Int.J.Curr.Microbiol.App.Sci (2025) *14*(11): 96-100

International Journal of Current Microbiology and Applied Sciences
***ISSN: 2319-7706* Volume 14 Number 11 (2025)**
Journal homepage: http://www.ijcmas.com

Review Article

https://doi.org/10.20546/ijcmas.2025.1411.011

Human Microbiome and Its Role in Immunity and Disease

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Keywords

Microbiome; Dysbiosis; Immune regulation; SCFAs; Gut-brain axis

Article Info

Received:
14 September 2025
Accepted:
22 October 2025
Available Online:
10 November 2025

A B S T R A C T

The human microbiome, a diverse community of microorganisms inhabiting the body, plays a pivotal role in keeping health and regulating immunity. Once regarded as passive inhabitants, these microbes are now recognised as active participants in immune development, metabolic regulation, and disease prevention. The gut microbiome serves as a major immunological interface, influencing the maturation of immune cells, cytokine balance, and mucosal defence mechanisms. Alterations in microbial composition known as dysbiosis can disrupt this balance, leading to immune dysregulation and chronic inflammation. Increasing evidence links dysbiosis to a wide range of disorders, including inflammatory bowel disease, obesity, diabetes, autoimmune conditions, and neuropsychiatric disorders. The microbiome's role extends beyond the gut, affecting systemic immunity and even modulating responses to infections, vaccines, and cancer therapies. Therapeutic strategies such as probiotics, prebiotics, dietary interventions, and fecal microbiota transplantation (FMT) are being explored to restore microbial homeostasis and enhance immune function. Despite remarkable advances, significant challenges remain in defining a "healthy" microbiome and standardising analytical methods. This review highlights current understanding of the human microbiome's contribution to immune regulation and disease pathogenesis, emphasising the need for integrative, personalised approaches in microbiome-based medicine. Continued research in this field holds immense promise for transforming prevention and treatment strategies across multiple domains of human health.

Introduction

The human body is host to a vast and complex community of microorganisms collectively known as the human microbiome (1,2). This diverse ecosystem—including bacteria, viruses, fungi, and archaea—exists primarily in the gut, but also inhabits the skin, oral cavity, respiratory tract, and genitourinary system. It is estimated that microbial cells in the body equal human cells in number, highlighting their integral role in maintaining physiological balance and health (3,4).

In recent years, the microbiome has appeared as a critical determinant of human health, influencing not only digestion and metabolism but also immune regulation, neurodevelopment, and disease

susceptibility. Far from being mere bystanders, these microorganisms engage in dynamic interactions with host tissues and immune cells, shaping immune system maturation and tolerance from early life (5,6). The concept of humans as "super-organisms"—a symbiotic partnership between human and microbial genomes—has redefined our understanding of health and disease.

The gut microbiome has drawn intense scientific interest due to its extensive impact on immune homeostasis. Through the production of metabolites such as short-chain fatty acids and the modulation of mucosal immunity, the gut flora helps maintain the delicate balance between immune defence and tolerance. When this equilibrium is disrupted—a condition termed dysbiosis—the resulting immune dysregulation can contribute to a wide range of disorders including inflammatory bowel disease, obesity, diabetes, autoimmune conditions, and even neuropsychiatric illnesses.

Recent technological advances, especially in next-generation sequencing and metagenomics, have enabled a deeper exploration of microbial diversity and its functional implications. These discoveries have opened new avenues for preventive and therapeutic strategies, from probiotics and dietary modulation to microbiome-based precision medicine (7,8,9).

This review aims to summarise current understanding of the human microbiome's role in immunity and disease, exploring its mechanisms of immune modulation, links with major disease processes, and emerging therapeutic prospects. By integrating existing evidence, it highlights how maintaining microbial balance may be a key frontier in promoting human health and preventing disease in the 21st century.

Over the past two decades, extensive research has transformed our understanding of the human microbiome from a collection of commensal organisms to a vital determinant of immune function and overall health. Early studies using culture-based methods offered limited insights into microbial diversity, but the introduction of 16S rRNA gene sequencing and metagenomic analysis has revolutionised this field. These technologies revealed that the human body harbours trillions of microorganisms, most of which are unculturable by traditional methods, and that their composition varies across individuals, body sites, and environments.

One of the earliest milestones in this field was the Human Microbiome Project (HMP) launched in 2007, which systematically characterised microbial communities across different body regions. The project laid the foundation for exploring how microbial balance contributes to health and how its disruption, or dysbiosis, relates to disease. Subsequent studies proved that the gut microbiota plays a significant role in shaping the immune system (10). Experimental models showed that germ-free animals show underdeveloped immune tissues and impaired immune responses, confirming that microbial exposure is essential for immune maturation.

Further research has proved that microbial metabolites such as short-chain fatty acids (SCFAs)—particularly butyrate and propionate—exert anti-inflammatory effects and promote regulatory T-cell differentiation. These interactions keep mucosal immunity and protect against over-activation of immune pathways. In contrast, disturbances in the gut microbial composition have been associated with diseases such as inflammatory bowel disease (IBD), obesity, type 2 diabetes, and various autoimmune conditions. Clinical studies have also shown that reduced microbial diversity correlates with increased inflammation and metabolic dysfunction.

Beyond the gut, the microbiome's influence extends to other organ systems, including the skin, respiratory tract, and the brain. The discovery of the gut–brain axis has opened new perspectives on how microbiota can influence mental health and neurological function. Alterations in gut flora have been linked to depression, anxiety, and neurodevelopment disorders, suggesting a bidirectional communication between the gut and the central nervous system mediated through immune, neural, and endocrine pathways.

Recent research has also explored therapeutic interventions aimed at modulating the microbiome. Probiotics and prebiotics have gained attention for their potential to restore microbial balance, while fecal microbiota transplantation (FMT) has shown remarkable success in treating recurrent Clostridioides difficile infection and is being investigated for broader applications. Dietary patterns, particularly those rich in fibre and plant-based foods, have been found to support microbial diversity and resilience, offering a natural means of promoting immune health.

Overall, the literature consistently highlights that the

microbiome is not a passive inhabitant but an active modulator of human physiology. Maintaining microbial equilibrium appears essential for immune stability and disease prevention. However, gaps stay in defining what constitutes a "healthy" microbiome, and inter-individual variability continues to challenge the development of universal therapeutic models. As ongoing research integrates genomics, metabolomics, and systems biology, the coming years are expected to deepen our understanding of host–microbe interactions and their role in personalised medicine.

Methodology

This paper is a narrative review based on a comprehensive analysis of published literature related to the human microbiome and its role in immunity and disease. A detailed search was conducted using electronic databases including PubMed, Google Scholar, ScienceDirect, and SpringerLink to find relevant articles published between 2007 and 2025. Keywords used in the search included "human microbiome," "gut flora," "immunity," "dysbiosis," "microbiota and disease," and "probiotics."

Both original research articles and review papers were considered to ensure a broad understanding of the topic. Preference was given to peer-reviewed studies, systematic reviews, and meta-analyses that explored the relationship between the microbiome, immune regulation, and disease mechanisms. Articles focusing on animal models were included only when they offered mechanistic insights relevant to human physiology.

The selected studies were analysed to find recurring patterns, emerging trends, and key findings about the microbiome's role in keeping immune balance, influencing disease progression, and shaping therapeutic approaches.

The information was synthesised under major thematic areas, including microbiome–immune interactions, dysbiosis and disease association, and microbiome-targeted therapies.

No experimental work or patient data were collected for this paper. All information presented is derived from previously published and publicly available sources. Proper citation and referencing have been kept throughout to ensure academic integrity.

Discussion

The relationship between the human microbiome and the immune system has redefined how health and disease are understood in modern medicine. Far from being a passive community of organisms, the microbiota functions as an active immunological partner that constantly interacts with the host. It influences the maturation of both innate and adaptive immunity, regulates cytokine production, and shapes the body's response to pathogens.

A balanced microbiome helps maintain immune tolerance through mechanisms such as regulatory T-cell activation and the secretion of short-chain fatty acids like butyrate, which have strong anti-inflammatory effects. When this balance is disrupted, a state known as dysbiosis the immune system can become overactive or misdirected, leading to chronic inflammation and increased vulnerability to disease.

Growing evidence links dysbiosis to a wide range of disorders. In gastrointestinal diseases such as inflammatory bowel disease (IBD) and irritable bowel syndrome (IBS), altered microbial diversity and reduced beneficial species like Bacteroides fragilis and Akkermansia muciniphila are consistently seen. Similarly, changes in the gut microbiome contribute to metabolic syndromes by influencing energy harvest, insulin resistance, and low-grade systemic inflammation. In autoimmune disorders such as rheumatoid arthritis and multiple sclerosis, microbiome alterations trigger abnormal immune activation against self-antigens. The microbiome also plays a crucial role in the gut–brain axis, influencing mood, cognition, and stress responses through neural, hormonal, and immunological pathways. Recent studies have shown correlations between altered gut flora and psychiatric conditions including depression and anxiety, highlighting the far-reaching influence of microbial homeostasis.

Clinically, this growing understanding has opened new therapeutic possibilities. Probiotics and prebiotics are being explored to restore healthy microbial communities and enhance immune function. Fecal microbiota transplantation (FMT), once limited to recurrent Clostridioides difficile infections, is now under investigation for inflammatory bowel disease and metabolic disorders. Dietary interventions—especially those rich in fibre and plant-based nutrients—also show promise in promoting microbial diversity and resilience.

Despite these advances, several challenges remain. There is no universal definition of a "healthy microbiome," as composition varies widely across individuals, diets, and environments. Standardisation of microbiome analysis, including sampling techniques and sequencing methods, is still lacking. Moreover, most research has focused on bacterial communities, while the roles of the virome and mycobiome remain poorly understood.

Future directions lie in integrating metabolomics, artificial intelligence, and personalised medicine to better interpret complex host–microbe interactions. Understanding how individual microbial signatures influence treatment response—such as vaccine efficacy or cancer immunotherapy—may revolutionise patient care. A multidisciplinary approach combining microbiology, genomics, nutrition, and clinical medicine will be essential to unlock the full therapeutic potential of the human microbiome.

Prevention and Strategies

Promoting microbial resilience requires lifestyle-driven and clinical approaches. Core strategies include:

• High-fiber, plant-forward diets promoting SCFA-producing microbiota

• Reduced ultra-processed foods and artificial sweeteners

• Rational antibiotic stewardship and avoidance of unnecessary antimicrobials

• Prebiotic- and synbiotic-based nutrition

• Probiotic supplementation in high-risk groups (post-antibiotics, ICU, elderly)

• Early-life interventions including breastfeeding and minimized C-section without indication

• Encouraging physical activity, stress reduction, and sleep hygiene

• Emerging therapies: precision probiotics, engineered bacteriotherapy, metabolite-replacement therapy, and controlled FMT

Public-health measures must integrate microbiome preservation in antimicrobial policies, nutrition programs, and maternal-child health frameworks to reduce inflammatory and metabolic disease burden.

In conclusion, the human microbiome has appeared as one of the most significant discoveries in modern biomedical science, fundamentally reshaping our understanding of health and disease. It functions as an active and dynamic partner of the human immune system, influencing immune maturation, tolerance, and defence against pathogens.

A balanced microbiome supports immune homeostasis through the production of key metabolites and regulation of inflammatory pathways, while its disruption—dysbiosis—has been linked to a wide spectrum of conditions ranging from inflammatory and metabolic disorders to autoimmune and neuropsychiatric diseases.

Ongoing research continues to reveal the complexity of host–microbe interactions, emphasising that microbial composition and diversity are vital indicators of immune stability.

As science advances, microbiome modulation through probiotics, dietary changes, and fecal microbiota transplantation offers promising avenues for disease prevention and treatment. However, defining a universally "healthy" microbiome remains challenging due to individual, genetic, and environmental variability.

Future research integrating metagenomics, metabolomics, and personalised medicine will be crucial in translating microbiome science into clinical practice. Understanding and harnessing the microbiome's potential could revolutionise preventive healthcare, therapeutics, and precision medicine — marking a change in basic assumptions in how human health is maintained and restored.

Author Contributions

Avinash Tiwari: Investigation, formal analysis, writing—original draft. Ayushi Shukla: Validation, methodology, writing—reviewing.

Data Availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethical Approval Not applicable.

Consent to Participate Not applicable.

Consent to Publish Not applicable.

Conflict of Interest The authors declare no competing interests.

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How to cite this article:

Avinash Tiwari and Ayushi Shukla. 2025. Human Microbiome and Its Role in Immunity and Disease. *Int.J.Curr.Microbiol.App.Sci.* 14(11): 96-100. **doi:** https://doi.org/10.20546/ijcmas.2025.1411.011