



(REVIEW ARTICLE)



## Microbiota and microbiome in relation to diabetes and obesity

Karla Yazmin Gámiz Villareal <sup>1</sup>, Alejandra Rodriguez Santillanes <sup>1,\*</sup> and Brissia Lazalde <sup>2</sup>

<sup>1</sup> Faculty of Medicine and Nutrition Juárez University of the State of Durango, Durango, Dgo, México.

<sup>2</sup> Department of Genetics, Faculty of Medicine and Nutrition, México.

GSC Advanced Research and Reviews, 2024, 19(03), 176–181

Publication history: Received on 07 May 2024; revised on 16 June 2024; accepted on 18 June 2024

Article DOI: <https://doi.org/10.30574/gscarr.2024.19.3.0224>

### Abstract

Millions of microorganisms compose the human gut microbiota, essential for maintaining metabolic health. Recent research has shown that the gut microbiome of people with obesity and diabetes changes significantly in composition and functionality. These changes are characterized by a decrease in diversity and an overrepresentation of certain microbial agents that have detrimental metabolic effects. Dysbiosis, an imbalance in the gut microbiota, contributes to the development and progression of metabolic disorders in several ways, including increased intestinal permeability, inflammation, and altered dietary energy utilization. This review focuses on how microbial populations affect glucose metabolism, insulin sensitivity, and adiposity, with the goal of elucidating the complex relationships between gut microbiota and metabolic health. In addition, we investigate treatment options such as probiotics, prebiotics and fecal microbiota transplants as potential avenues to regulate the gut microbiome. Understanding the complex interplay between the host and the microbiome promises new ways to diagnose and treat these metabolic disorders.

**Keywords:** Microbiota; Type 2 diabetes; Microbiome; Obesity.

### 1. Introduction

The microbiota plays a key role in various metabolic, nutritional, physiological and immunological processes, the human microbiota is established after birth and begins as a dynamic ecosystem, this same has been pointed out as a participant in two diseases which are obesity and diabetes, the latter is a comprehensive metabolic disease caused by the interaction between genetic factors and environmental factors [1]. As for obesity, it is traditionally defined as an excess of body fat detrimental to health and is usually assessed in clinical practice by body mass index (BMI) [2].

It is influenced by the metainflammation observed in obesity and type 2 diabetes (T2DM), which are characterized by an altered gut microbiota composition, which has been observed to contribute to the development of insulin resistance and progression to T2DM. Thus, this imbalance can lead to metabolic disorders and increased central appetite, resulting in obesity [3,4].

#### 1.1. Gut microbiota in metabolic diseases

Metabolic disorders are defined as a group of diseases in which normal metabolic processes are disrupted due to the accumulation of large amounts of a metabolite or deficiency of one or more metabolites. Metabolic disorders have a variety of clinical presentations ranging from acute symptoms in the neonatal period to a slower, more gradual onset later in life. Metabolic diseases can be inherited or acquired throughout life. Inherited metabolic disorders are the result of a genetic defect in the functioning of an intermediate metabolic pathway, whereas acquired disorders are the result of external factors, with lifestyle-related factors being the main causes, a related cause being the microbiota. [5].

\* Corresponding author: Alejandra Rodriguez Santillanes.

The gut microbiota is central to human health, playing a key role in digestion, production of metabolites with potential to alter human metabolism (e.g., short-chain fatty acids), and development of the immune system. The immunomodulatory properties of the intestinal microbiota are of particular interest in the context of the metainflammation observed in obesity and T2D [6]. The intestinal microbiota of the gastrointestinal tract (GIT) develops during infancy. The process of microbial colonization depends on a variety of host factors, but diet is the most prominent factor [7].

Diet affects multiple aspects of human health. It is well documented that inadequate nutrition patterns, e.g., a Western-style diet or a high-fat diet, are associated with chronic diseases of civilization, such as obesity and T2D. Different dietary patterns, in particular, the macronutrient and micronutrient composition of the diet and the nutritional sources of macronutrients, contribute to the remodeling of the GM (gastrointestinal microbiota). Even short-term dietary changes (a few days) can modulate the composition of the GM and actively affect host metabolism [8].

### **1.2. Gut microbiota and intestinal epigenetics control the metabolic and physiological state of the host**

In recent years, epigenetic modification has been considered to play a role in the mechanisms of inflammation, obesity and metabolic diseases. Epigenetics is the study of phenotypic changes caused by dynamic and reversible changes in gene expression while leaving the underlying DNA sequence unchanged, including changes in chromatin conformation and their effect on cellular transcription. In eukaryotes, the main mechanisms are DNA methylation, histone post-transcriptional modification, chromatin recombination and regulation of gene expression by ncRNAs (non-coding RNAs). As an environmental factor, the gut microbiota can trigger epigenetic modifications in the host under the influence of diet, drugs (antibiotics) and other factors. In particular, changes in epigenetic markers may be determined by the gut microbiota and its derived metabolites [9]. The microbiome, low-grade inflammation and gut microbiota may also trigger epigenetic modifications in the host.

### **1.3. The microbiome, low-grade inflammation and insulin resistance.**

Inflammation is described as a series of vascularized tissue responses to injury or infection. These responses are a protective response necessary for survival, but prolonged exposure to stimuli and mobilization of immune cells can be detrimental. This chronic, low-grade inflammation, triggered by the entry of fragments of bacteria into the circulation through a defective intestinal barrier has considerable knock-on effects on host adiposity and insulin resistance [10]. Metabolic cells, such as adipocytes and hepatocytes, are in close contact with immune cells and blood vessels. This proximity establishes a constant communication between metabolism and immune responses. In fact, several studies have demonstrated an increase in proinflammatory markers in adipose tissue of obese individuals, with enlarged adipocytes in mice and humans showing macrophage infiltration and dying adipocytes surrounded by crown-shaped structures formed by phagocytic macrophages. These same adipocytes, together with macrophages, produce proinflammatory cytokines and chemokines [11]. In other words, low-grade inflammation has been widely associated with alterations in glucometabolic pathways, as seen in people with obesity and T2D. Several cytokines are increased in the circulation of people with metabolic syndrome and have negative effects on peripheral tissue metabolism and, just as insulin production is impaired in diabetes, we also have that, similarly, obese subjects had a higher inflammatory tone and more severe asthma, which was related to the gut microbiota [12].

### **1.4. Correction of the microbiota as treatment alternative.**

Just as it has been mentioned that the imbalance of such microbiota is able to trigger each function, we also have that the same is able to provide us with treatment, which several types of interventions have been shown to correct the imbalance of the microbiota and restore the beneficial metabolic outcomes of a normal microbiota. Among these, fecal microbiota transplantation (FMT) is an emerging and promising technology used to improve clinical outcomes of various pathological conditions through modifications in the composition of the gut microbiota. Similarly, obese subjects had higher inflammatory tone and more severe asthma, which was related to the gut microbiota.

Current studies focusing on this relationship have provided promising avenues of research that include altering the efficiency of digestion, exploring the role of bacteria in the production of short-chain fatty acids (SCFA) along with other metabolites, and studying the impact of diet and microbiota transplants in altering, or restoring the microbial composition profile. Remodeling the composition of the gut microbiome through diet, genetics, and other medical procedures, such as FMT, could lead to new treatment strategies for many common pathological processes [13].

### **1.5. Probiotics and prebiotics as treatment of the microbiome.**

The International Scientific Association for Probiotics and Prebiotics (ISAPP) defines probiotics as live microorganisms that, when administered in adequate amounts, confer a health benefit to the host. They benefit health by modulating

host mucosal immune function, improving dysbiosis or promoting nutrient absorption. Similarly, ISAPP defines a prebiotic as a substrate selectively utilized by host microorganisms that confers a health benefit. Prebiotics are organic substances that are not digested or absorbed by the host, but can selectively promote the metabolism and proliferation of probiotics.

Prebiotics are safe and effective, and have a high therapeutic effect along with minimal side effects. Prebiotics have also been shown to be effective against genetically induced obesity at doses lower than the commonly used grams per day and for a limited period of only 2 weeks [14].

Probiotics have been shown to improve glucose metabolism and insulin sensitivity in patients with T2D [15]. The most popular probiotics are members of the lactobacillus and bifidobacteria groups, which are able to interfere with dysbiotic intestinal biodiversity [16].

### **1.6. Regulation of the microbiota by the immune system**

The immune system has a fundamental role in the regulation of the symbiotic relationship between the microbiota and the host. It allows a proper interaction between the microbiota and the intestinal mucosa by recognizing microbial proteins as self-antigens. Conversely, the intestinal microbiota responds by producing proinflammatory cytokines (e.g., IL-1, IL-6 or TNF alpha) that protect the host from pathogens. An innate immune signaling complex called the "inflammasome" is activated and assembles to protect against potentially pathogenic agents. Once activated, active proinflammatory cytokines (e.g., IL-18 and IL-1b) are produced, which in turn induce cell death through various mechanisms, thus maintaining intestinal homeostasis. Activation of the inflammasome has been associated with neuroinflammatory conditions and appears to play an essential role in the progression of several neurological disorders [17].

### **1.7. The microbiota and its contribution to insulin and feeding processes.**

Insulin concentrations also appear to be altered as a function of gut microbiota. Transplantation of gut microbiota from lean subjects to patients with metabolic syndrome increased insulin sensitivity. This effect is probably related to the reduction of chronic low-grade inflammation resulting from LPS (liposaccharide) translocation and, consequently, increased activation of the insulin signaling cascade [18]. The gut microbiota has been implicated in the control of food intake and satiety through gut peptide signaling, in which bacterial products activate enteroendocrine cells by modulating paracrine signaling molecules produced by enterocytes. The intestinal microbiota can increase the production of certain SCFA, which have been shown to be associated with increased production of peptide YY (PYY), ghrelin, insulin, and glucagon-like peptide 1 (GLP-1) [19]. Similarly, the microbiota is immersed in most studies investigating the relationships between obesity and the gut microbiome, use very small sample sizes, and employ various analytical methods to infer gut microbial composition. These factors are likely responsible for the considerable heterogeneity observed in the results [20].

### **1.8. Dietary fiber as a regulator of gut microbiota composition.**

Overweight and obesity, lifestyle, genetic predisposition, and gut microbiota dysbiosis have been pointed out as possible risk factors in the development of T2DM. In particular, low fiber intake and the consumption of foods rich in fats and sugars, common in the Western lifestyle, have been observed to contribute to the depletion of certain bacterial taxa. Therefore, it is possible that a high intake of dietary fiber alters the gut environment and provides the necessary substrate for microbial bloom [21]. Since higher dietary fiber intake alters nutritional niches in the gut, allowing beneficial bacteria to expand their populations [22], a high-fiber diet may prevent protein fermentation and promote eubiosis of the gut microbiota [23]. Recent findings have shown that regular fiber intake can favor a "virtuous circle", consisting in the overgrowth of microbial groups that ferment fiber while inhibiting other species.

In this context, the prebiotic effect of dietary fibers could be a feasible strategy to prevent T2D, through modulation of the metabolic response [24]. Dietary fiber can also improve glycemic control in type 1 diabetes and prediabetes and favorably influence a number of cardiometabolic risk factors, in addition to glycemic control (cholesterol [total, LDL, high-density lipoprotein (HDL)], triglycerides, body weight, body mass index, waist circumference, fasting insulin, homeostatic model assessment of insulin resistance [HOMA IR], blood pressure, and C-reactive protein [CRP] [25].

### **1.9. Physical activity related to gut microbiota in obesity and diabetes**

Regular aerobic exercise has been reported to alter the gut microbiota in various species, including humans. However, it has been difficult to discern whether exercise affects the gut microbiota independently of the composition of the usual diet. [26]. Indeed, physical training improves obesity status by increasing insulin sensitivity, reducing systemic

inflammation, and improving VO<sub>2</sub> max. Physical activity performed in short but continuous doses can increase the abundance of health-promoting bacteria (*Bifidobacterium* spp., *Akkermansia muciniphila*, *Roseburia hominis*, and *Faecalibacterium prausnitzii*) in the gut microbiota. However, a sedentary lifestyle is inversely related to the richness of the gut microbiota [27].

Low-intensity exercise may influence the TGI by reducing stool transit time and thus the contact time between pathogens and the gastrointestinal mucosal layer. As a consequence, it appears that exercise has protective effects, reducing the risk of colon cancer, diverticulosis, inflammatory bowel disease, among other metabolic diseases. Moreover, even in the presence of a high-fat diet, exercise can reduce inflammatory infiltrate and protect the morphology and integrity of the intestine [28].

---

## 2. Conclusions

To date, advances in the knowledge of the implications of the microbiota in the development of metabolic diseases such as obesity and diabetes have been of great importance, and the dissemination of this knowledge in the medical community is of utmost importance, since it is an area of opportunity for treatment not only through the use of probiotics and prebiotics, but also through changes in lifestyle with the aim of preventing the development of these diseases and their complications.

---

## Compliance with ethical standards

### *Disclosure of conflict of interest*

No conflict of interest to be disclosed.

---

## References

- [1] Huang F, Lai J, Qian L, Hong W, Li L. Differentiation of Uc-MSCs into insulin secreting islet-like clusters by trypsin through TGF-beta signaling pathway. *Differentiation*. 2024 Jan 1;135:100744–4.<https://www.sciencedirect.com/science/article/abs/pii/S0301468123000920?via%3Dihub>
- [2] Gómez Puente JM, Martínez-Marcos M. Overweight and obesity: effectiveness of interventions in adults. *Clinical nursing* [Internet]. 2018 [cited 2019 Sep 13];28(1):65–74. Available from:<https://www.ncbi.nlm.nih.gov/pubmed/29274691>
- [3] Scheithauer TPM, Rampanelli E, Nieuwdorp M, Vallance BA, Verchere CB, van Raalte DH, et al. Gut Microbiota as a Trigger for Metabolic Inflammation in Obesity and Type 2 Diabetes. *Frontiers in Immunology*. 2020 Oct 16;11.<https://pubmed.ncbi.nlm.nih.gov/33178196/>
- [4] Liu BN, Liu XT, Liang ZH, Wang JH. World Journal of Gastroenterology Gut microbiota in obesity Manuscript source: Invited manuscript. *World J Gastroenterol* [Internet]. 2021;27(25):3837–50. Available from:<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8291023/pdf/WJG-27-3837.pdf>
- [5] Moreno-Indias I, Salgado-Somoza A, Azzouzi H el, Murri M. Editorial: Emerging Roles of the Gut Microbiota in the Pathogenesis of Metabolic Disorders. *Frontiers in Endocrinology*. 2021 Aug 13;12. Available from:<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8414896/>
- [6] Li D, Li Y, Yang S, Lu J, Jin X, Wu M. Diet-gut microbiota-epigenetics in metabolic diseases: From mechanisms to therapeutics. *Biomedicine & Pharmacotherapy*. 2022 Sep;153:113290. Available from:<https://www.sciencedirect.com/science/article/pii/S0753332222006795?via%3Dihub#sec0015>
- [7] Al Bander Z, Nitert MD, Mousa A, Naderpoor N. The Gut Microbiota and Inflammation: An Overview. *International Journal of Environmental Research and Public Health* [Internet]. 2020 Oct 1;17(20). Available from:<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7589951/>
- [8] Moszak M, Szulińska M, Bogdański P. You Are What You Eat-The Relationship between Diet, Microbiota, and Metabolic Disorders-A Review. *Nutrients* [Internet]. 2020 Apr 15;12(4). Available from:<https://www.ncbi.nlm.nih.gov/pubmed/32326604>
- [9] Li D, Li Y, Yang S, Lu J, Jin X, Wu M. Diet-gut microbiota-epigenetics in metabolic diseases: From mechanisms to therapeutics. *Biomedicine & Pharmacotherapy*. 2022 Sep;153:113290. Available from:<https://www.sciencedirect.com/science/article/pii/S0753332222006795?via%3Dihub#sec0015>

- [10] Patterson E, Ryan PM, Cryan JF, Dinan TG, Ross RP, Fitzgerald GF, et al. Gut microbiota, obesity and diabetes. *Postgraduate Medical Journal* [Internet]. 2016 Feb 24;92(1087):286–300. Available from:<https://pmj.bmj.com/content/92/1087/286>
- [11] Dabke K, Hendrick G, Devkota S. The gut microbiome and metabolic syndrome. *Journal of Clinical Investigation*. 2019 Oct 1;129(10):4050–7. Available from:<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6763239/>
- [12] Napolitano M, Covasa M. Microbiota Transplant in the Treatment of Obesity and Diabetes: Current and Future Perspectives. *Frontiers in Microbiology* [Internet]. 2020 Nov 12 [cited 2021 Mar 7];11. Available from:<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7693552/pdf/fmicb-11-590370.pdf>
- [13] Napolitano M, Covasa M. Microbiota Transplant in the Treatment of Obesity and Diabetes: Current and Future Perspectives. *Frontiers in Microbiology* [Internet]. 2020 Nov 12;11. Available from:<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7693552/pdf/fmicb-11-590370.pdf>
- [14] WANG Y, WEN L, TANG H, QU J, RAO B. Probiotics and Prebiotics as Dietary Supplements for the Adjunctive Treatment of Type 2 Diabetes. *Polish Journal of Microbiology*. 2023 Mar 1;72(1):3–9. Available from:<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10280329/>
- [15] Wu J, Yang K, Fan H, Wei M, Xiong Q. Targeting the gut microbiota and its metabolites for type 2 diabetes mellitus. *Frontiers in Endocrinology*. 2023 May 9;14. Available from:<https://pubmed.ncbi.nlm.nih.gov/37229456/>
- [16] Araujo R, Borges-Canha M, Pimentel-Nunes P. Microbiota Modulation in Patients with Metabolic Syndrome. *Nutrients*. 2022 Oct 25;14(21):4490. Available from:<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9658393/>
- [17] Longo S, Rizza S, Federici M. Microbiota-gut-brain axis: relationships among the vagus nerve, gut microbiota, obesity, and diabetes. *Acta Diabetologica* [Internet]. 2023 Apr 14;60(8):1007–17. Available from:<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10289935/#:~:text=The%20MGBA%20involves%20p,athways%20such>
- [18] Gomes AC, Hoffmann C, Mota JF. The human gut microbiota: Metabolism and perspective in obesity. *Gut Microbes*. 2018 Apr 18;9(4):1–18. Available from:<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6219651/>
- [19] Cox HM, Tough IR, Woolston AM, Zhang L, Nguyen AD, Sainsbury A, et al. Peptide YY Is Critical for Acylethanolamine Receptor Gpr119-Induced Activation of Gastrointestinal Mucosal Responses. *Cell Metabolism*. 2010 Jun;11(6):532–42. Available from:<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2890049/>
- [20] Wesolowska-Andersen A, Bahl M, Carvalho V, Kristiansen K, Sicheritz-Pontén T, Gupta R, et al. Choice of bacterial DNA extraction method from fecal material influences community structure as evaluated by metagenomic analysis. *Microbiome*. 2014;2(1):19. Available from:<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4063427/>
- [21] Eye O, Feng QQ, Eye OO, Wang XH. The Role of Dietary Fiber in Modulating Gut Microbiota Dysbiosis in Patients with Type 2 Diabetes: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *Nutrients*. 2020 Oct 23;12(11):3239. Available from:<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7690692/>
- [22] Cronin P, Joyce SA, O'Toole PW, O'Connor EM. Dietary Fiber Modulates the Gut Microbiota. *Nutrients* [Internet]. 2021 May 13;13(5):1655. Available from:<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8153313/>
- [23] Ojo O, Ojo OO, Zand N, Wang X. The Effect of Dietary Fiber on Gut Microbiota, Lipid Profile, and Inflammatory Markers in Patients with Type 2 Diabetes: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *Nutrients*. 2021 May 26;13(6):1805. Available from:<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8228854/>
- [24] Salamone D, Rivellesse AA, Vetrani C. The relationship between gut microbiota, short-chain fatty acids and type 2 diabetes mellitus: the possible role of dietary fiber. *Diabetological Act*. 2021 May 10; Available from:<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8316221/>
- [25] Reynolds AN, Akerman AP, Mann J. Dietary fiber and whole grains in diabetes management: Systematic review and meta-analyses. Ma RCW, editor. *PLOS Medicine* [Internet]. 2020 Mar 6;17(3):e1003053. Available from:<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7059907/>
- [26] MITCHELL CM, DAVY BM, HULVER MW, NEILSON AP, BENNETT BJ, DAVY KP. Does Exercise Alter Gut Microbial Composition? A Systematic Review. *Medicine & Science in Sports & Exercise*. 2019 Jan;51(1):160–7. Available from:[https://journals.lww.com/acsm-mse/fulltext/2019/01000/does\\_exercise\\_alter\\_gut\\_microbial\\_composition\\_a.20.aspx](https://journals.lww.com/acsm-mse/fulltext/2019/01000/does_exercise_alter_gut_microbial_composition_a.20.aspx)

- [27] Aragón-Vela J, Solis-Urra P, Ruiz-Ojeda FJ, Álvarez-Mercado AI, Olivares-Arancibia J, Plaza-Diaz J. Impact of Exercise on Gut Microbiota in Obesity. *Nutrients*. 2021 Nov 10;13(11):3999. Available from:<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8624603/#B54-nutrients-13-03999>
- [28] Monda V, Villano I, Messina A, Valenzano A, Esposito T, Moscatelli F, et al. Exercise modifies the gut Microbiota with positive health effects. *Oxid Med Cell Longev* [Internet]. 2017 [cited 2024 May 18];2017:1–8. Available in:<http://dx.doi.org/10.1155/2017/3831972>