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Gut Microbiota Dynamics in Obesity and Metabolic Regulation

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General Background: Obesity is one of the fastest-growing global public health challenges, contributing to over 60% of deaths linked to elevated body mass index (BMI). **Specific Background:** Emerging evidence highlights the gut microbiota as a critical factor in the onset and progression of obesity by influencing dietary energy extraction and regulating host genes involved in fat storage and metabolism. **Knowledge Gap:** While the relationship between gut microbiota and metabolic health is increasingly recognized, the mechanisms through which microbial modulation can be translated into effective preventive or therapeutic strategies remain insufficiently explored. **Aim:** This study emphasizes the role of gut microbiota in health and disease, with a focus on the potential of probiotics and prebiotics to improve gut and immune health. **Results:** Findings demonstrate that gut microbiota composition is highly variable and shaped by diet, nutrients, lifestyle, and environmental exposures, suggesting its potential as a modifiable factor in obesity prevention. **Novelty:** This review underscores the dynamic nature of gut microbiota and positions its modulation through dietary and microbial interventions as a promising strategy for obesity management. **Implications:** Promoting microbial balance with prebiotics, probiotics, fermented foods, fruits, and vegetables, while reducing intake of saturated fats and refined sugars, offers a feasible and evidence-based approach for the prevention and treatment of obesity.

Highlights:

- Gut microbiota influences energy balance and fat storage, impacting obesity development
- Probiotics and prebiotics can help restore microbial balance for obesity prevention
- Dietary patterns and lifestyle strongly shape gut microbial composition and diversity

Keywords: Gut Microbiota, Obesity, Prevention, Dietary Strategies

Introduction

Obesity is a persistent and health recurring condition characterized by excessive or abnormal fat accumulation [1]. Since 2000, global obesity rates among adults have risen by 1.5-fold, with over 1.9 billion overweight adults recorded in 2016. Prevalence has also increased among children and adolescents aged 5–19, climbing from 2.9% to 6.8 [2]. Over the past few decades, microbiome research has evolved into a major scientific focus. Historical studies date back to the mid-1880s, when Theodor Escherich reported on microorganisms, leading to the isolation of Escherichia coli. Subsequent discoveries included Veillon Ella parvula was first identified in 1898, followed by the discovery of Bifidobacterium species in 1900. Throughout the 20th century, microbial taxa were isolated from various human sites including nasal mucosa, oral cavities, skin, the gastrointestinal tract, and the urogenital tract collectively forming the human microbiota. In the 21st century, microbiome science has emerged as a cutting-edge research domain [3]. While genetic factors influence body weight 32 genes have been linked to BMI [4], other contributors include the abundance of inexpensive, calorie-dense foods and reduced physical activity. More recently, shifts in gut microbiota composition have been proposed as a potential cause of obesity. Studies show that fecal samples can contain up to 3.3 million non-redundant microbial genes [5], but the influence of diet and lifestyle on microbiota dynamics remains poorly understood. Advanced molecular techniques have now enabled more accurate profiling of intestinal bacterial flora, including uncultivable species. This has revealed associations between microbiota imbalances and obesity. Variations in methodologies, however, partly explain inconsistencies in identifying specific microbiota changes linked to obesity [6].

Obesity can be classified as either simple—primarily resulting from excessive intake of carbohydrates and/or fats or secondary, which stems from metabolic or hormonal disorders, hypothalamic-pituitary conditions, or other diseases [7]. While obesity fundamentally reflects an imbalance between calorie intake and expenditure [8], the key determinant is not just caloric intake but also absorption efficiency [9]. When adipose tissue’s capacity to store triglycerides is exceeded, excess lipids spill into circulation, leading to ectopic fat deposition in the liver, skeletal muscle, and pancreas, which contributes to insulin resistance. Additionally, inflammation in adipose tissue triggers pro-inflammatory cytokine production, further disrupting glucose regulation [10]. Gut microbiota is thought to influence obesity and related metabolic disorders by affecting adiposity and glucose metabolism. Diet is the primary factor shaping gut microbiota balance [11], and understanding this relationship may open new avenues for prevention and treatment strategies.

1.Gut Microbiota

Plays the gut microbiota a fundamental role in maintaining human physiological functions. These microbial communities ferment water-soluble fibers to generate short-chain fatty acids (SCFAs) and energy otherwise unavailable to the host, and they synthesize essential vitamins such as riboflavin (B2), folic acid, vitamin K, and biotin. Additionally, they metabolize xenobiotics, inhibit colonization by pathogenic microorganisms, preserve he health and stability of the intestinal epithelium, and contribute to the development of a well-functioning immune system [12]. The microbiota also regulates intestinal motility, influencing the efficiency of nutrient and energy absorption from food [13]. When microbial composition is disrupted, homeostasis can be compromised, increasing the risk of metabolic diseases such as Adiposity, insulin resistance, and cardiovascular complications [14]. These roles highlight the microbiome’s critical contribution to metabolism and weight regulation. The human gut harbors

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extremely dense microbial populations, with approximately 10^{11}–10^{12} microorganisms per gram of intestinal content, the vast majority (about 95%) being anaerobes. Early studies using culture-based methods identified dominant cultivable species such as Bacteroides, Eubacterium, Bifidobacterium, *Peptostreptococcus, Fusobacterium, Ruminococcus, Clostridium, and Lactobacillus* [15].

The influence of modern diets and lifestyles on gut microbial ecology remains incompletely understood. However, lifestyle factors are believed to modulate microbiota composition (Figure 1). A large-scale study by Qin et al. revealed that only approximately one-third of bacterial gene clusters were characterized consistently present across diverse European populations. Nearly 40% of each individual's genes were shared with at least half of the study cohort, with 99.1% of these being bacterial in origin, a small fraction archaeal, and only 0.1% eukaryotic or viral [16].

Gut microbiota contributes to numerous essential physiological processes, including pathogen defense, immune modulation [17], digestion and nutrient metabolism ([18], epithelial cell turnover [19], regulation of insulin sensitivity [20], and even neurological and behavioral functions [21].

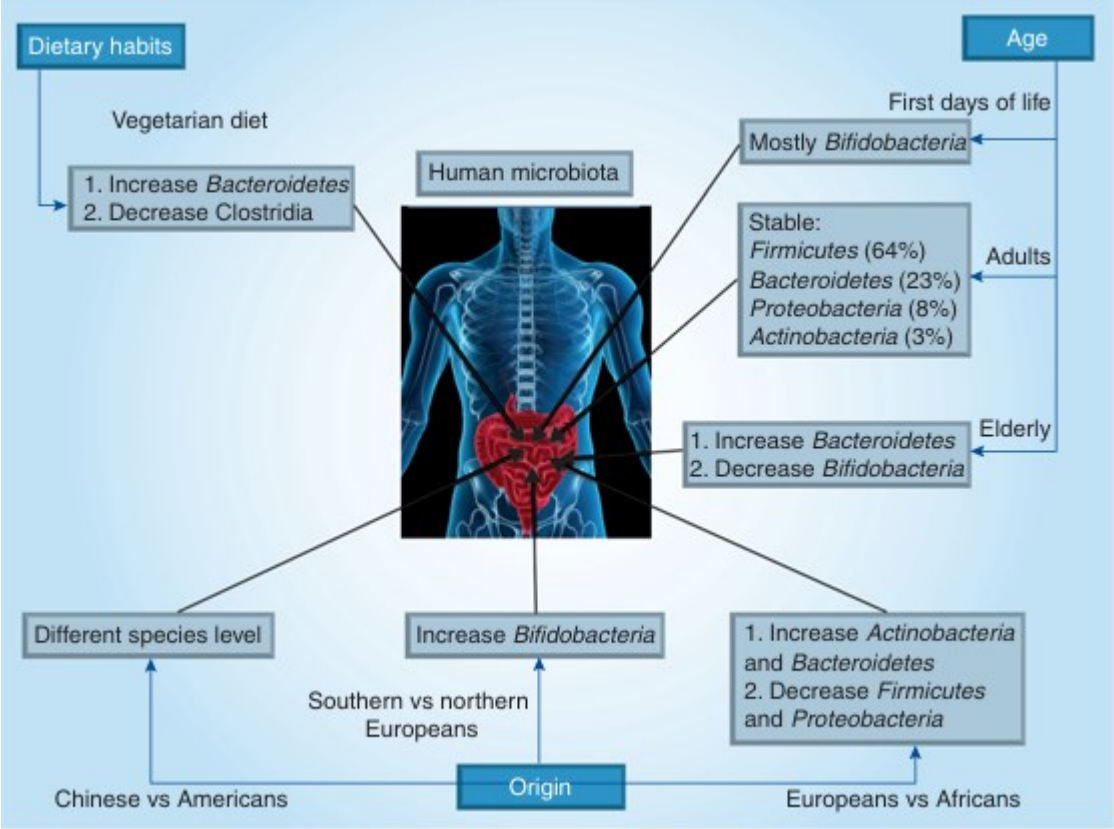

Figure 1. Factors for the composition of the human gut microbiota.

Microbial distribution along the gastrointestinal (GI) tract reflects localized physiological conditions [22]. The small intestine's environment favors fast-growing, facultative anaerobes capable of adhering to epithelial surfaces such as Lactobacillaceae while the colon supports a dense, diverse community dominated by anaerobes specialized in fermenting complex carbohydrates, including Prevotellaceae, Lachnospiraceae, and Rikenellaceae [23]. The GI tract protects the host by maintaining a selective barrier composed of physical layers (epithelium and mucus), biochemical defenses (enzymes and antimicrobial proteins), and immunological mechanisms (secretory IgA and immune cells associated with epithelial

tissue) [24]. Microorganisms that fail to contribute beneficial functions may be regulated or eliminated over time [25].

2.Influence of Gut Microbiota on Adiposity and Metabolic Health

The gut microbiota plays a pivotal role in regulating energy balance, metabolic activity, immune responses, and inflammation [26]. Growing evidence suggests that Dysbiosis in the composition and functional capacity of the gut microbiota has been increasingly implicated in the pathogenesis of obesity and its associated metabolic complications, including insulin resistance, type 2 diabetes mellitus, and chronic low-grade systemic inflammation [27].

3. Microbial Composition in Obesity

Obese individuals often exhibit:

1.An increased Firmicutes-to-Bacteroidetes ratio
2.Reduced alpha-diversity (lower species richness and evenness)
3. Enrichment of Actinobacteria and Proteobacteria populations [28].

The link between gut microbiota and obesity was first demonstrated in germ-free mouse models. When gut microbes from conventionally raised mice were transplanted into germ-free mice, the recipients displayed increased fat accumulation and higher insulin resistance even when consuming less food. This finding confirmed that gut microbes can promote adipose tissue expansion in the host [29]. Analyses using 16S rRNA gene sequencing have revealed a notable decline associated with obesity, particularly in terms of microbial diversity and specific taxa abundance in Bacteroidetes and a proportional increase in Firmicutes [30]. Further work by Turnbaugh et al. confirmed that obese mice possess gut microbiota with an enhanced capacity for energy extraction from the diet. Similar trends have been observed in humans for example; obese children tend to have higher Firmicutes and lower Bacteroidetes abundance [31].

4. Specific Bacterial Associations

Certain bacterial taxa have been linked to weight regulation. The family Christensenellaceae is negatively correlated with body mass index (BMI) and is associated with weight loss [31]. Akkermansia muciniphila has shown promising effects in improving metabolic health in overweight and obese individuals [33]. Traditional probiotics such as Lactobacillus and Bifidobacterium also play important roles in maintaining intestinal balance, though their effects on body weight appear to be species- and strain-specific [34, 35].

a.Types of Obesity and Microbial Patterns

Obesity can be classified into subcutaneous and visceral forms. Interestingly, while a high Firmicutes/Bacteroidetes ratio is a general marker of obesity, its relationship with adipose tissue type varies. In morbid obesity, Firmicutes abundance correlates with brown adipocyte markers in subcutaneous fat but not in visceral fat, suggesting a potential protective role in subcutaneous obesity [36]. Additionally, dietary interventions such as very-low-calorie diets have been shown to shift gut microbial profiles, with changes in Roseburia and Christensenellaceae associated with altered metabolic pathways [37]. In animal models, increasing Akkermansia populations has reduced body weight and visceral fat in mice fed high-fat, high-sugar diets [38].

b. Microbial Diversity and Health

Reduced diversity in the gut microbiome is a recurring observation in obesity research [39]. Lower alpha-diversity has been documented in obese individuals compared to healthy controls, although beta-diversity differences are often insignificant. Some studies, however, argue that diversity is not universally linked to disease, with significant associations present in only about one-third of cases [40]. Given that microbial ecosystems can exhibit resilience and stability, the role of diversity in obesity remains complex and context-dependent.

5. Probiotics and Prebiotics: Their Role In Supporting Your Immune System

Probiotics are defined as “live microorganisms (e.g. bacteriaand yeasts) that, when administered in a viable form and adequate amounts, are beneficial to human health [41] This definitionsti pulates that a probiotic must be alive when administered, have a health benefit to the host (or person taking it) and be delivered at an effective dose. The definition implies that a probiotic must be safe for the intended use and must be a defined entity to allow for appropriate identification to the strain level. A review paper Hill *et al* [42] suggested there isno requirement for probiotics to demonstrate properties in preclinical studies such as gastrointestinal colonisation, ability tosurvive gastrointestinal transit, adherence to the gut mucosa, antipathogenic properties and ability to balance the host gastrointestinal lmucosa. According to Sanders et al, the crux of the definition above is that probiotics are those live microorganisms that confer a health benefit to the individual. They add that to demonstrate a health benefit, the need is for human trials, using a well-defined intervention with well-defined microbial strains. Ideally, the impact of probiotics and prebiotics on the gut microbial population should be studied as part of such human trials [43].

The concept of prebiotics is newer than that of probiotics. They were most recently defined as “a substrate that is selectively used by host micro-organisms conferring a health benefit” [44]. All compounds currently considered to be prebiotics are either carbohydrates accessible to the gut microbiota or they can be fermentable dietary fiber. Examples of such carbohydrates would be inulin and other Fructo-Oligosaccharides (FOS) that microorganisms in the gastrointestinal tract use as metabolic fuel. Other substances such as polyphenols and polyunsaturated fatty acids that can be converted to conjugated fatty acids might fit with the definition of a prebiotic, assuming convincing weight of evidence in the target host Symbiotic contain a mixture of prebiotics and probiotics” [45].

Prebiotics, a concept more recent than probiotics, are described as substrates selectively utilized by host microorganisms to provide a health benefit [46]. Typically, prebiotics are carbohydrates accessible to gut microbes or fermentable dietary fibers—such as inulin and fructo-oligosaccharides (FOS)—that serve as metabolic fuel for beneficial bacteria. Other compounds, including polyphenols and polyunsaturated fatty acids, may also fit this definition if sufficient evidence supports their role in promoting beneficial microbial growth. While probiotics are live organisms, prebiotics are non-living substances that selectively enhance the growth and activity of beneficial microbes. Common sources include plant-based oligosaccharides, mucin-derived glycans, and undigested dietary components [47]. Their benefits range from improved gut health to enhanced immune function.

Symbiotic are formulations that combine probiotics and prebiotics to achieve synergistic or complementary effects. In synergistic symbiotic, the prebiotic component is specifically chosen to enhance the activity of the selected probiotic strain. In complementary symbiotic, each component

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independently provides a health benefit [48, 59]. Research is ongoing into "Opti biotics"—optimized symbiotic designed to maximize the growth and benefits of probiotic strains Figer2 [50].

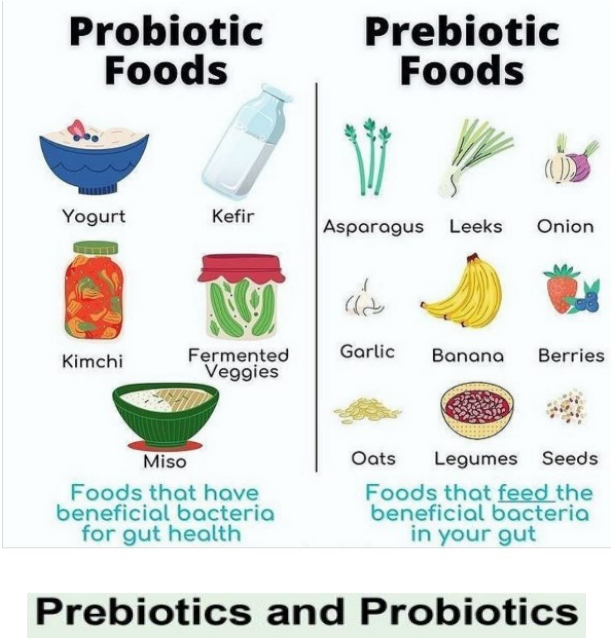

Figure 2. Prebiotic and Probiotic

6. Lifestyle and Environmental Determinants of Gut Microbiome Structure and Function.

The (GI) tract contains an estimated 100 trillion microorganisms—about ten times the number of human somatic cells. Although the majority of microorganisms within the gut ecosystem are bacterial, it also comprises yeasts, unicellular eukaryotes, viruses, and small parasitic helminths. These microbial communities exhibit considerable variation in their composition, abundance, and functional roles along the gastrointestinal tract.", and function along different segments of the GI tract, with the largest and most diverse communities residing in the large intestine. Here, microbes contribute to the fermentation of undigested food components—particularly dietary fibers—and to fecal bulk formation, In adults, common bacterial genera include Bifidobacterium, Lactobacillus, Bacteroides, Clostridium, Escherichia, Streptococcus, and Ruminococcus. Approximately 60% of gut bacteria belong to the phyla Bacteroidetes and Firmicutes [51]. Methane-producing microorganisms, classified as Archaea, are found in about half of the population [52].

Alterations in gut microbial composition, commonly referred to as dysbiosis, have been increasingly implicated in the pathogenesis of conditions such as inflammatory bowel disease. Maintaining a balanced and diverse microbiota is therefore crucial for health, with dietary fiber intake being one of the most effective strategies for supporting microbial diversity. Probiotic supplementation may also help sustain a beneficial microbial [53]. Microbial metabolic activity is influenced by nutrient availability, pH levels, and the overall gut environment [54]. Fermentation of fibers and proteins in the colon produces short-chain fatty acids (SCFAs) such as acetate, propionate, and butyrate which serve as key energy sources for colonocytes, support gut barrier integrity, and regulate immune responses beyond the gut, including in the lungs [55]. Microbial enzymes also play an essential role in degrading complex polysaccharides that humans cannot digest without microbial assistance [56].

Microbial colonization begins during or shortly after birth, with mode of delivery influencing early microbial exposure. Infants delivered vaginally tend to have higher gut bacterial counts in the first month than those born via caesarean section [57]. Breastfeeding further shapes early microbiota development by supplying oligosaccharides that selectively promote Bifidobacterium and Lactobacillus, strengthening immune function and potentially lowering the risk of allergies and asthma [58, 59]. Microbiota composition continues to change over a person's lifetime, influenced by genetics, diet, hormonal fluctuations (e.g., during puberty, pregnancy, and menopause), and aging. With age, Bacteroidetes tend to decrease while Firmicutes increase [60]. Stress is another factor, impacting gut-brain axis signaling and altering microbiota profiles, including reducing beneficial Lactobacillus populations [61]. Conversely, physical activity, as shown in professional athletes, is associated with increased gut microbial diversity [62]. Travel, infections, and environmental exposures can also produce lasting changes in microbial composition and function [63].

7. Modulatory Effects of Diet and Nutrient Profiles on Gut Microbiome Ecology.

Data from 2017–2018 indicate that the prevalence of obesity in the United States rose to 42.4%, up from 30.5% in 2000 [64]. Being overweight or obese is now recognized as a major risk factor for type 2 diabetes, with trends in both conditions showing strikingly similar patterns. More than 34 million Americans have diabetes, and 90–95% of these cases are type 2, of which roughly 89% occur in overweight or obese individuals. A primary contributor to both obesity and type 2 diabetes is the consumption of diets high in fat and sugar but low in dietary fiber [65]. The gut microbiome plays a central role in nutrient absorption, energy extraction, and inflammation regulation, all of which can influence obesity and metabolic disease risk [66]. Microbes help harvest energy from food, maintain a balance between beneficial and opportunistic bacteria, and produce bioactive compounds such as vitamins (e.g., vitamin K) and neurotransmitters like serotonin. Imbalances in microbial composition can therefore contribute to disease development [67].

Both short-term and long-term dietary patterns significantly shape gut microbiome diversity. For example, chronic low-grade inflammation a hallmark of obesity and type 2 diabetes—has been linked to diet-induced changes in microbial composition [68, 69]. Animal studies provide strong evidence for diet–microbiota interactions. Mice fed a high-fat, high-sugar diet show decreased Bacteroidetes and increased Firmicutes and Mollicutes populations [70]. Similarly, high-fat diets have been associated with increased Proteobacteria and Firmicutes, along with higher levels of Enterobacteriaceae, Escherichia, Klebsiella, and Shigella [71]. Conversely, beneficial genera such as Bifidobacterium and Lactobacillus tend to decline, particularly under ketogenic diet conditions, where ketone bodies—such as beta-hydroxybutyrate may inhibit their growth [72].

Dietary fiber intake is another critical determinant of microbiome composition. A landmark comparative study showed that children in rural Burkina Faso, whose diets were rich in fiber and resistant starch, had higher Bacteroidetes levels and greater SCFA production than European children consuming lower-fiber, Western-style diets [73]. High-fiber diets have also been associated with increased abundance of SCFA-producing bacteria such as Ruminococcus bromii, Faecalibacterium prausnitzii, and Eubacterium rectale, which are positively correlated with butyrate production [74, 75],These findings suggest that dietary interventions—particularly increasing fiber and reducing high-fat, high-sugar intake—can beneficially reshape the gut microbiota, enhance SCFA production, and potentially lower the risk of obesity and type 2 diabetes [76].

8. Metabolites produced by the gut microbiota

In last years, the gut microbiome has emerged as a pivotal regulator of health and disease, participating in processes ranging from immune modulation to the control of epigenetic changes [77]. Comprising approximately 100 trillion microorganisms [78], the gut microbiome generates a diverse array of secondary metabolites that exert significant effects not only on intestinal homeostasis but also on systemic immune regulation, inflammatory signaling pathways, and the pathogenesis of complex diseases, including cancer [78]. The composition of the gut microbiota is shaped by multiple factors, including diet, age, antibiotic use, and environmental exposures. When this balance is disrupted—a state known as dysbiosis it has been linked to the onset and progression of various diseases, including cancer and infectious conditions [79]. Functioning as a biochemical factory, the gut microbiota transforms dietary components and endogenous substrates into bioactive metabolites whose effects extend far beyond the gastrointestinal tract [80].

Recent studies have shown that gut microbes can metabolize dietary compounds into secondary metabolites that actively mediate host–microbe interactions [81]. These metabolites have been found to influence tumor initiation and prevention across multiple cancer types, including colorectal, liver, esophageal, gastric, and pancreatic cancers [82]. In addition, certain bacterial genotoxins contribute directly to colorectal cancer progression. For instance, some Escherichia coli strains belonging to phylogenetic group B2 carry a genomic island known as the polyketide synthase (pks) gene cluster, which encodes the production of colibactin. Colibactin induces genetic mutations, DNA damage, and chromosomal instability in colonocytes, thereby promoting tumorigenesis and enhancing cancer cell proliferation [83]. Similarly, the cytolethal distending toxin produced by Campylobacter jejuni causes DNA double-strand breaks and has been implicated in colon tumor development [84].

Current academic trends emphasize the potential of targeting secondary gut antimicrobial pathways to promote beneficial microbiota and reduce the risk of infectious diseases. Studies reveal that an imbalance between beneficial and harmful microbes accelerates pathogenic growth. The stability of the gut microbiome is influenced by numerous factors including nutrition, the immune system, host genetics, and environmental exposures [83]. Pathogenicity is further regulated by immune responses, genetic predispositions, age, and environmental influences [85]. Harmful bacteria produce metabolites that activate Th17 cells, which in turn coordinate immune responses. Th17 cells, along with myofibroblasts and intestinal epithelial cells, secrete cytokines that promote tissue repair, protect healthy cells, and enhance the immune system’s ability to combat viruses, fungi, and protozoa [86]. Moreover, primary bile acids (PBAs) and secondary bile acids (SBAs) work synergistically to maintain intestinal homeostasis. However, excessive levels of SBAs have been associated with increased proliferation of infectious microbes. Elevated SBAs can enhance the infectivity of fungal pathogens such as Candida albicans and viruses, including coronaviruses [87].

Conclusion

Dysbiosis of the gut microbiota has been strongly associated with the onset and progression of obesity. Numerous microbial taxa have been implicated in obesity pathogenesis through mechanisms that include enhancing host energy harvest, increasing central appetite regulation, promoting adipose tissue storage, contributing to chronic low-grade inflammation, and modulating circadian rhythms. Given the

remarkable complexity and diversity of the gut microbiota, the precise molecular and physiological mechanisms underlying its role in obesity remain incompletely understood.

Obesity is recognized as a multifactorial condition arising from the interplay of genetic predisposition and environmental influences. Although current knowledge regarding the gut microbiota's contribution to obesity is still in its early stages, the rapid pace of recent discoveries underscores its emerging significance. Substantial evidence now supports the notion that both the composition of the gut microbiota and its metabolite profile play pivotal roles in obesity development and in obesity-associated comorbidities. The structural and functional characteristics of the gut microbiota, as well as the factors influencing its homeostasis, vary not only between adults and infants but also across different stages of early life. Of particular importance are gut microbiota-derived metabolites—whether produced exclusively by microbial metabolism, generated through host–microbe co-metabolism, or synthesized from dietary substrates—which exert profound effects on metabolic regulation. These metabolites are increasingly recognized as key mediators in both the initiation and progression of obesity. Consequently, modulation of gut microbiota composition and metabolite production—through targeted dietary interventions, prebiotics, probiotics, and pharmacological agents—represents a promising therapeutic and preventive strategy for metabolic disorders, including obesity.

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