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Review Article

# The effect of the gut microbiome on obesity: Mechanisms, interactions, and therapeutic implications: A comprehensive review

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ABSTRACT

Discovery of the gut microbiome as a crucial element in obesity. Recent research has not only linked changes to the gut microflora with development of obesity but also provided novel insights into it pathophysiology. Here we present a review paper with the latest highlights on how microbiota contribute to obesity and unravel possible molecular mechanisms by which gut microorganisms can modulate energy balance, metabolic control of body weight homeostasis and inflammation. Furthermore, we investigate the crosstalk of diet with genetics and microbiome in obesity pathophysiology as well as the gut–brain axis related to metabolic regulation, and consider future implications from this knowledge for management of obesity.



## 1. Introduction

Obesity is a growing global phenomenon with urgent need to identify causes of the condition, and interventions. Historically, defining characteristics of obesity have focused on the imbalance in the homeostasis between caloric intake and expenditure; although even with this basic understanding there is increasing awareness regarding components beyond energy balance such as genetics, environment and implication of gut microbiota.[1] The gut microbiome is a rich, complex community of microorganisms that resides in the human gastrointestinal tract and affects numerous physiological processes such as digestion, metabolism or immune function. Growing evidence supports a role of the gut microbiome in modulating obesity; emerging data indicate that changes in its composition and function could mediate both weight development and maintenance.[2]

## 2. Mechanisms of Microbiome Influence on Obesity

### 2.1. Energy harvesting and storage

The human gut microbiome contribute mainly to the fermentative metabolism of complex polysaccharides and produce SCFAs (short chain fatty acids), including acetate, propionate and butyrate. SCFAs play a significant role in energy metabolism; these molecules are able to supplement calories and to interfere with lipid deposition and appetite.[3,4]

### 2.2. Modulation of host metabolism

The Human gut microbiota plays an important role in host metabolism in several ways for example through influencing bile acid metabolism lipogenesis and glycaemic homeostasis. The earlier studies have also proved that microbiome derived SCFAs such as butyrate increase the insulin sensitivity and decreases the inflammation which are major factors in obesity and metabolic syndrome.

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### 2.3. Inflammatory pathways

Abdominal obesity is defined by low grade chronic inflammation, which is partly attributed by the alteration in Gut microbiota. Disruption of the equilibriums of the intestinal microbiota can result in hyperpermeability of the intestinal barrier and subsequent translocation of lipopolysaccharides (LPS) into circulation and resultant chronic inflammation.[4] They maintain an inflammatory state that is associated with other features such as insulin resistance and dysfunction of adipose tissues, which further aggravates obesity.

Regulation of appetite and energy expenditure: It has been established that the factors arising from gut microbiota productions of metabolites that impact on the CNS in relation to appetite and energy expenditure. For example, some of SCFAs and all other short-chain fatty acids are capable of modulating the secretion of hormones like ghrelin, PYY and GLP-1 which control hunger and satiety.[5]

## 3. Interaction-Matrix of Diet, Genotype and Microbiota

### 3.1. Dietary influence

Food intake also plays a central role in defining the composition of gut microbiota. Diets that are rich in fats and sugars, common to Western societies, are linked to low levels of microbial diversity and an expansion of bacteria that favour adipose tissue accumulation.[6] On the other hand, a diet with high-fibre and plant-based foods enhances the growth of beneficial microbiota that produce SCFAs that as opposed to obesity.

### 3.2. Genetic factors

This is the case given that host genetics can be used to determine how the gut microbiome affects the possibility of obesity. Researchers have determined Microbiome genes that are responsible for its composition and function and are believed to influence metabolic characteristics. This again points to the fact that obesity is not a simple disease, and that people may need individualised approaches for this.

### 3.3. Microbiome-gene-diet interactions

It showed that feeding patterns, genes, and microbes in the belly make a circle that determines obesity. For instance, some genotypes might synergize with a high fat diet to disturb the microbiota composition and result in an increase of fat mass and metabolic impairment.[7] Knowledge of these interactions is therefore important as it will help in the formulation of intervention strategies.

## 4. Therapeutic Implications

### 4.1. Probiotics and prebiotics

Synbiotics—a combination of probiotics, live bacteria that can impart health benefits, and prebiotics, nondigestible food ingredients that encourage the growth of the useful bacteria have proved helpful in altering and controlling the microbiome to tackle obesity.[8,9] Some clinical trials also indicate that obese people can reduce their body weight and improve their metabolic profile by taking certain strains of friendly bacteria including Lactobacillus- and Bifidobacterium.

### 4.2. Faecal microbiota transplantation (FMT)

FMT aims at the implantation of stool donors from a lean donor to an obese recipient with the view of modulating microbial composition and function.[10] Evidence from early human trials shows that FMT can affect insulin resistance positively and help with weight loss, however the effectiveness of FMT as treatment strategy for obesity and related diseases in the long term is still not clear.[11]

### 4.3. Dietary interventions

Some of the dietary changes that can be applied in the management of obesity include changing of gut microbiome. High fiber, polyphenol consumption coupled with fermentation yields increased microbiome ratio and positive metabolic modifications.[12]

### 4.4. Precision medicine

Obesity in the future will probably be treated through precision medicine model in which treatment depends on the patient's genes, microbiome and extended dieting habits. This is in agreement with the argument that with knowledge of causes of obesity that is specific to each candidate, better treatment measures can be applied.

## 5. Discussion

The intricate relationship between the gut microbiome and obesity is area of extensive research, revealing both challenges and opportunities for therapeutic intervention. The findings presented in this review underscore the complexity of obesity as a condition that goes beyond simple caloric imbalance, highlighting the significant role of gut microbiota in energy regulation, metabolism, and inflammation.

One of the key mechanisms by which the gut microbiome influences obesity is through the production of short-chain fatty acids (SCFAs). These metabolites not only serve as an additional energy source but also play a role in modulating host metabolism, including enhancing insulin sensitivity and reducing inflammation. The disruption of the gut microbiota's balance, particularly the increase in Firmicutes and decrease in Bacteroidetes, has been associated with increased energy harvest and fat deposition. This altered microbial composition is further compounded by diets high in fats and sugars, which are prevalent in Western societies, leading to decreased microbial diversity and a shift towards a pro-obesity microbiota profile.

Moreover, the gut microbiota's role in regulating inflammatory pathways is crucial in understanding obesity. Chronic low-grade inflammation, often observed in abdominal obesity, is linked to increased intestinal permeability and the translocation of lipopolysaccharides (LPS) into the bloodstream, which triggers systemic inflammation. This inflammatory state not only exacerbates insulin resistance but also contributes to adipose tissue dysfunction, further promoting obesity.[11]

The interaction between diet, genetics, and the gut microbiome adds another layer of complexity to obesity. The concept of "personalized nutrition" based on an individual's genetic makeup and gut microbiota composition is gaining traction as a potential strategy for managing obesity. For instance, specific genotypes may interact with dietary components to influence the microbiota's composition and function, thereby affecting an individual's propensity for weight gain or loss. This highlights the importance of considering individual differences in microbiota and genetic factors when designing dietary interventions for obesity management.

Therapeutically, the manipulation of the gut microbiome offers promising avenues for treating obesity. Probiotics, prebiotics, and synbiotics have shown potential in modulating the gut microbiota to promote a healthier metabolic profile and aid in weight loss. However, the efficacy of these interventions can vary based on the individual's baseline microbiota composition and diet. Faecal Microbiota Transplantation (FMT) represents another innovative approach, with early studies suggesting it can improve insulin sensitivity and induce weight loss in obese individuals. However, the long-term effectiveness and safety of FMT as a treatment for obesity remain unclear, necessitating further research.[13,14]

Dietary interventions aimed at altering the gut microbiome, such as increasing fiber and polyphenol intake, have also been shown to positively influence metabolic outcomes.[15] These dietary changes can enhance the growth of beneficial bacteria that produce SCFAs, which are associated with improved metabolic health and reduced obesity risk.

## 6. Conclusion

The gut microbiota is known to contribute to obesity and obesity related metabolic processes that affect the host's metabolism, energy expenditure and inflammation. These features suggest that the relations between diet genetics and the microbiome are intricate and require further exploration in order to come up with proper therapeutic approaches. As the knowledge expands, other therapies involving microbiome modification like use of probiotics, prebiotics, FMT, and diets form potentials strategies in dealing with obesity. Nevertheless, more researches are required to expound these processes and also to implement the knowledge acquired into practice.

## 7. Conflict of Interest

None.

## 8. Source of Funding

None.

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