

# Microbiome, Obesity and its treatment

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**ABSTRACT:** *The prevalence of Obesity kept rising over the last decade. To deal with this global health challenge, current therapies, however, have certain limitations. After discovering mechanisms between microbiota and human body and comparing lean and obese individuals, it is found that manipulating microbiome could probably be a solution. Based on recent findings, microbiome-based therapies are introduced, along with speculation for possible treatment.*

**KEYWORDS:** *Microbiome; Obesity; Gut microbiota composition; Microbiome-based Treatment; Probiotics; Prebiotics; Fecal Transplant*

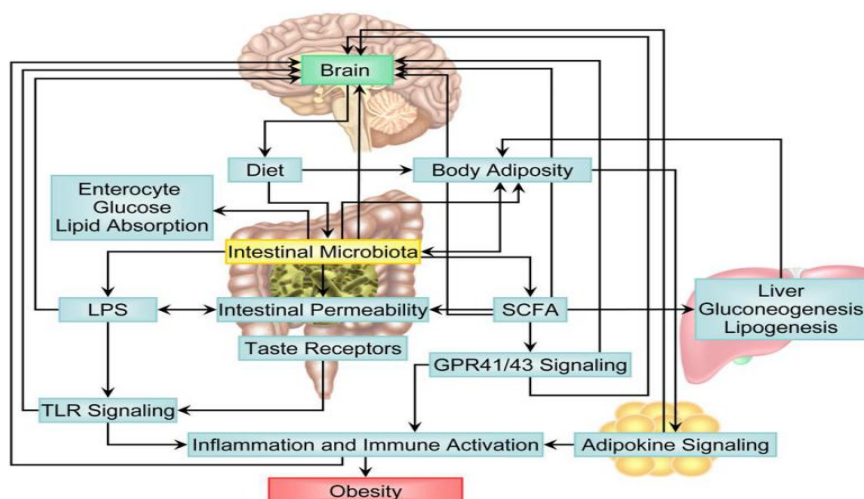
## Introduction

Obesity is defined as an abnormal accumulation of body fat, often 20% or more over an individual's ideal body weight. There is a great deal of problems that may derive from obesity, namely diabetes, osteoporosis, cardiovascular disease, fatty liver disease, cancer, etc. In the past decades, the prevalence of obesity (Body mass index, BMI  $\geq$  30) kept increasing, with 10.8% in men and 14.9% in women.[1] The severity of this disease has exceeded normal expectation and effective treatment of obesity is urgently needed.

However, as one of multifactorial diseases, the development of obesity is still under evaluation. Genetics, unbalanced diet, lack of exercise, age, environment and sleeping quality are considered contributive to obesity.[1] According to those factors, currently there are three main ways to treat obesity: the first one, which is lifestyle intervention including diet change and regular exercise, nevertheless, needs long term maintenance with low effect. The second method of using anti-obesity drugs, however, has potential psychological and physiological side effects including depression, anxiety, block of absorption (e.g. Melbine) and suppression of appetite (e.g. Saxenda).[1] Considering the limited qualifying conditions (BMI > 40) for obesity patients to have a surgery (gastric bypass, lap sleeve, etc.) and potential risks, this option is not always suitable.

Recent researches of microbiota and fecal microbiota transplant reveal that microbiome can be an important contributor to pathogenesis of obesity. It is found that conventionally-raised (CON-V) mice that harbored microbiota at birth

contained 42% more body fat as germ-free (GF) mice without gut microbiota.[1]



After transmitting microbiota from CON-R mice to GF mice, body fat in GF mice significantly increase despite a decrease in food intake.[1] All of these results support the fact that microbiota have relationship with body fat, which paved way for further studies of its possible mechanisms and how this can be used to develop new treatment of obesity.

### Mechanisms between Gut microbiome and obesity

Microbiota can affect body fat in a variety of ways, including improvement on energy and nutrition absorptions, changes in metabolic pathways and influences in brain activity.

Obesity can be explained by the gut-related bacteria mechanism, such as microbial fermentation which decomposes polysaccharides into monosaccharides and generates short-chain fatty acid (SCFA), which leads to higher efficiency of energy absorption.[1] Microbes that contribute to obesity include: *Clostridium ramosum*, *B. thetaiotaomicron*, and *M. smithii*.[2]

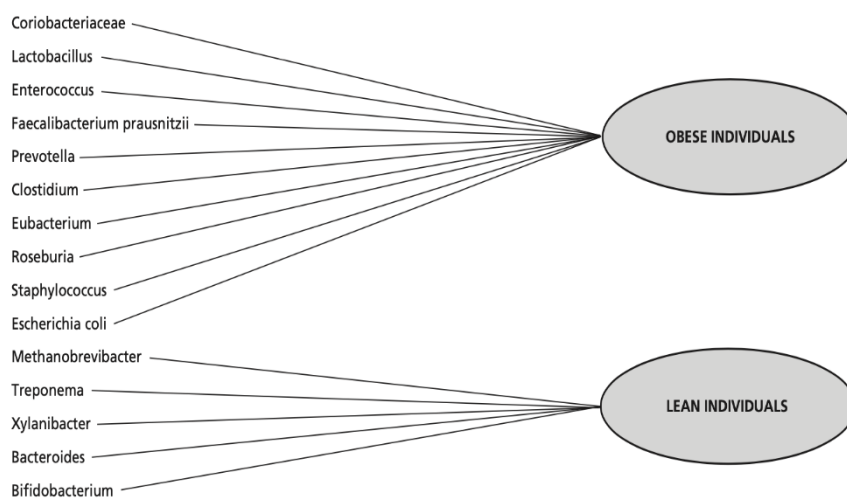
Microbes are able to affect essential amino acids pathway which is associated with obesity and insulin resistance.[2] Also, Researchers have found that microbial activities of dietary choline is relevant to the composition of microbiota. Microbes are able to metabolize choline into trimethylamine-N-oxide (TMAO). Moreover,

disproportionate gut microbiota may lead to excessive absorption of fat and cholesterol since unsuitable amount of bile acids is secreted by anaerobic bacteria.

It has been suggested that microbiota could manipulate host behaviors by changing food preferences. A research indicates that germ-free host tends to consume more sweet solution than normal hosts.[3] It also suggests that there are more sweet receptors in proximal bowels than in tongue.[3]

### Gut microbiota composition in obese individuals

Human gut microbiota consist of more than 30 species, where Firmicutes, Bacteroidetes, Proteobacteria and Actinobacteria are reported to contribute towards obesity.[1]



**Figure 2** Population of bacteria found to increase in obese and lean individuals.

Summary of evidence for consistent changes in the gut microbiome of obese human subjects versus lean individuals. Reproduced with permission from Angelakis E, Armougom F, Million M, et al. The relationship between gut microbiota and weight gain in humans. *Future Microbiol.* 2012 Jan;7(1):91-109.<sup>66</sup>

However, detailed composition of microbiota in obese individuals differ in various experiments and researches due to differences in age, ethnicity, lifestyle and geography among people. So in conclusion, there are no absolute or specific changes in ratio between certain bacteria in obese individuals because of a variety of factors, however, composition of a person's microbiota will change as it gets obese.

### **Microbiome-based treatment of obesity**

It is confirmed that obese individuals have disproportionate gut microbiota. In order to treat obesity, extra microbes or forces are needed to improve the composition of microbiota. Manipulating the gut microbiota may be an essential and logical strategy for weight loss, which can be achieved by following intake.

Probiotics, defined as “live microorganisms that, when administered in adequate amounts, confer a health benefit on the host”, can directly alter microbiota composition and improve adiposity measures.[4] These are commensal microbes that inhibit adhesion to mucosal surface of obesogenic bacteria, enhance gut epithelial barriers and modulate immune system.[4] As obesity is a chronic inflammatory disease, functions of probiotics fit well with anti-obesity treatment and gradually have distinct impact on reduction of body fat and BMI.

Prebiotics, different from probiotics, are actually undigestible nutrients which improve and stimulate growth and replication of beneficial gut microbiota. They usually consist of oligosaccharides, lead to changes in both activity and function of beneficial microbiota and then reduce adiposity.[4] Inulin, a naturally-derived prebiotic, is reported to significantly stimulate growth of Bifidobacterium and A muciniphila, which negatively correlates with body weight.[4]

Theoretically, antibiotics may also help treat obesity, as long as antibiotics particularly towards obesogenic bacteria is developed. However, previous hypothesis shows that antibiotics lead to disruptions in microbiome.[5] Further reports give out that antibiotics result in pathophysiological development of IBS and Crohn’s disease.[5] Thus, use of antibiotics remain controversial and need further support.

Other than changing the proportion of different species in gut microbiota, synthetic biology also contributes to treatment of obesity. Engineered probiotics can directly deliver by-products and substances which can cause weight loss. Administration of N-acyl ethanolamides (NAEs) can inhibit fat absorption, delay gastric emptying and reduce food intake.[1] And overweight mice, when treated with bioengineered Bifidobacterium that secrete Oxyntomodulin (OXM), exhibited reduced appetite and decreased body weight.[1]

Another possible treatment of obesity is fecal transplant, which is a brand new domain in past decades. Previous fecal transplant experiments successfully prove the feasibility of this method, and currently it has been adopted to treat IBD, IBS, RCDI, etc. Meanwhile, it also faces plenty challenges such as how to avoid spread of undetected diseases in feces. Further researches specific to human that study relationship between fecal transplant and obesity are needed to validate security and effectiveness of this method.

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