2026 Volume: 02 Issue: 04 www.ijrpa.com ISSN 2456-9995 Review Article

International Journal Research Publication Analysis

Page: 01-16

GUT MICROBIOTA AND DIABETES MELLITUS: A COMPREHENSIVE REVIEW OF MOLECULAR MECHANISMS AND CLINICAL IMPLICATIONS

Isha Dhiman[1*], Jyoti Bajwa[2], Jeewanjot Singh[3], Danish Ellahi Malik[4], Zaffar Iqbal[5]

Assistant Professor[1], Associate Professor[2], Assistant Professor[3], Student[4], Student[5]

Desh Bhagat University, Mandi Gobindgarh, Punjab, India.

Article Received: 05 March 2026

Article Revised: 23 March 2026

Published on: 13 April 2026

***Corresponding Author: Isha Dhiman**

Assistant Professor , Desh Bhagat University, Mandi Gobindgarh, Punjab, India.

DOI: https://doi-doi.org/101555/ijrpa.6734

ABSTRACT

Diabetes mellitus (DM) is a complex metabolic disorder characterized by chronic hyperglycemia resulting from impaired insulin secretion, insulin resistance. In recent years, the gut microbiota has emerged as a critical factor influencing the pathogenesis and progression of diabetes. This review provides a comprehensive overview of the molecular mechanisms linking gut microbiota and diabetes mellitus, including dysbiosis, short-chain fatty acid (SCFA) production, inflammation, immune responses, and gut barrier dysfunction. The review also highlights the clinical implications of these findings, emphasizing the potential of gut microbiota as a diagnostic biomarker and therapeutic target. Microbiome-based interventions, including dietary modifications, probiotics, prebiotics, synbiotics, and fecal microbiota transplantation, show promising results in improving metabolic outcomes. However, current research is limited by inter-individual variability, lack of standardized methodologies, and insufficient long-term clinical evidence. Future directions include the application of advanced omics technologies, personalized medicine approaches, and well-designed clinical trials to better understand host–microbiome interactions and optimize therapeutic strategies. Overall, targeting the gut microbiota represents a promising and innovative approach for the prevention and management of diabetes mellitus.

KEYWORDS: Diabetes mellitus; Dysbiosis; Gut microbes; Prebiotics; Probiotics.

1. INTRODUCTION

1.1 Overview of Diabetes Mellitus

Diabetes mellitus (DM) is a group of chronic, heterogeneous metabolic disorders characterized by persistent hyperglycemia resulting from defects in insulin secretion, insulin action, or a combination of both. It represents a major global health concern due to its rapidly increasing prevalence and its association with significant morbidity and mortality. The fundamental pathophysiology of diabetes involves disruption in glucose homeostasis, a tightly regulated process primarily controlled by insulin secreted from pancreatic β-cells. In diabetic conditions, impaired insulin secretion, peripheral insulin resistance, and increased hepatic glucose production collectively contribute to elevated blood glucose levels [1]. These metabolic abnormalities not only affect carbohydrate metabolism but also alter lipid and protein metabolism, leading to widespread systemic effects.

Diabetes mellitus is broadly classified into several types based on its etiology. Type 1 diabetes mellitus (T1DM) is an autoimmune disorder characterized by the destruction of pancreatic β-cells, resulting in absolute insulin deficiency. In contrast, type 2 diabetes mellitus (T2DM), which accounts for the majority of cases, is primarily associated with insulin resistance and relative insulin deficiency, often linked to obesity, sedentary lifestyle, and genetic predisposition. Gestational diabetes mellitus (GDM) occurs during pregnancy due to increased insulin resistance and poses risks for both maternal and fetal health. Additionally, other specific forms of diabetes include monogenic diabetes, pancreatic disease-related diabetes, and drug- or hormone-induced diabetes [2].

In recent years, diabetes mellitus has been increasingly recognized as a multifactorial disorder influenced by complex interactions between genetic, environmental, and lifestyle factors. Emerging evidence highlights the significant role of gut microbiota in the regulation of metabolic homeostasis, immune responses, and inflammatory pathways, thereby contributing to the onset and progression of diabetes [3]. Understanding the intricate mechanisms underlying diabetes is essential for developing novel therapeutic strategies, particularly those targeting the gut microbiome, which has gained considerable attention in the context of metabolic diseases.

2. Importance of Gut Microbiota

The gut microbiota, a complex and dynamic community of trillions of microorganisms residing in the human gastrointestinal tract, plays a crucial role in maintaining host metabolic, immunological, and physiological homeostasis. Composed primarily of bacteria belonging to

the phyla Firmicutes, Bacteroidetes, Actinobacteria, and Proteobacteria, the gut microbiota functions as a metabolic "organ" that contributes to digestion, nutrient absorption, and energy regulation [4]. It is actively involved in the fermentation of indigestible dietary components, leading to the production of bioactive metabolites such as short-chain fatty acids (SCFAs), including acetate, propionate, and butyrate, which are essential for maintaining intestinal integrity, modulating immune responses, and regulating glucose and lipid metabolism. The importance of gut microbiota extends beyond basic physiological functions to its significant role in host immunity [5]. It contributes to the development and maturation of the immune system by maintaining a balance between pro-inflammatory and anti-inflammatory responses. A healthy gut microbiome supports the integrity of the intestinal barrier, preventing the translocation of harmful pathogens and endotoxins such as lipopolysaccharides (LPS) into systemic circulation [6]. Disruption of this balance, known as dysbiosis, can lead to increased intestinal permeability ("leaky gut"), triggering chronic low-grade inflammation, which is a key factor in the pathogenesis of metabolic disorders, including diabetes mellitus.

In the context of metabolic health, gut microbiota plays a pivotal role in regulating energy homeostasis, insulin sensitivity, and fat storage. Alterations in microbial composition have been associated with obesity and type 2 diabetes, where an imbalance in microbial populations can influence host metabolism through various mechanisms, including modulation of bile acid metabolism, regulation of incretin hormones such as glucagon-like peptide-1 (GLP-1), and interaction with host signaling pathways involved in glucose metabolism [7]. Furthermore, gut microbiota-derived metabolites can act as signaling molecules that influence gene expression and metabolic pathways in peripheral tissues, thereby contributing to insulin resistance and β-cell dysfunction. Recent advances in microbiome research have highlighted the bidirectional relationship between gut microbiota and host metabolism, emphasizing its potential as a therapeutic target. Strategies such as dietary interventions, probiotics, prebiotics, synbiotics, and fecal microbiota transplantation (FMT) have shown promise in modulating gut microbial composition and improving metabolic outcomes [8]. Therefore, understanding the importance of gut microbiota is essential for elucidating its role in the development and progression of diabetes mellitus and for exploring novel microbiome-based therapeutic approaches aimed at restoring metabolic balance and improving clinical outcomes as shown in **Fig 1** [9].

This review aims to provide a comprehensive and detailed analysis of the molecular mechanisms linking gut microbiota and diabetes mellitus. It focuses on key pathways such as dysbiosis, microbial metabolites, immune modulation, and intestinal barrier dysfunction. The

review also explores the clinical implications of these mechanisms, including emerging therapeutic strategies, diagnostic tools, and personalized medicine approaches. Furthermore, it discusses the challenges, limitations, and future directions in this rapidly evolving field.

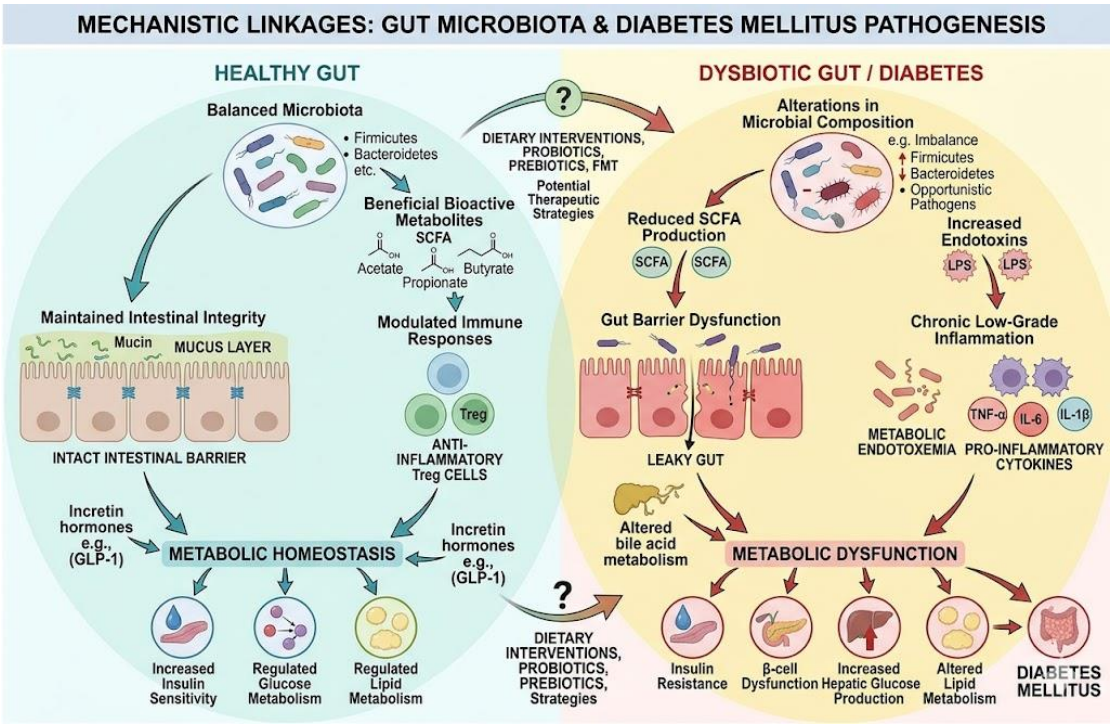

Fig 1. Mechanistic linkages of gut microbiota and diabetes mellitus pathogenesis.

3. Molecular Mechanisms Linking Gut Microbiota and Diabetes

3.1 Dysbiosis and Metabolic Disorders

Dysbiosis refers to an imbalance in the composition, diversity, and functional capacity of the gut microbiota, which disrupts the symbiotic relationship between the host and intestinal microorganisms. This altered microbial state has been increasingly implicated in the development and progression of metabolic disorders, including obesity, insulin resistance, and diabetes mellitus [10]. In a healthy gut, a diverse and stable microbial community contributes to metabolic homeostasis by aiding digestion, producing beneficial metabolites, and maintaining intestinal barrier integrity. However, dysbiosis is characterized by a reduction in beneficial microbes, particularly short-chain fatty acid (SCFA)-producing bacteria, and an increase in pathogenic or opportunistic species, leading to impaired metabolic functions [11].

One of the primary consequences of dysbiosis is the disruption of energy balance and nutrient metabolism. Altered gut microbial composition can enhance the extraction of energy from the diet, promote fat deposition, and influence host metabolic pathways involved in glucose and

lipid metabolism. In individuals with metabolic disorders, an increased ratio of Firmicutes to Bacteroidetes has often been reported, although findings may vary depending on population and environmental factors [12]. This imbalance contributes to excessive caloric harvest and storage, thereby predisposing individuals to obesity, a major risk factor for type 2 diabetes. Dysbiosis also plays a critical role in promoting chronic low-grade inflammation, a hallmark of metabolic diseases. The disruption of gut barrier integrity leads to increased intestinal permeability, allowing the translocation of microbial components such as lipopolysaccharides (LPS) into the bloodstream. This condition, known as metabolic endotoxemia, activates immune responses through pattern recognition receptors such as Toll-like receptors, resulting in the release of pro-inflammatory cytokines. These inflammatory mediators interfere with insulin signaling pathways, ultimately contributing to insulin resistance and impaired glucose homeostasis [13].

In addition, dysbiosis is associated with a decrease in the production of SCFAs, particularly butyrate, which is essential for maintaining intestinal epithelial health and exerting anti-inflammatory effects. Reduced SCFA levels impair gut barrier function, decrease insulin sensitivity, and disrupt hormonal regulation of appetite and glucose metabolism [14]. Furthermore, alterations in gut microbiota affect bile acid metabolism and signaling pathways involving receptors such as FXR and TGR5, which play key roles in regulating lipid and glucose metabolism [15]. Emerging evidence also suggests that dysbiosis influences host gene expression and metabolic pathways through epigenetic mechanisms. Microbial metabolites can modulate histone modification and DNA methylation, thereby affecting genes involved in inflammation, insulin signaling, and energy metabolism. These changes further exacerbate metabolic dysfunction and contribute to the pathogenesis of diabetes and related disorders as shown in **Table 1** [16].

Table 1. Molecular mechanisms linking gut microbiota and diabetes mellitus.

S. No.	Key Aspect	Description	References
1	Microbial Imbalance	Dysbiosis involves reduced beneficial microbes and increased pathogenic species	[17]
2	Altered Energy Metabolism	Enhances energy extraction, fat deposition, and disrupts glucose/lipid pathways	[18]
3	Chronic Inflammation	Increased gut permeability leads to LPS entry and low-grade inflammation	[19]
4	Reduced SCFA Production	Decrease in butyrate impairs gut barrier, insulin sensitivity, and immunity	[20]
5	Metabolic & Epigenetic Effects	Alters bile acid signaling and gene expression affecting metabolic functions	[21]

3.2 Short-Chain Fatty Acids (SCFAs)

Short-chain fatty acids (SCFAs) are key microbial metabolites produced in the colon through the fermentation of non-digestible dietary fibers by gut microbiota. The principal SCFAs - acetate, propionate, and butyrate play a fundamental role in maintaining metabolic homeostasis and have emerged as critical mediators linking gut microbiota to host physiology, particularly in the context of diabetes mellitus [22]. These metabolites serve not only as an energy source for colonocytes but also function as signaling molecules that influence a wide range of metabolic and immunological processes. Among SCFAs, butyrate is especially important for maintaining intestinal health, as it serves as the primary energy source for colonic epithelial cells and helps preserve the integrity of the gut barrier. By enhancing the expression of tight junction proteins, butyrate reduces intestinal permeability and prevents the translocation of harmful microbial components such as lipopolysaccharides (LPS) into systemic circulation. This protective effect limits metabolic endotoxemia and chronic low-grade inflammation, both of which are strongly associated with insulin resistance and the development of type 2 diabetes [23]. SCFAs also exert systemic metabolic effects through their interaction with G-protein-coupled receptors, particularly GPR41 and GPR43, expressed on intestinal epithelial cells, adipose tissue, and immune cells. Activation of these receptors regulates energy balance, enhances insulin sensitivity, and modulates inflammatory responses [24]. Additionally, SCFAs stimulate the secretion of incretin hormones such as glucagon-like peptide-1 (GLP-1) and peptide YY (PYY) from enteroendocrine cells, thereby improving glucose tolerance, promoting insulin secretion, and regulating appetite.

Furthermore, SCFAs play a significant role in modulating lipid metabolism and hepatic glucose production. Propionate serves as a substrate for gluconeogenesis in the liver, while acetate is involved in cholesterol and fatty acid synthesis [25]. Through these mechanisms, SCFAs contribute to the regulation of systemic energy metabolism. They also influence immune function by promoting the differentiation of regulatory T cells (Tregs) and suppressing pro-inflammatory pathways, thereby maintaining immune homeostasis. In individuals with diabetes and related metabolic disorders, a reduction in SCFA-producing bacteria is commonly observed, leading to decreased SCFA levels [26]. This deficiency is associated with impaired gut barrier function, increased inflammation, and altered metabolic signaling, all of which contribute to the progression of insulin resistance and hyperglycemia. Therefore, SCFAs represent a crucial mechanistic link between gut microbiota and metabolic health, and strategies aimed at enhancing SCFA production -such as dietary fiber intake,

prebiotics, and probiotics - hold significant therapeutic potential in the prevention and management of diabetes mellitus [27].

3.3 Inflammation and Immune Modulation

Inflammation and immune modulation represent central mechanisms through which gut microbiota influence the development and progression of diabetes mellitus. Under physiological conditions, the gut microbiota maintains a balanced interaction with the host immune system, promoting immune tolerance while preserving the ability to respond to pathogens. This balance is achieved through continuous crosstalk between microbial components and host immune cells, which helps regulate both innate and adaptive immune responses [28]. However, alterations in gut microbial composition, or dysbiosis, can disrupt this equilibrium and lead to a state of chronic low-grade inflammation, a key contributor to metabolic disorders such as insulin resistance and type 2 diabetes.

One of the primary pathways linking gut microbiota to inflammation is the increased translocation of microbial-derived molecules, particularly lipopolysaccharides (LPS), into systemic circulation due to impaired intestinal barrier function. This condition, often referred to as metabolic endotoxemia, activates pattern recognition receptors such as Toll-like receptors (especially TLR4) on immune cells [29]. Activation of these receptors triggers intracellular signaling cascades, including the nuclear factor-kappa B (NF-κB) pathway, leading to the production of pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and interleukin-1β (IL-1β). These cytokines interfere with insulin signaling pathways in peripheral tissues, thereby contributing to insulin resistance and impaired glucose metabolism. Gut microbiota also plays a crucial role in modulating immune cell populations and their functions. Beneficial microbial metabolites, particularly short-chain fatty acids (SCFAs), promote the differentiation and expansion of regulatory T cells (Tregs), which are essential for maintaining immune tolerance and suppressing excessive inflammatory responses [30]. At the same time, dysbiosis may enhance the activation of pro-inflammatory immune cells such as Th1 and Th17 cells, further exacerbating systemic inflammation. This imbalance between anti-inflammatory and pro-inflammatory immune responses contributes to the pathogenesis of both type 1 and type 2 diabetes, with autoimmune destruction of pancreatic β-cells being a hallmark of type 1 diabetes [31].

In addition, gut microbiota influences the production of cytokines and chemokines that regulate immune signaling and metabolic pathways. Changes in microbial composition can alter the secretion of anti-inflammatory cytokines such as interleukin-10 (IL-10) and increase

pro-inflammatory mediators, thereby shifting the immune balance toward a pro-inflammatory state [32]. Chronic inflammation induced by these mechanisms affects multiple organs, including adipose tissue, liver, and skeletal muscle, all of which play critical roles in glucose metabolism. Furthermore, emerging evidence suggests that gut microbiota can modulate immune responses through epigenetic mechanisms. Microbial metabolites are capable of influencing gene expression in immune cells by altering histone acetylation and DNA methylation patterns, thereby regulating inflammatory pathways and metabolic functions. This highlights the complex interplay between the gut microbiome and host immune system in shaping disease outcomes as shown in **Fig 2** [33].

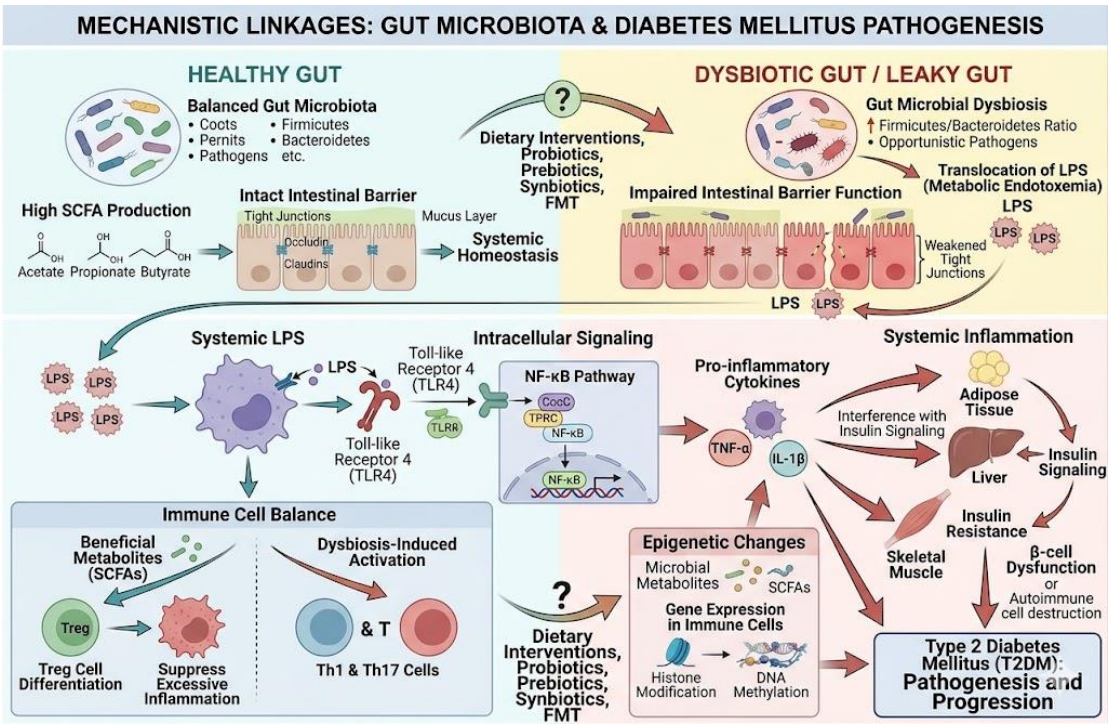

Fig 2. Mechanistic linkages: Gut microbiota and diabetes mellitus pathogenesis.

3.4 Gut Barrier Dysfunction

Gut barrier dysfunction is a critical mechanism linking gut microbiota alterations to the development of metabolic disorders, including diabetes mellitus. The intestinal barrier is a highly specialized and selectively permeable structure composed of epithelial cells, tight junction proteins (such as occludin, claudins, and zonula occludens), mucus layers, and immune components that collectively function to prevent the translocation of harmful luminal contents while allowing the absorption of nutrients [34]. Under normal conditions, this barrier maintains intestinal homeostasis by restricting the passage of pathogens, toxins, and microbial products into systemic circulation. However, disruption of this barrier, often

referred to as “leaky gut,” leads to increased intestinal permeability and plays a pivotal role in metabolic dysregulation.

Gut microbiota is essential for maintaining the integrity of the intestinal barrier. Beneficial microbes, particularly those producing short-chain fatty acids (SCFAs) such as butyrate, support epithelial cell health and enhance the expression of tight junction proteins. Butyrate serves as a primary energy source for colonocytes and promotes mucin production, thereby strengthening the mucus layer and protecting the intestinal lining [35]. In contrast, dysbiosis-characterized by a reduction in beneficial bacteria and an increase in pathogenic species-impairs these protective mechanisms, leading to weakened tight junctions and compromised barrier function. One of the major consequences of gut barrier dysfunction is the translocation of microbial components such as lipopolysaccharides (LPS) from the gut lumen into the bloodstream, a condition known as metabolic endotoxemia. Circulating LPS activates immune receptors, particularly Toll-like receptor 4 (TLR4), on immune and metabolic cells, triggering inflammatory signaling pathways such as nuclear factor-kappa B (NF-κB) [36]. This results in the release of pro-inflammatory cytokines, which interfere with insulin signaling pathways in key metabolic tissues including the liver, adipose tissue, and skeletal muscle. Consequently, chronic low-grade inflammation induced by gut barrier dysfunction contributes significantly to the development of insulin resistance and type 2 diabetes [37]. Additionally, gut barrier dysfunction influences metabolic regulation by altering the interaction between gut microbiota and host endocrine signaling. Increased permeability can disrupt the secretion of gut-derived hormones such as glucagon-like peptide-1 (GLP-1), which plays a crucial role in insulin secretion and glucose homeostasis. Furthermore, impaired barrier integrity may lead to systemic exposure to bacterial metabolites that negatively affect pancreatic β-cell function and survival [38].

Emerging evidence also highlights the role of dietary and environmental factors in modulating gut barrier integrity. Diets low in fiber and high in fat have been shown to promote dysbiosis and reduce SCFA production, thereby weakening the intestinal barrier. Conversely, interventions such as prebiotics, probiotics, and dietary fiber supplementation can enhance gut barrier function by restoring microbial balance and increasing SCFA production.

4. Clinical Implications and Therapeutic Strategies

The growing understanding of the relationship between gut microbiota and diabetes mellitus has significant clinical implications, offering novel opportunities for the prevention,

diagnosis, and treatment of metabolic disorders. The recognition that gut microbiota plays a central role in regulating glucose homeostasis, inflammation, and energy metabolism has shifted the focus toward microbiome-targeted therapeutic strategies as complementary approaches to conventional diabetes management [39]. These insights not only enhance our understanding of disease pathogenesis but also open new avenues for personalized medicine. One of the key clinical implications lies in the potential use of gut microbiota as a diagnostic and prognostic biomarker. Alterations in microbial composition and diversity have been associated with the onset and progression of type 2 diabetes, suggesting that specific microbial signatures could be used for early detection and risk assessment. Advances in metagenomics and metabolomics have enabled the identification of microbial metabolites, such as short-chain fatty acids (SCFAs) and bile acids, which may serve as indicators of metabolic health and therapeutic response [39].

Dietary interventions remain one of the most effective and accessible strategies for modulating gut microbiota. Diets rich in dietary fiber promote the growth of beneficial bacteria and enhance SCFA production, thereby improving insulin sensitivity and reducing inflammation [40]. Conversely, high-fat and low-fiber diets contribute to dysbiosis and metabolic dysfunction. Therefore, personalized nutritional approaches aimed at restoring microbial balance are increasingly being emphasized in diabetes management. The use of probiotics, prebiotics, and synbiotics has gained considerable attention as therapeutic strategies targeting the gut microbiome. Probiotics, which are live beneficial microorganisms, can help restore microbial balance, improve gut barrier integrity, and reduce inflammation [41]. Prebiotics, typically non-digestible fibers, selectively stimulate the growth of beneficial bacteria, while synbiotics combine both approaches to enhance therapeutic efficacy. Clinical studies have demonstrated that these interventions can improve glycemic control, lipid profiles, and inflammatory markers in individuals with diabetes. Another promising therapeutic approach is fecal microbiota transplantation (FMT), which involves the transfer of gut microbiota from a healthy donor to a recipient to restore microbial diversity and function. Although still in the experimental stage for metabolic diseases, FMT has shown potential in improving insulin sensitivity and metabolic outcomes, highlighting the importance of microbiota composition in disease modulation [42].

In addition, pharmacological interventions may also exert part of their therapeutic effects through modulation of gut microbiota. For instance, commonly used antidiabetic drugs such as metformin have been shown to alter gut microbial composition, increasing the abundance of beneficial bacteria and enhancing SCFA production. This suggests that the gut microbiome

may serve as an important mediator of drug efficacy and response variability among patients. Furthermore, emerging strategies such as postbiotics (bioactive microbial metabolites) and microbiota-derived therapies are being explored for their potential to directly influence metabolic pathways without the need for live microorganisms. These approaches may offer safer and more targeted alternatives in the future [43].

5. Limitations in Current Research and Future roadmap

Despite growing evidence linking gut microbiota to diabetes mellitus, several limitations remain in current research. High inter-individual variability in microbiota composition, influenced by diet, genetics, and environment, makes it difficult to define consistent microbial patterns associated with the disease. Most studies are observational, limiting the ability to establish causality between dysbiosis and diabetes. Additionally, lack of standardization in methodologies, including sample processing and sequencing techniques, leads to inconsistent findings. The functional roles of many microbial species and their interactions with the host are still not fully understood. Confounding factors such as diet and medications, particularly antidiabetic drugs, further complicate data interpretation. Moreover, limited long-term clinical trials and population diversity reduce the generalizability of results. These challenges highlight the need for more robust, standardized, and mechanistic studies to effectively translate microbiome research into clinical practice.

Future research should focus on establishing causal relationships between gut microbiota and diabetes through well-designed longitudinal and clinical studies. Advanced omics technologies are needed to better understand microbial functions and host interactions. Standardization of research methods will improve reproducibility of findings. Personalized approaches based on individual microbiome profiles may enhance treatment outcomes. Additionally, the development of novel therapies such as next-generation probiotics, postbiotics, and microbiome-based interventions requires further investigation through long-term clinical trials to ensure their safety and efficacy.

6. CONCLUSION

In conclusion, the gut microbiota plays a crucial role in the pathogenesis and progression of diabetes mellitus through multiple interconnected mechanisms, including dysbiosis, altered metabolite production, immune modulation, inflammation, and gut barrier dysfunction. These interactions significantly influence metabolic homeostasis, insulin sensitivity, and glucose regulation. Growing evidence highlights the gut microbiome as a key link between

environmental factors and host metabolism, emphasizing its importance in understanding diabetes at a molecular level. Moreover, emerging microbiome-based therapeutic strategies, such as dietary interventions, probiotics, prebiotics, and fecal microbiota transplantation, offer promising avenues for improving metabolic outcomes and complementing conventional treatments. However, several challenges, including variability in microbial composition, limited clinical evidence, and lack of standardized methodologies, must be addressed before these approaches can be widely implemented in clinical practice.

Overall, a deeper understanding of gut microbiota and its complex interactions with the host will be essential for the development of personalized and effective therapeutic strategies. Continued research in this field holds significant potential to transform the prevention, diagnosis, and management of diabetes mellitus in the future.

REFERENCE

1. M. S. Popoviciu *et al.*, "Diabetes Mellitus Secondary to Endocrine Diseases: An Update of Diagnostic and Treatment Particularities," (in eng), *Int J Mol Sci,* vol. 24, no. 16, Aug 11 2023, doi: 10.3390/ijms241612676.
2. M. S. Popoviciu, N. Kaka, Y. Sethi, N. Patel, H. Chopra, and S. Cavalu, "Type 1 Diabetes Mellitus and Autoimmune Diseases: A Critical Review of the Association and the Application of Personalized Medicine," (in eng), *J Pers Med,* vol. 13, no. 3, Feb 26 2023, doi: 10.3390/jpm13030422.
3. H. Kaur and S. A. Ali, "Probiotics and gut microbiota: mechanistic insights into gut immune homeostasis through TLR pathway regulation," (in eng), *Food Funct,* vol. 13, no. 14, pp. 7423-7447, Jul 18 2022, doi: 10.1039/d2fo00911k.
4. M. Colella *et al.*, "Microbiota revolution: How gut microbes regulate our lives," (in eng), *World J Gastroenterol,* vol. 29, no. 28, pp. 4368-4383, Jul 28 2023, doi: 10.3748/wjg.v29.i28.4368.
5. X. F. Liu *et al.*, "Regulation of short-chain fatty acids in the immune system," (in eng), *Front Immunol,* vol. 14, p. 1186892, 2023, doi: 10.3389/fimmu.2023.1186892.
6. F. Di Vincenzo, A. Del Gaudio, V. Petito, L. R. Lopetuso, and F. Scaldaferri, "Gut microbiota, intestinal permeability, and systemic inflammation: a narrative review," (in eng), *Intern Emerg Med,* vol. 19, no. 2, pp. 275-293, Mar 2024, doi: 10.1007/s11739-023-03374-w.
7. S. Sasidharan Pillai, C. A. Gagnon, C. Foster, and A. P. Ashraf, "Exploring the Gut Microbiota: Key Insights Into Its Role in Obesity, Metabolic Syndrome, and Type 2

Diabetes," (in eng), *J Clin Endocrinol Metab,* vol. 109, no. 11, pp. 2709-2719, Oct 15 2024, doi: 10.1210/clinem/dgae499.

8. E. Zikou, C. Koliaki, and K. Makrilakis, "The Role of Fecal Microbiota Transplantation (FMT) in the Management of Metabolic Diseases in Humans: A Narrative Review," (in eng), *Biomedicines,* vol. 12, no. 8, Aug 16 2024, doi: 10.3390/biomedicines12081871.
9. V. Shukla, S. Singh, S. Verma, S. Verma, A. A. Rizvi, and M. Abbas, "Targeting the microbiome to improve human health with the approach of personalized medicine: Latest aspects and current updates," (in eng), *Clin Nutr ESPEN,* vol. 63, pp. 813-820, Oct 2024, doi: 10.1016/j.clnesp.2024.08.005.
10. M. R. Bidell, A. L. V. Hobbs, and T. P. Lodise, "Gut microbiome health and dysbiosis: A clinical primer," (in eng), *Pharmacotherapy,* vol. 42, no. 11, pp. 849-857, Nov 2022, doi: 10.1002/phar.2731.
11. A. Ambat *et al.*, "Enhancing recovery from gut microbiome dysbiosis and alleviating DSS-induced colitis in mice with a consortium of rare short-chain fatty acid-producing bacteria," (in eng), *Gut Microbes,* vol. 16, no. 1, p. 2382324, Jan-Dec 2024, doi: 10.1080/19490976.2024.2382324.
12. E. M. Brown, J. Clardy, and R. J. Xavier, "Gut microbiome lipid metabolism and its impact on host physiology," (in eng), *Cell Host Microbe,* vol. 31, no. 2, pp. 173-186, Feb 8 2023, doi: 10.1016/j.chom.2023.01.009.
13. T. R. Dmytriv, K. B. Storey, and V. I. Lushchak, "Intestinal barrier permeability: the influence of gut microbiota, nutrition, and exercise," (in eng), *Front Physiol,* vol. 15, p. 1380713, 2024, doi: 10.3389/fphys.2024.1380713.
14. N. Recharla, R. Geesala, and X. Z. Shi, "Gut Microbial Metabolite Butyrate and Its Therapeutic Role in Inflammatory Bowel Disease: A Literature Review," (in eng), *Nutrients,* vol. 15, no. 10, May 11 2023, doi: 10.3390/nu15102275.
15. H. Yu, R. Nie, and C. Shen, "The role of bile acids in regulating glucose and lipid metabolism," (in eng), *Endocr J,* vol. 70, no. 4, pp. 359-374, Apr 28 2023, doi: 10.1507/endocrj.EJ22-0544.
16. X. Lin *et al.*, "The Gut Microbial Regulation of Epigenetic Modification from a Metabolic Perspective," (in eng), *Int J Mol Sci,* vol. 25, no. 13, Jun 29 2024, doi: 10.3390/ijms25137175.
17. T. Hrncir, "Gut Microbiota Dysbiosis: Triggers, Consequences, Diagnostic and Therapeutic Options," (in eng), *Microorganisms,* vol. 10, no. 3, Mar 7 2022, doi: 10.3390/microorganisms10030578.

18. Z. F. Chen, Y. F. Shen, D. W. Gao, D. F. Lin, W. Z. Ma, and D. G. Chang, "Metabolic pathways and male fertility: exploring the role of Sertoli cells in energy homeostasis and spermatogenesis," (in eng), *Am J Physiol Endocrinol Metab,* vol. 329, no. 1, pp. E160-e178, Jul 1 2025, doi: 10.1152/ajpendo.00074.2025.
19. C. Vetrani *et al.*, "From Gut Microbiota through Low-Grade Inflammation to Obesity: Key Players and Potential Targets," (in eng), *Nutrients,* vol. 14, no. 10, May 18 2022, doi: 10.3390/nu14102103.
20. C. H. Kim, "Complex regulatory effects of gut microbial short-chain fatty acids on immune tolerance and autoimmunity," (in eng), *Cell Mol Immunol,* vol. 20, no. 4, pp. 341-350, Apr 2023, doi: 10.1038/s41423-023-00987-1.
21. Y. Fan *et al.*, "Caloric restriction remodels the hepatic chromatin landscape and bile acid metabolism by modulating the gut microbiota," (in eng), *Genome Biol,* vol. 24, no. 1, p. 98, Apr 30 2023, doi: 10.1186/s13059-023-02938-5.
22. A. Mayorga-Ramos, C. Barba-Ostria, D. Simancas-Racines, and L. P. Guamán, "Protective role of butyrate in obesity and diabetes: New insights," (in eng), *Front Nutr,* vol. 9, p. 1067647, 2022, doi: 10.3389/fnut.2022.1067647.
23. L. Z. Shu, Y. D. Ding, Q. M. Xue, W. Cai, and H. Deng, "Direct and indirect effects of pathogenic bacteria on the integrity of intestinal barrier," (in eng), *Ther Adv Gastroenterol,* vol. 16, p. 17562848231176427, 2023, doi: 10.1177/17562848231176427.
24. Y. Zhao *et al.*, "Linking Short-Chain Fatty Acids to Systemic Homeostasis: Mechanisms, Therapeutic Potential, and Future Directions," (in eng), *J Nutr Metab,* vol. 2025, p. 8870958, 2025, doi: 10.1155/jnme/8870958.
25. Y. Zeng, Y. Wu, Q. Zhang, and X. Xiao, "Crosstalk between glucagon-like peptide 1 and gut microbiota in metabolic diseases," (in eng), *mBio,* vol. 15, no. 1, p. e0203223, Jan 16 2024, doi: 10.1128/mbio.02032-23.
26. P. Shi *et al.*, "Recent advances in regulatory immune cells: exploring the world beyond Tregs," (in eng), *Front Immunol,* vol. 16, p. 1530301, 2025, doi: 10.3389/fimmu.2025.1530301.
27. Q. Mao *et al.*, "Research Progress on the Correlation of Atopic Dermatitis with Gut Microbiota," (in eng), *Clin Cosmet Investig Dermatol,* vol. 17, pp. 1613-1619, 2024, doi: 10.2147/ccid.S442551.
28. K. A. Warrick, C. N. Vallez, H. E. Meibers, and C. Pasare, "Bidirectional Communication Between the Innate and Adaptive Immune Systems," (in eng), *Annu Rev*

Immunol, vol. 43, no. 1, pp. 489-514, Apr 2025, doi: 10.1146/annurev-immunol-083122-040624.

29. M. Kalyan *et al.*, "Role of Endogenous Lipopolysaccharides in Neurological Disorders," (in eng), *Cells,* vol. 11, no. 24, Dec 14 2022, doi: 10.3390/cells11244038.
30. H. Fang *et al.*, "Postbiotic Impact on Host Metabolism and Immunity Provides Therapeutic Potential in Metabolic Disease," (in eng), *Endocr Rev,* vol. 46, no. 1, pp. 60-79, Jan 10 2025, doi: 10.1210/endrev/bnae025.
31. L. Pirola and J. C. Ferraz, "Role of pro- and anti-inflammatory phenomena in the physiopathology of type 2 diabetes and obesity," (in eng), *World J Biol Chem,* vol. 8, no. 2, pp. 120-128, May 26 2017, doi: 10.4331/wjbc.v8.i2.120.
32. D. Lobo-Silva, G. M. Carriche, A. G. Castro, S. Roque, and M. Saraiva, "Balancing the immune response in the brain: IL-10 and its regulation," (in eng), *J Neuroinflammation,* vol. 13, no. 1, p. 297, Nov 24 2016, doi: 10.1186/s12974-016-0763-8.
33. B. Kim, A. Song, A. Son, and Y. Shin, "Gut microbiota and epigenetic choreography: Implications for human health: A review," (in eng), *Medicine (Baltimore),* vol. 103, no. 29, p. e39051, Jul 19 2024, doi: 10.1097/md.0000000000039051.
34. M. Gieryńska, L. Szulc-Dąbrowska, J. Struzik, M. B. Mielcarska, and K. P. Gregorczyk-Zboroch, "Integrity of the Intestinal Barrier: The Involvement of Epithelial Cells and Microbiota-A Mutual Relationship," (in eng), *Animals (Basel),* vol. 12, no. 2, Jan 8 2022, doi: 10.3390/ani12020145.
35. Y. R. Chae, Y. R. Lee, Y. S. Kim, and H. Y. Park, "Diet-Induced Gut Dysbiosis and Leaky Gut Syndrome," (in eng), *J Microbiol Biotechnol,* vol. 34, no. 4, pp. 747-756, Apr 28 2024, doi: 10.4014/jmb.2312.12031.
36. F. Violi, V. Castellani, D. Menichelli, P. Pignatelli, and D. Pastori, "Gut barrier dysfunction and endotoxemia in heart failure: A dangerous connubium?," (in eng), *Am Heart J,* vol. 264, pp. 40-48, Oct 2023, doi: 10.1016/j.ahj.2023.06.002.
37. M. Liu, B. Huang, L. Wang, Q. Lu, and R. Liu, "Peanut skin procyanidins ameliorate insulin resistance via modulation of gut microbiota and gut barrier in type 2 diabetic mice," (in eng), *J Sci Food Agric,* vol. 102, no. 13, pp. 5935-5947, Oct 2022, doi: 10.1002/jsfa.11945.
38. J. Smarkusz-Zarzecka, L. Ostrowska, and M. Radziszewska, "The Impact of Environmental Factors on the Secretion of Gastrointestinal Hormones," (in eng), *Nutrients,* vol. 17, no. 15, Aug 2 2025, doi: 10.3390/nu17152544.

39. P. Kleinová *et al.*, "Nutritional and Metabolic Interventions to Prevent and Treat Protein-Energy Wasting in Nondialysis CKD-Narrative Review," (in eng), *Nutrients,* vol. 18, no. 3, Jan 24 2026, doi: 10.3390/nu18030390.
40. M. Mazhar, Y. Zhu, and L. Qin, "The Interplay of Dietary Fibers and Intestinal Microbiota Affects Type 2 Diabetes by Generating Short-Chain Fatty Acids," (in eng), *Foods,* vol. 12, no. 5, Feb 28 2023, doi: 10.3390/foods12051023.
41. A. E. Quaglio, D. O. Magro, M. Imbrizi, E. C. De Oliveira, L. C. Di Stasi, and L. Y. Sassaki, "Creeping fat and gut microbiota in Crohn's disease," (in eng), *World J Gastroenterol,* vol. 31, no. 1, p. 102042, Jan 7 2025, doi: 10.3748/wjg.v31.i1.102042.
42. M. Biazzo and G. Deidda, "Fecal Microbiota Transplantation as New Therapeutic Avenue for Human Diseases," (in eng), *J Clin Med,* vol. 11, no. 14, Jul 15 2022, doi: 10.3390/jcm11144119.
43. W. Liu, Z. Luo, J. Zhou, and B. Sun, "Gut Microbiota and Antidiabetic Drugs: Perspectives of Personalized Treatment in Type 2 Diabetes Mellitus," (in eng), *Front Cell Infect Microbiol,* vol. 12, p. 853771, 2022, doi: 10.3389/fcimb.2022.853771.