant's immune system and overall health (Dominguez-Bello et al., 2010) (Yang et al.,2024) Breastfeeding further enriches the gut microbiota with beneficial strains like *Bifidobacterium,* facilitated by human milk oligosaccharides (HMO) (Yang et al., 2024).

The critical role of the microbiome in shaping immune system development has been highlighted through studies examining factors that influence microbiome composition and stability. These factors include external influences, such as limited exposure to microbial components during fetal development, delivery by Cesarean section, and antibiotic use (Moore et al., 2023). Internal factors, like the underdeveloped state of the gut in preterm infants, also contribute to disruptions in microbiome establishment (Dogra et al., 2021)

2.2 Factors Influencing Microbiome Development

The makeup of the gut microbiome is determined by:

- **Host Genetics**: Genetic predisposition affects microbial diversity and susceptibility to dysbiosis. The gut microbiome is established through environmental exposure beginning at birth and plays a pivotal role in the interplay between environmental and genetic factors that influence host phenotype (Virolainen et al., 2023). While the microbiome is shaped by external factors such as diet, lifestyle, and early microbial exposures, it is also influenced by the host's genetic framework, creating a dynamic feedback loop of mutual adaptation. This dual role positions the microbiome as both an environmentally responsive entity and a host-modulated system. Given its adaptability, the microbiome represents a promising target for therapeutic intervention. Modulating its composition and function offers potential pathways for managing health and disease (GTEx Consortium, 2020). Understanding the intricate relationship between host genetics and microbiome dynamics is crucial for optimizing these interventions. By tailoring microbiome modifications to align with an individual's genetic predispositions, it may become possible to develop precision-based strategies to mitigate disease risk, enhance therapeutic outcomes, and promote overall health. This approach highlights the transformative potential of microbiome-based therapies in personalized medicine (Goodrich et al., 2014).
- **Dietary Patterns**: High-fiber diets support microbial diversity, whereas high-fat, low-fiber diets are linked to reduced diversity (Bailén et al., 2020). The composition of the gut microbiota is significantly influenced by dietary patterns, as various nutrients and food components serve as substrates for microbial metabolism. This intricate relationship underscores the role of diet as a major determinant of microbial diversity and functionality, which in turn impacts overall health (Kris-Etherton et al., 2018). However, while it is well-established that diet modulates gut microbiota, the specific associations between distinct dietary habits and microbial profiles across diverse human populations remain insufficiently explored and understood. Unraveling these connections is critical for advancing personalized nutrition strategies. Dietary interventions tailored to optimize gut microbiota could offer innovative approaches to managing conditions such as obesity, diabetes, and gastrointestinal disorders. For example, fiber-rich diets are widely recognized for supporting the proliferation of beneficial microorganisms that generate short-chain fatty acids, which play a crucial role in maintaining gut health and overall well-being, while high-fat, low-fiber diets may favor the proliferation of less favorable microbial populations (Bojková et al., 2020). Future research must focus on characterizing how specific dietary components interact with microbial communities in different cultural, geographical, and genetic contexts. Such insights could enable dietitians to design targeted dietary plans that not only address individual nutritional needs but also enhance microbial health, paving the way for more effective and personalized therapeutic interventions (De Filippo et al., 2010).
- **Antibiotic Use**: Early and excessive antibiotic exposure can disrupt microbial colonization, increasing the risk of allergies and autoimmune disorders. Exposure to antibiotics and other disruptive factors during early life can interfere with the natural transmission and stepwise development of a diverse, balanced gut microbiota (Patangia et al., 2022). Such disruptions have been associated with a heightened risk of developing metabolic and immune-related disorders. These disruptions can impair the establishment of microbial communities essential for immune system training and metabolic regulation, potentially contributing to conditions such as asthma, allergies, autoimmune diseases, obesity, and heightened vulnerability to opportunistic infections (Vidovic & Vidovic, 2020). Repeated and early administration of antibiotics can disrupt the balance of the gut microbiome and may contribute to the development and long-term survival of antibiotic-resistant bacterial strains. Such strains can colonize the gut, creating reservoirs of resistance genes that may be transferred to other pathogenic or commensal

microorganisms. This phenomenon exacerbates the global challenge of AMR, as resistant pathogens can compromise the efficacy of future antibiotic treatments (Abbas et al., 2025). Strategies such as promoting the use of narrow-spectrum antibiotics, encouraging breastfeeding to support natural microbial transmission, and developing probiotics or prebiotics tailored to restore microbial balance after antibiotic exposure hold promise. Additionally, public health initiatives aimed at reducing unnecessary antibiotic prescriptions and enhancing awareness of AMR are essential for mitigating long-term health consequences and preserving the effectiveness of antimicrobial therapies (Zhang et al., 2021).

3. The Gut Microbiome and Systemic Health

3.1 Metabolic Functions

Gut microbiota plays a crucial role in fermenting dietary fibers, which results in the generation of short-chain fatty acids (SCFAs) including propionate, acetate, and butyrate (Portincasa et al., 2022). These SCFAs are indispensable for host health, functioning as primary energy sources for colonic epithelial cells, and contributing to anti-inflammatory mechanisms that preserve gut integrity and modulate immune responses. In addition to SCFA synthesis, the gut microbiota plays a critical role in regulating bile acid metabolism, a process fundamental to efficient lipid digestion and the maintenance of cholesterol balance. This multifaceted interaction underscores the microbiota's essential contribution to both gastrointestinal health and systemic metabolic regulation (Louis et al., 2014). The interaction between gut microbes and dietary or host-derived compounds further highlights the complexity of the gut microbial ecosystem. Specific microbial species contribute to the release, modification, and conversion of diet-derived phytochemicals, bile acids, and glycoconjugates (Abdul Rahim et al., 2019). These metabolic activities not only shape the microbial community but also influence the host's metabolic pathways and overall health. For example, microbial transformations of bile acids can regulate signaling pathways involved in glucose and lipid metabolism, while phytochemical metabolites may exert antioxidant or anti-inflammatory effects (Morrison & Preston, 2016).

3.2 Immune Modulation

The gut microbiome educates the immune system, promoting tolerance to commensals while defending against pathogens. Pattern recognition receptors like Toll-like receptors (TLRs) mediate microbial interactions with immune cells, ensuring immune homeostasis (Wicherska-Pawłowska et al., 2021). The microbiota plays a central role in the development and regulation of the host's immune system. It facilitates immune maturation by promoting interactions between microbial populations and immune cells, thereby influencing the host's capacity to differentiate between harmful pathogens and harmless antigens. This dynamic interaction not only establishes immune homeostasis but also plays a critical role in the regulation of inflammatory responses and the maintenance of tolerance to commensal microbes and dietary antigens (Herwald & Egesten, 2017). Through these processes, microbiota is essential in ensuring the immune system's adaptability and proper function throughout the host's lifespan. Consequently, the immune system has evolved in parallel to maintaining a mutually beneficial relationship with the diverse and ever-changing microbial communities residing within the host. This bidirectional interaction is critical for immune homeostasis, enabling the body to mount protective responses against pathogens while maintaining tolerance to harmless antigens and self-tissues (Abe et al., 2019). Under optimal conditions, this microbiota-immune system alliance fosters a balanced immune environment that supports both defense and regulation. However, in many high-income countries, modern lifestyle factors—including the widespread use of antibiotics, shifts in dietary patterns, and the reduction of exposure to natural microbial partners such as helminths—have disrupted this delicate balance (Harris, 2023). These changes may lead to a microbiota characterized by reduced diversity and resilience, impairing its ability to support robust immune function. This dysbiosis is increasingly linked to the rise in immune-mediated conditions such as allergies, autoimmune diseases, and chronic inflammatory disorders (Zaiss & Harris, 2016). Addressing these challenges requires a multifaceted approach, including the promotion of judicious antibiotic use, the adoption of dietary strategies that support microbial diversity, and the exploration of interventions to restore beneficial host-microbiota relationships. Advancing our understanding of this intricate partnership between the microbiota and the immune system could pave the way for innovative therapies targeting immune dysregulation and related diseases (Belkaid and Hand, 2014).

3.3 Gut-Brain Axis

The gut-brain axis represents a bidirectional communication network influenced by microbial metabolites like SCFAs, tryptophan derivatives, and neuroactive compounds such as gamma-aminobutyric acid (GABA). The concept of the gut-brain axis has long been recognized for its role in maintaining physiological balance and homeostasis (Sun et al., 2024). In recent years, however, significant advancements have highlighted the critical involvement of microbiota as a major modulator of gut-brain interactions. Recent research highlights the significance of the microbiota-gut-brain axis, where microbial populations impact brain function and behavior, thereby contributing to overall health shown in Figure 1. The bidirectional communication between the gut microbiota and the central nervous system is crucial in regulating mood, stress responses, and cognitive functions (Carabotti et al., 2015). This emerging understanding provides a new perspective on how disturbances in the microbiome, such as dysbiosis, could contribute to neurological and psychiatric conditions, opening new avenues for potential therapeutic interventions targeting the microbiome (Cryan et al., 2019).

4. The Microbiome in Disease States

4.1 Dysbiosis and Its Implications

Dysbiosis, characterized by an imbalance in microbial composition, is commonly associated with a range of chronic diseases. As microbiome research has expanded, the term "dysbiosis" has gained increasing prominence, particularly when microbial patterns are linked to health and disease (Kandpal et al., 2022). While some have critiqued the ambiguity surrounding the scientific definition and implications of dysbiosis, its usage continues to proliferate in the field (Hooks & O'Malley, 2017).

- **Metabolic Disorders**: Increased *Firmicutes/Bacteroidetes* ratio correlates with obesity and insulin resistance. Human gut microbiota is

essential in regulating both health and disease states. It is increasingly recognized that modifying the gut microbiota could serve as a therapeutic strategy for addressing a range of diseases (Liu et al., 2021).

- **Autoimmune Conditions**: Dysbiosis disrupts immune tolerance, contributing to conditions like rheumatoid arthritis and multiple sclerosis (Cekanaviciute et al., 2017).

Colorectal Cancer: Microbial metabolites, such as hydrogen sulfide, can promote carcinogenesis, while beneficial strains produce butyrate, inhibiting tumor growth. This contribution arises not only from the pro-carcinogenic actions of certain pathogens but also from the broader microbial community, particularly its metabolic products (Yu et al., 2022). Recent studies have highlighted that short-chain fatty acids, including acetate, propionate, and butyrate, help suppress inflammation and cancer progression. Conversely, certain microbial byproducts, including secondary bile acids, have been associated with the facilitation of carcinogenic processes (Louis et al., 2014).

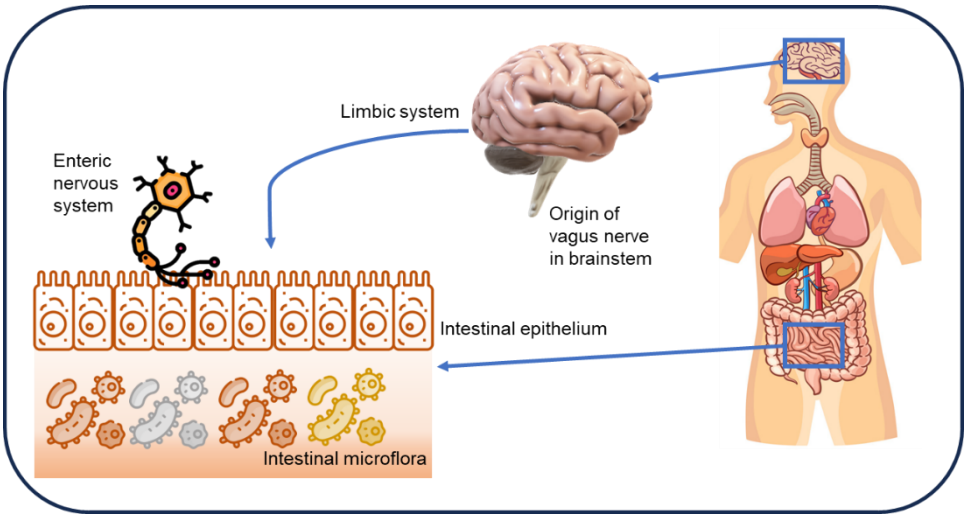

Fig. 2: Gut-Brain Axis

4.2 Microbial Biomarkers

Emerging research suggests that microbial signatures can serve as biomarkers for disease prediction and therapeutic response. Recent advances in next-generation sequencing technologies have enabled deeper insights into the intricate relationships between the gut microbiota and these diseases, uncovering potential correlations between specific bacterial populations and disease states (Afzaal et al., 2022). However, the identification of universally applicable gut microbial biomarkers for these conditions remains in the early stages. While numerous studies have explored the links between gut microbiota and intestinal diseases, suggesting various bacterial signatures that may serve as potential biomarkers, the complexity, and variability of the microbiome across individuals have made it challenging to establish consistent markers for clinical application. Advancements in research may enable a deeper understanding of microbial interactions, potentially leading to the development of diagnostic tools and tailored therapies for gastrointestinal diseases (Mancabelli et al., 2017)

5. Advances in Microbiome Science

5.1 Technological Innovations

- **Metagenomics and Transcriptomics**: These tools allow researchers to profile microbial communities and their functional roles (Quince et al., 2017). In the human microbiome, metatranscriptomics (MTX) offers promising potential for advancing both fundamental biological understanding and the identification of epidemiological biomarkers. These biomarkers could serve as high-dimensional diagnostic tools, providing insights into current health status and offering prognostic information for future health outcomes. MTX occupies a distinct role within molecular epidemiology due to its ability to capture the dynamic and responsive nature of microbial gene expression (Eybpoosh et al., 2017). Unlike human genetics, which remains largely stable over time, the expression of genes within the microbiome changes more rapidly, reflecting recent environmental exposures and microbial interactions. This temporal responsiveness allows MTX to provide a "shorter memory" of microbial activity, offering a real-time snapshot of the microbiome's response to external factors. Furthermore, MTX can be highly personalized, offering greater specificity than human transcriptomes due to the microbiome's adaptability and individual variability (Schupack et al., 2022). Similar to how tissue-specific transcription profiles reflect localized molecular activity, MTX can capture gene expression that is unique to specific body sites, providing detailed insights into the microbial function at those locations. In some cases, combining human and microbial transcriptional profiles can offer a comprehensive view of host-microbe interactions, further enriching our understanding of health and disease (Nayak et al., 2021). While much attention has been given to microbiome diversity and membership through metagenomics (MGX), as well as to human transcriptional biomarkers, the application of MTX to population health and clinical practice is still in its early stages, with much research needed to fully explore its potential for diagnostic and therapeutic purposes (Zhang et al., 2021).

CRISPR-Cas Systems: Genome editing technologies allow for the precise modification of probiotics, enabling targeted therapeutic interventions. CRISPR-Cas systems, particularly the class 2 single effector nucleases such as Cas9 and Cas12, have become widely utilized tools for genome editing and transcriptional regulation across various organisms. Their small size and portability make them highly efficient for directing genome modifications in plants, animals, and microbes, facilitating advancements in genetic engineering and enabling the development of customized probiotics with specific functional traits (Hidalgo-Cantabrana et al., 2019).

5.2 Emerging Concepts

- **Virome and Mycobiome**: The gut virome and fungal microbiome are gaining attention for their roles in shaping microbial ecosystems (Norman et al., 2015). Early evidence of the role of fungi in regulating gut homeostasis comes from the use of *Saccharomyces boulardii*, a yeast traditionally included in herbal medicine in Southeast Asia for its effectiveness in reducing severe diarrhea in cholera patients. *S. boulardii* continues to be widely used as a probiotic to prevent diarrhea and protect against intestinal colonization by *Clostridium difficile* following antibiotic treatment, also showing efficacy in preventing recurrent *C. difficile* infections. The beneficial effects of *S. boulardii* are attributed to its ability to neutralize pathogen toxins, inhibit the growth and invasion of intestinal pathogens, and enhance host immune responses (Terciolo et al., 2019). Additionally, it exerts anti-inflammatory effects, which have been beneficial in conditions like ulcerative colitis, and *C. difficile* colitis. More recently, another probiotic yeast, *Candida kefyr*, has shown promise in animal models, where it reduces colitis severity by altering the gut microbiota, specifically by decreasing the abundance of *Bacteroides* and lowering IL-6 production, ultimately attenuating intestinal inflammation (Matijašić et al., 2021).
- **Postbiotics**: Metabolites like SCFAs and enzymes are being explored for their therapeutic potential beyond live probiotics (Aguilar-Toalá et al., 2018). Probiotics are live microorganisms that, when consumed in sufficient quantities, have the potential to provide various health benefits to the host. These beneficial microbes interact with the gastrointestinal tract, influencing its composition and function, and may contribute to the maintenance of a balanced microbiota, supporting overall immune health, digestive function, and even systemic physiological processes (Hou et al., 2022). These beneficial microbes have garnered increasing attention for their diverse therapeutic potential. As highlighted by Zucko et al., probiotics offer a broad spectrum of health benefits, extending from the relief of gastrointestinal issues to their role in managing conditions such as allergies, obesity, and depression (Zucko et al., 2020). Additionally, they have been shown to aid in the treatment of bacterial vaginosis and support the overall health of the gastrointestinal tract. The growing body of evidence underscores the versatility of probiotics in contributing to various aspects of human health, prompting ongoing research into their use in both preventive and therapeutic applications (Vera-Santander et al., 2023).

6. Therapeutic and Preventive Strategies

6.1 Diet-Based Interventions

Plant-based, fiber-rich diets promote microbial diversity and SCFA production, while excessive red meat and processed foods are linked to dysbiosis (David et al., 2014). Dietary components are fundamental in regulating body homeostasis by modulating the composition of the gut microbiota, supplying vital nutrients, and triggering a range of physiological processes. Changes in dietary patterns, whether short-term or long-term, can significantly disrupt the balance of the gut microbiota, leading to metabolic dysfunctions and disturbances in physiological processes. This emerging concern is supported by recent studies highlighting the impact of dietary habits on health outcomes (Mizia et al., 2021). Diets rich in fats, and carbohydrates, and low in fiber are often associated with the development of gut dysbiosis, a condition that can contribute to a range of health issues. In contrast, dietary patterns like vegan and vegetarian diets, rich in fruits and vegetables, have demonstrated anti-inflammatory effects and contribute to the restoration of a balanced gut microbiota (Soldán et al., 2024). These dietary approaches support gut health and may help mitigate the risk of dysbiosis. These findings emphasize the significant role of diet in shaping the gut microbiota and its potential to influence overall health outcomes. Gut microbiota plays a critical role in regulating several metabolic processes, including cholesterol metabolism, blood glucose control, and insulin sensitivity. This microbial imbalance can contribute to the onset and progression of conditions such as cardiovascular disease, type 2 diabetes, and obesity (Iatcu et al., 2021). By altering key metabolic pathways, dysbiosis can affect processes like inflammation, insulin sensitivity, and lipid metabolism, further exacerbating these health issues. Additionally, the disruption of gut microbiota may impair the regulation of energy homeostasis, influencing both the development and severity of these chronic diseases. Recent research has significantly advanced our understanding of the gut microbiome's influence on mood and behavior, revealing its potential in mental health regulation. One emerging therapeutic approach, known as rebiosis, focuses on restoring microbiome balance by enhancing microbial resilience in the gut through the use of probiotics or prebiotics (Zhou et al., 2024). Over the past few decades, the health benefits of probiotics and prebiotics have been the subject of extensive research, particularly regarding their role in promoting gut health and preventing or treating various diseases. Additionally, the concept of psychobiotics has emerged as a novel antidepressant strategy, utilizing probiotics to modulate the gut-brain axis and potentially influencing mental health conditions (Adithya et al., 2021)

6.2 Probiotics and Prebiotics

- **Probiotics**: Live microorganisms, such as *Lactobacillus* and *Bifidobacterium*, play a vital role in restoring microbial equilibrium within the gut. By enhancing the diversity and composition of the microbiota, these beneficial microbes contribute to the maintenance of a healthy gut environment (Rinninella et al., 2019). They work by outcompeting pathogenic microorganisms, producing antimicrobial compounds, and modulating immune responses, which collectively support the restoration of microbial balance and promote overall gut health.
- **Prebiotics**: Non-digestible fibers, such as inulin, act as fuel for beneficial microbes, promoting their proliferation and enhancing their metabolic functions. The probiotic and prebiotic fields are currently shaped by a variety of factors. Recent advancements in technology, particularly in data collection and analytical techniques, have created new opportunities for discovering novel probiotics and prebiotics, while also advancing our understanding of their interactions with both the microbiome and the host (Kumar et al., 2020). Increasing attention is being directed toward investigating the wide range of applications of these substances for various health conditions, anatomical regions, demographic groups, and modes of administration. Additionally, the development of regulatory policies, clinical recommendations, and industry trends is playing a critical role in shaping the integration of probiotics and prebiotics within the fields of nutrition and healthcare (Cunningham et al., 2021). As research in these areas progresses, a thorough and integrated examination of current trends and their future implications is becoming increasingly crucial, as shown in Figure 3 (Cunningham, et al., 2021).

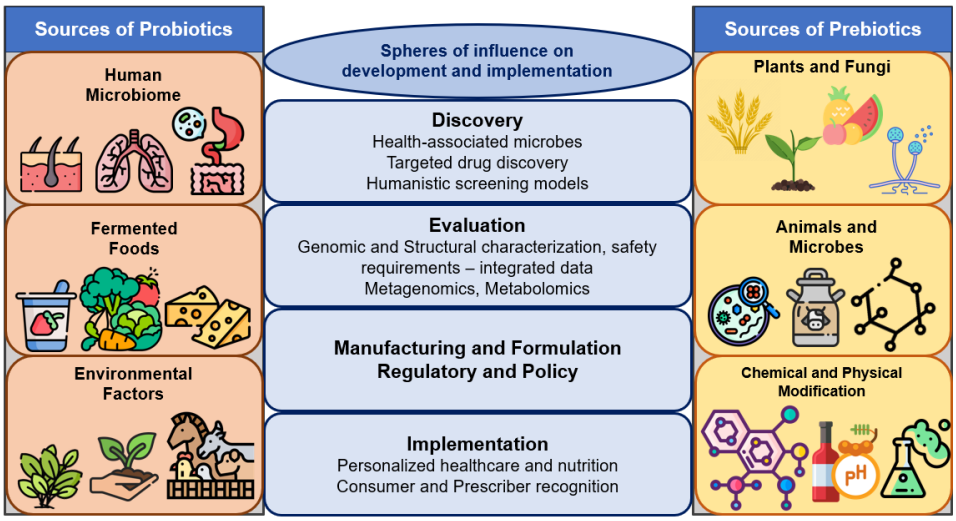

Fig. 3: Influences on the Future of Prebiotics and Probiotics (Retrieved from Drawio)

6.3 Fecal Microbiota Transplantation (FMT)

FMT is a groundbreaking therapy for *Clostridioides difficile* infections, with ongoing research exploring its applications in metabolic and autoimmune disorders (Biazzo & Deidda, 2022). The human body hosts a diverse array of microorganisms, with the majority residing in the gut, collectively known as the gut microbiota. In recent decades, mounting evidence has linked various human diseases to disruptions in the gut microbiota, known as dysbiosis. This has led to the hypothesis that restoring a healthy balance and composition of microbiota could improve clinical outcomes (Hou et al., 2022). Among the strategies to modulate the microbiota, supplementation with prebiotics and probiotics has shown promising results, although the main challenge remains the limited diversity of microbial species available for use as probiotics. In contrast, fecal microbiota transplantation (FMT) offers a more direct approach by transferring fecal matter from a healthy donor to a recipient's intestines, intending to reshape the recipient's gut microbial community to promote health (Chandrasekaran et al., 2024).

7. Future Directions

Microbiome profiling could enable personalized interventions, tailoring diets, and therapies to individual microbial compositions (Turnbaugh et al., 2009). AI and machine learning are revolutionizing microbiome research, facilitating the prediction of disease outcomes and therapeutic responses (Shah et al., 2021). Privacy concerns and equitable access to microbiome-based therapies are critical issues as the field advances (Zhu et al., 2021).

8. Conclusion

The microbiome revolution has fundamentally reshaped our understanding of gut health and its integral role in systemic human physiology. The gut microbiota, a complex and dynamic microbial community, orchestrates critical functions such as nutrient metabolism, immune modulation, and communication with the central nervous system. Disruptions in this delicate ecosystem, known as dysbiosis, are increasingly associated with a wide range of diseases, including metabolic disorders, autoimmune diseases, gastrointestinal pathologies, and neurodegenerative conditions. These discoveries have driven the development of novel therapeutic approaches, including targeted prebiotics, engineered probiotics, fecal microbiota transplantation, and microbiota-derived metabolites, to restore microbial homeostasis and optimize health. Moreover, the microbiome's ability to influence drug metabolism and host genetics underscores its critical role in precision medicine. By integrating microbiome research into diagnostics, therapeutics, and personalized interventions, the field promises to advance sustainable and targeted healthcare solutions. Continued exploration of the gut microbiome's vast capabilities will pave the way for innovative strategies to improve human health and combat chronic diseases effectively.

References

Abbas, R. Z., Qureshi, M. A., & Saeed, Z. (2025). Botanical compounds: A promising control strategy against Trypanosoma cruzi. *Boletín Latinoamericano y del Caribe de Plantas Medicinales y Aromáticas*, *24*(3), 308-327.

Abdul Rahim, M. B. H., Chilloux, J., Martinez-Gili, L., Neves, A. L., Myridakis, A., Gooderham, N., & Dumas, M. E. (2019). Diet-induced metabolic changes of the human gut microbiome: Importance of short-chain fatty acids, methylamines, and indoles. *Acta Diabetologica, 56*, 493–500.

Abe, T., Marutani, Y., & Shoji, I. (2019). Cytosolic DNA-sensing immune response and viral infection. *Microbiology and Immunology, 63*(2), 51–64. https://doi.org/10.1111/1348-0421.12669

Adithya, K. K., Rajeev, R., Selvin, J., & Seghal Kiran, G. (2021). Dietary influence on the dynamics of the human gut microbiome: Prospective implications in interventional therapies. *ACS Food Science & Technology, 1*(5), 717–736. http://dx.doi.org/10.1021/acsfoodscitech.0c00075

Afzaal, M., Saeed, F., Shah, Y. A., Hussain, M., Rabail, R., Socol, C. T., & Aadil, R. M. (2022). Human gut microbiota in health and disease: Unveiling the relationship. *Frontiers in Microbiology, 13*, 999001. https://doi.org/10.3389/fmicb.2022.999001

Aguilar-Toalá, J. E., Garcia-Varela, R., Garcia, H. S., Mata-Haro, V., González-Córdova, A. F., Vallejo-Cordoba, B., & Hernández-Mendoza, A.

(2018). Postbiotics: An evolving term within the functional foods field. *Trends in Food Science & Technology, 75*, 105–114. http://dx.doi.org/10.1016/j.tifs.2018.03.009

Bailén, M., Bressa, C., Martínez-López, S., González-Soltero, R., Montalvo Lominchar, M. G., San Juan, C., & Larrosa, M. (2020). Microbiota features associated with a high-fat/low-fiber diet in healthy adults. *Frontiers in Nutrition, 7*, 583608. https://doi.org/10.3389/fnut.2020.583608

Biazzo, M., & Deidda, G. (2022). Fecal microbiota transplantation as a new therapeutic avenue for human diseases. *Journal of Clinical Medicine, 11*(14), 4119. https://doi.org/10.3390/jcm11144119

Bojková, B., Winklewski, P. J., & Wszedybyl-Winklewska, M. (2020). Dietary fat and cancer—which is good, which is bad, and the body of evidence. *International Journal of Molecular Sciences, 21*(11), 4114. https://doi.org/10.3390/ijms21114114

Carabotti, M., Scirocco, A., Maselli, M. A., & Severi, C. (2015). The gut-brain axis: Interactions between enteric microbiota, central and enteric nervous systems. *Annals of Gastroenterology, 28*(2), 203–209.

Cekanaviciute, E., Yoo, B. B., Runia, T. F., Debelius, J. W., Singh, S., Nelson, C. A., & Baranzini, S. E. (2017). Gut bacteria from multiple sclerosis patients modulate human T cells and exacerbate symptoms in mouse models. *Proceedings of the National Academy of Sciences, 114*(40), 10713–10718. https://doi.org/10.1073/pnas.1711235114

Chandrasekaran, P., Weiskirchen, S., & Weiskirchen, R. (2024). Effects of probiotics on gut microbiota: An overview. *International Journal of Molecular Sciences, 25*(11), 6022. https://doi.org/10.3390/ijms25116022

Cryan, J. F., O'Riordan, K. J., Cowan, C. S., Sandhu, K. V., Bastiaanssen, T. F., Boehme, M., & Dinan, T. G. (2019). The microbiota-gut-brain axis. *Physiological Reviews*. https://doi.org/10.1152/physrev.00018.2018

Cunningham, M., Azcarate-Peril, M. A., Barnard, A., Benoit, V., Grimaldi, R., Guyonnet, D., & Gibson, G. R. (2021). Shaping the future of probiotics and prebiotics. *Trends in Microbiology, 29*(8), 667–685. https://doi.org/10.1016/j.tim.2021.01.003

David, L. A., Maurice, C. F., Carmody, R. N., Gootenberg, D. B., Button, J. E., Wolfe, B. E., & Turnbaugh, P. J. (2014). Diet rapidly and reproducibly alters the human gut microbiome. *Nature, 505*(7484), 559–563. https://doi.org/10.1038/nature12820

De Filippo, C., Cavalieri, D., Di Paola, M., Ramazzotti, M., Poullet, J. B., Massart, S., & Lionetti, P. (2010). Impact of diet in shaping gut microbiota revealed by a comparative study in children from Europe and rural Africa. *Proceedings of the National Academy of Sciences, 107*(33), 14691–14696. https://doi.org/10.1073/pnas.1005963107

Deleu, S., Machiels, K., Raes, J., Verbeke, K., & Vermeire, S. (2021). Short-chain fatty acids and their producing organisms: An overlooked therapy for IBD? *EBioMedicine, 66*, 103293. https://doi.org/10.1016/j.ebiom.2021.103293

Dogra, S. K., Chung, C. K., Wang, D., Sakwinska, O., Colombo Mottaz, S., & Sprenger, N. (2021). Nurturing the early life gut microbiome and immune maturation for long-term health. *Microorganisms, 9*(10), 2110. https://doi.org/10.3390/microorganisms9102110

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

Eybpoosh, S., Haghdoost, A. A., Mostafavi, E., Bahrampour, A., Azadmanesh, K., & Zolala, F. (2017). Molecular epidemiology of infectious diseases. *Electronic Physician, 9*(8), 5149–5158. https://doi.org/10.19082/5149

Goodrich, J. K., Waters, J. L., Poole, A. C., Sutter, J. L., Koren, O., Blekhman, R., & Ley, R. E. (2014). Human genetics shape the gut microbiome. *Cell, 159*(4), 789–799. https://doi.org/10.1016/j.cell.2014.09.053

GTEx Consortium. (2020). The GTEx Consortium atlas of genetic regulatory effects across human tissues. *Science, 369*(6509), 1318–1330. https://doi.org/10.1126/science.aaz1776

Harris, N. L. (2023). Networking between helminths, microbes, and mammals. *Cell Host & Microbe, 31*(4), 464–471. https://doi.org/10.1016/j.chom.2023.02.008

Heczko, P. B., Giemza, M., Ponikiewska, W., & Strus, M. (2024). Importance of *Lactobacilli* for human health. *Microorganisms, 12*(12), 2382. https://doi.org/10.3390/microorganisms12122382

Herwald, H., & Egesten, A. (2017). Cells of innate and adaptive immunity: A matter of class? *Journal of Innate Immunity, 9*(2), 109. https://doi.org/10.1159/000457176

Hidalgo-Cantabrana, C., Goh, Y. J., Pan, M., Sanozky-Dawes, R., & Barrangou, R. (2019). Genome editing using the endogenous type I CRISPR-Cas system in *Lactobacillus crispatus*. *Proceedings of the National Academy of Sciences, 116*(32), 15774–15783. https://doi.org/10.1073/pnas.1905421116

Hooks, K. B., & O'Malley, M. A. (2017). Dysbiosis and its discontents. *mBio, 8*(5), e01011-17. https://doi.org/10.1128/mbio.01492-17

Hou, K., Wu, Z. X., Chen, X. Y., Wang, J. Q., Zhang, D., Xiao, C., & Chen, Z. S. (2022). Microbiota in health and diseases. *Signal Transduction and Targeted Therapy, 7*(1), 135. https://doi.org/10.1038/s41392-022-00974-4

Iatcu, C. O., Steen, A., & Covasa, M. (2021). Gut microbiota and complications of type-2 diabetes. *Nutrients, 14*(1), 166. https://doi.org/10.3390/nu14010166

Kandpal, M., Indari, O., Baral, B., Jakhmola, S., Tiwari, D., Bhandari, V., & Jha, H. C. (2022). Dysbiosis of gut microbiota from the perspective of the gut–brain axis: Role in the provocation of neurological disorders. *Metabolites, 12*(11), 1064. https://doi.org/10.3390/metabo12111064

Kris-Etherton, P. M., Petersen, K., & Van Horn, L. (2018). Convincing evidence supports reducing saturated fat to decrease cardiovascular disease risk. *BMJ Nutrition, Prevention & Health, 1*(1), 23. https://doi.org/10.1136/bmjnph-2018-000009

Kumar, R., Sood, U., Gupta, V., Singh, M., Scaria, J., & Lal, R. (2020). Recent advancements in the development of modern probiotics for restoring human gut microbiome dysbiosis. *Indian Journal of Microbiology, 60*(1), 12–25. https://doi.org/10.1007/s12088-019-00808-y

Liu, H., Shiver, A. L., Price, M. N., Carlson, H. K., Trotter, V. V., Chen, Y., & Deutschbauer, A. M. (2021). Functional genetics of human gut commensal *Bacteroides thetaiotaomicron* reveals metabolic requirements for growth across environments. *Cell Reports, 34*(9), Article

108789. https://doi.org/10.1016/j.celrep.2021.108789
Louis, P., Hold, G. L., & Flint, H. J. (2014). The gut microbiota, bacterial metabolites, and colorectal cancer. *Nature Reviews Microbiology, 12*(10), 661–672. https://doi.org/10.1038/nrmicro3344
Lu, S., Zhao, Q., Guan, Y., Sun, Z., Li, W., Guo, S., & Zhang, A. (2024). The communication mechanism of the gut-brain axis and its effect on central nervous system diseases: A systematic review. *Biomedicine & Pharmacotherapy, 178*, 117207. https://doi.org/10.1016/j.biopha.2024.117207
Mancabelli, L., Milani, C., Lugli, G. A., Turroni, F., Cocconi, D., van Sinderen, D., & Ventura, M. (2017). Identification of universal gut microbial biomarkers of common human intestinal diseases by meta-analysis. *FEMS Microbiology Ecology, 93*(12), fix153. https://doi.org/10.1093/femsec/fix153
Matijašić, M., Meštrović, T., Čipčić Paljetak, H., Perić, M., Barešić, A., & Verbanac, D. (2020). Gut microbiota beyond bacteria—Mycobiome, virome, archaeome, and eukaryotic parasites in IBD. *International Journal of Molecular Sciences, 21*(8), 2668. https://doi.org/10.3390/ijms21082668
Mizia, S., Felińczak, A., Włodarek, D., & Syrkiewicz-Świtała, M. (2021). Evaluation of eating habits and their impact on health among adolescents and young adults: A cross-sectional study. *International Journal of Environmental Research and Public Health, 18*(8), 3996. https://doi.org/10.3390/ijerph18083996
Moore, J., Navarro, S., McCarthy, K., Rashid, R. B., Phipps, S., Amoako, A., Callaway, L., & Eley, V. (2023). State of the art: Intrapartum antibiotics in cesarean section, the infant microbiota and allergic diseases. *Acta Obstetricia et Gynecologica Scandinavica, 102*(7), 811–820. https://doi.org/10.1111/aogs.14577
Morrison, D. J., & Preston, T. (2016). Formation of short-chain fatty acids by the gut microbiota and their impact on human metabolism. *Gut Microbes, 7*(3), 189–200. https://doi.org/10.1080/19490976.2015.1134082
Nayak, R. R., Alexander, M., Deshpande, I., Stapleton-Gray, K., Rimal, B., Patterson, A. D., Ubeda, C., Scher, J. U., & Turnbaugh, P. J. (2021). Methotrexate impacts conserved pathways in diverse human gut bacteria leading to decreased host immune activation. *Cell Host & Microbe, 29*(3), 362–377.e11. https://doi.org/10.1016/j.chom.2020.12.008
Patangia, D. V., Anthony Ryan, C., Dempsey, E., Paul Ross, R., & Stanton, C. (2022). Impact of antibiotics on the human microbiome and consequences for host health. *MicrobiologyOpen, 11*(1), e1260. https://doi.org/10.1002/mbo3.1260
Portincasa, P., Bonfrate, L., Vacca, M., De Angelis, M., Farella, I., Lanza, E., Khalil, M., Wang, D. Q., Sperandio, M., & Di Ciaula, A. (2022). Gut microbiota and short-chain fatty acids: Implications in glucose homeostasis. *International Journal of Molecular Sciences, 23*(3), 1105. https://doi.org/10.3390/ijms23031105
Quince, C., Walker, A. W., Simpson, J. T., Loman, N. J., & Segata, N. (2017). Shotgun metagenomics, from sampling to analysis. *Nature Biotechnology, 35*(9), 833–844. https://doi.org/10.1038/nbt.3935
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? A changing ecosystem across age, environment, diet, and diseases. *Microorganisms, 7*(1), 14. https://doi.org/10.3390/microorganisms7010014
Saheb Kashaf, S., Proctor, D. M., Deming, C., et al. (2021). Integrating cultivation and metagenomics for a multi-kingdom view of skin microbiome diversity and functions. *Nature Microbiology*. https://doi.org/10.1038/s41564-021-01011-w
Schupack, D. A., Mars, R. A. T., Voelker, D. H., Abeykoon, J. P., & Kashyap, P. C. (2022). The promise of the gut microbiome as part of individualized treatment strategies. *Nature Reviews Gastroenterology & Hepatology, 19*(1), 7–25. https://doi.org/10.1038/s41575-021-00499-1
Sender, R., Fuchs, S., & Milo, R. (2016). Are we really vastly outnumbered? Revisiting the ratio of bacterial to host cells in humans. *Cell, 164*(3), 337–340. https://doi.org/10.1016/j.cell.2016.01.013
Soldán, M., Argalášová, Ľ., Hadvinová, L., Galileo, B., & Babjaková, J. (2024). The effect of dietary types on gut microbiota composition and development of non-communicable diseases: A narrative review. *Nutrients, 16*(18), 3134. https://doi.org/10.3390/nu16183134
Sun, X., Shukla, M., Wang, W., & Li, S. (2024). Unlocking gut-liver-brain axis communication metabolites: Energy metabolism, immunity, and barriers. *npj Biofilms and Microbiomes, 10*(1), 136. https://doi.org/10.1038/s41522-024-00610-9
Terciolo, C., Dapoigny, M., & Andre, F. (2019). Beneficial effects of *Saccharomyces boulardii* CNCM I-745 on clinical disorders associated with intestinal barrier disruption. *Clinical and Experimental Gastroenterology, 12*, 67–82. https://doi.org/10.2147/CEG.S181590
Turnbaugh, P. J., Ley, R. E., Hamady, M., Fraser-Liggett, C. M., Knight, R., & Gordon, J. I. (2007). The human microbiome project. *Nature, 449*(7164), 804–810. https://doi.org/10.1038/nature06244
Vera-Santander, V. E., Hernández-Figueroa, R. H., Jiménez-Munguía, M. T., Mani-López, E., & López-Malo, A. (2023). Health benefits of consuming foods with bacterial probiotics, postbiotics, and their metabolites: A review. *Molecules, 28*(3), 1230. https://doi.org/10.3390/molecules28031230
Vidovic, N., & Vidovic, S. (2020). Antimicrobial resistance and food animals: Influence of livestock environment on the emergence and dissemination of antimicrobial resistance. *Antibiotics, 9*(2), 52. https://doi.org/10.3390/antibiotics9020052
Virolainen, S. J., VonHandorf, A., Viel, K. C. M. F., Weirauch, M. T., & Kottyan, L. C. (2023). Gene-environment interactions and their impact on human health. *Genes and Immunity, 24*(1), 1–11. https://doi.org/10.1038/s41435-022-00192-6
Wicherska-Pawłowska, K., Wróbel, T., & Rybka, J. (2021). Toll-like receptors (TLRs), NOD-like receptors (NLRs), and RIG-I-like receptors (RLRs) in innate immunity: TLRs, NLRs, and RLRs ligands as immunotherapeutic agents for hematopoietic diseases. *International Journal of Molecular Sciences, 22*(24), 13397. https://doi.org/10.3390/ijms222413397
Yang, S., Cai, J., Su, Q., Li, Q., & Meng, X. (2024). Human milk oligosaccharides combine with *Bifidobacterium longum* to form the "golden shield" of the infant intestine: Metabolic strategies, health effects, and mechanisms of action. *Gut Microbes, 16*(1), Article 2430418.

http://dx.doi.org/10.3390/microorganisms11061553

Yoo, S., Jung, S. C., Kwak, K., & Kim, J. S. (2024). The role of prebiotics in modulating gut microbiota: Implications for human health. *International Journal of Molecular Sciences, 25*(9), Article 4834. https://doi.org/10.3390/ijms25094834

Yu, J. S., Correia-Melo, C., Zorrilla, F., Herrera-Dominguez, L., Wu, M. Y., Hartl, J., & Ralser, M. (2022). Microbial communities form rich extracellular metabolomes that foster metabolic interactions and promote drug tolerance. *Nature Microbiology, 7*(4), 542–555. https://doi.org/10.1038/s41564-022-01072-5

Zaiss, M. M., & Harris, N. L. (2016). Interactions between the intestinal microbiome and helminth parasites. *Parasite Immunology, 38*(1), 5–11. https://doi.org/10.1111/pim.12274

Zhang, X., Borbet, T. C., Fallegger, A., Wipperman, M. F., Blaser, M. J., & Müller, A. (2021). An antibiotic-impacted microbiota compromises the development of colonic regulatory T cells and predisposes to dysregulated immune responses. *mBio, 12*(1), Article e03474-20. https://doi.org/10.1128/mBio.03474-20

Zhang, Y., Thompson, K. N., Branck, T., Yan, Y., Nguyen, L. H., Franzosa, E. A., & Huttenhower, C. (2021). Metatranscriptomics for the human microbiome and microbial community functional profiling. *Annual Review of Biomedical Data Science, 4*(1), 279–311. https://doi.org/10.1146/annurev-biodatasci-031121-103035

Zhou, P., Chen, C., Patil, S., & Dong, S. (2024). Unveiling the therapeutic symphony of probiotics, prebiotics, and postbiotics in gut-immune harmony. *Frontiers in Nutrition, 11*, Article 1355542. https://doi.org/10.3389/fnut.2024.1355542

Zucko, J., Starcevic, A., Diminic, J., Oros, D., Mortazavian, A. M., & Putnik, P. (2020). Probiotic—Friend or foe? *Current Opinion in Food Science, 32*, 45–49. http://dx.doi.org/10.1016/j.cofs.2020.01.007