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The gut microbiota effect on obesity and associated metabolic disorders: A Review

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Abstract

The microbiome plays a significant role as a novel factor of biology that indirectly causes obesity through interactions with the host and diet. It affects sugar and fat metabolism and contributes to the regulation of a host's intestinal immunity. This is one of the mechanisms through which it contributes response to diet and the pathophysiology of diet-induced obesity. Obesity is a modern disease that has reached epidemic proportions in all societies due to the metabolic disorders and chronic inflammation it causes. Energy-rich diets and a sedentary lifestyle without exercise are factors that lead to obesity. This review aims to shed light on an important problem facing societies, the resulting threat to human health, and how to treat it using modern applications.

Keywords: gut microbiome, Dysbiosis, insulin resistance

1. Introduction

Recent research underscores the strong connection between gut microbiota and obesity, and later alters the microbiota of the gut, which is in turn closely related to obesity pathogenesis, as it affects host immunity & metabolism. Thus, interventions involving microbiota of the gut could be used to prevent and treat obesity [1]. An imbalance in the microbiota of the gut affects the metabolism process, which is closely linked to causing obesity, as it affects the body's immunity and metabolism. Therefore, interventions that focus on beneficial gut bacteria and their balance can be used to prevent or treat obesity [1,2]. Obesity is one of the most common and serious medical conditions in modern society. Depend on WHO data, the obese population is increasing. Obesity effect by causes glucose intolerance, hypertension, metabolic disorders, dyslipidemia & hyperuricemia, a risk factor for ischemic heart disease, atherosclerosis. Therefore, the prevention, pathogenesis, and obesity treatment merit further investigation. Laboratory experiments have been conducted since 2004, when [2] found for the first time that transferring bacteria from the feces of conventionally raised mice to experimental mice called GF mice increased fat mass and insulin resistance. The increased fat storage was't due to increased food intake rather than a decrease in a fat-inhibiting factor [2,3,4]. In 2006, it was first shown that gut bacteria differ with obesity, and the researchers' results at the time showed that the ratio of Firmicutes to Bacteroides bacteria in humans and obese rodents increased[3]. Numerous studies have been conducted on gut microbes in obese patients to clarify the balance between different ethnic groups and some differences in geographical location and surrounding environment. These

differences may be attributed to interactions between multipleffactorshas dietyandeculturalkbackground [3,4,5,6].

In 2013studies conducted that transferring gut bacteria from obese human models or mice to gluten-free mice led to obesity later [4,5]. Furthermore, it was proven that disruption of gut bacteria resulting from antibiotic use in childhood increases the risk of obesity in adulthood[3,4,5]. obesity is closely linked to metabolic diseases. Studies on Oscillospira bacteria decrease with obesity and are expected to be candidates for the next generation of probiotics because they produce short-chain fatty acids such as butyrate. analyzed the gut microbiomes of about 420 twins and found that an abundance (Christensenellaceaek) lower BMI, transplanting cChristensenella-minuta into Gf-mice reduced weight gain [4].

A study by a researcher [5] showed that the relative abundance of Amuciniphila, which affects glucose metabolism, decreases in mice and humans with obesity and diabetes. In China, a metagenome analysis, serum metabolomics profiling revealed an abundance of kglutamate-fermenting. *B. thetaiotaomicron* reduced with obesity elevation with serum glutamine (Gln). Bariatric surgery and *B. thetaiotaomicron* administration decreased (Gln) levels in mice [6,7]. Hencek, *B. thetaiotaomicron* affects AA cycling and has anti-obesity effects [6]. *B. thetaiotaomicron* upregulates intestinal lipidiabsorptionutransportersupromoteshhepatichlipid biosynthesis, which may cause obesity and impaired glucose tolerance in high-fat diet-fed mice [7].

2. Obesity treatmentjaltersaagutfmicrobiota

A study by [8] indicates that weight loss plays an effective role in improving metabolic disorders associated with obesity, such as high blood pressure and diabetes. Another study of [9] showed that reducing food intake and changing hormone levels that affect fat digestion, bile acid secretion, energy metabolism, and microbiota of gut, metabolic effects of gastric sleeve surgery were eliminated in mice with disruptions in the FXR gene, suggesting that FXR signaling contributes to mreduced bodykweight and improved glycemic control after bariatric surgery [10]. Another group demonstrated the mechanism by which Roux-en-Y gastric bypass (RYBG) improves metabolism in rodents, specifically, it reduces bile acids with an increase (GLP-1) glucagon-like peptide 1, via L-cell proliferation. The reduction with bilelacids, the effect in Lactobacillus bacteria that decreased it, leads to intestinal L-cell proliferation, increased GLP-1 secretion, and improvements in glycemic control [11]. A study of [12] analyzed 40 subjects before and after RYBG that showed that RYBG improved chronic inflammation but increased proinflammatory bacteria andDlevels of (LPS) lipopolysaccharide and flagellin-specific immunoglobulin A (IgA) increased. Thus, increased intestinal IgA levels after bariatric surgery neutralize immunogenic bacteria and their components, leading to improved systemic inflammation [9,10,11].

2.1Gut microbiota and glucose metabolism

A metagenomic analysis of patients of Chinese descent with type 2 diabetes revealed a decreaseSin butyrateSproducingSbacteria, an increase in methane metabolism and H_2S production, increase in the expression of genes regulating resistance to oxidative stress [13]. A metagenomic analysis of a cohort of 145 healthy European women with impaired glucose tolerance and type 2 diabetes identified changes in the gut microbiota dysbiosis [14]. metagenomic profiles differ between diabetic and healthy individuals and can be a good predictor of impaired glucose metabolism. However, regional and ethnic differences in gut microbiota must be taken into account. Nevertheless, there is a strong link between microbial imbalance and impaired glucose metabolism. Furthermore, gut dysbiosis is

already present in the stage of impaired glucose tolerance, even before the onset of type 2 diabetes [14,15,16]. A metagenomic analysis of approximately 1,500 Swedish individuals showed that prediabetes and type 2 diabetes are characterized by changes in the gut microbiota and their functional genes, as well as a decrease in the abundance of butyrate-producing bacteria and the machine using a random forest algorithm to distinguish between individuals with prediabetes and diabetes and demonstrated that bacterial compositional/functional changes are associated with insulin resistance in the stage of impaired glucose tolerance [16]. Analyzing gut microbiota could help detect glucose intolerance at an early stage and improve intervention. A machine learning model to predict the development of type 2 diabetes in healthy and prediabetic patients has been challenging [17]. A metagenomic analysis of 74 type 1 diabetes patients and nearly 300 healthy controls revealed microbial differences between the two groups; *P. copri* and *Eubacterium siraeum* were more prevalent in type 1 diabetes patients, while Firmicutes and Faecalibacterium prausnitzii were more prevalent in the control group. The altered bacterial species and metabolic pathways were associated with glycemic control [18]. Gut microbiota is also associated with type 1 and type 2 diabetes (T1DM and T2DM), stool specimens of patients with type 1 diabetes using proteomics & discovered reduced intestinal barrier function, proteins affecting intestinal inflammation, and changes in the gut microbiota even before disease onset [18]. Tracking the gut microbiota in children congenitally predisposed to type 1 diabetes revealed temporary increases in the abundance of *Ruminococcus gnavus* and *Streptococcus infantarius* bacteria and a decrease in microbial diversity before disease onset [19]. immunological mechanism, the commensal gut bacterium Parabacteroides distasonis possesses a homologue similar to the insulin beta chain, a target protein of the autoimmune response in type 1 diabetes[20]. The presence of these bacteria can lead to the production of autoimmune antibodies that contribute to the development of type 1 diabetes [20]. Ruminococcus spp. may prevent the onset of type 1 diabetes by stimulating CD8+ regulatory T cells [21], suggesting a close interaction between the gut microbiota, the immune system, and the development of type 1 diabetes.

3. Short-chain fatty acids

The ShortOchainDfatty acids SCFA butyrate has a metabolic effect through its protein-coupled receptors AGPRs [22]. It is involved inHsecretionPPYY peptides in the intestinal cells, which in turn regulate insulin secretion by stimulating pancreatic β-cells [22,23]. Experiments on mice lacking receptors showed reduced PYY peptide secretion after consuming Short-Chain Fatty acids [22,23,24]. Short-chain fatty acids regulate energy metabolism and enhance sympathetic activation by GPR41 signaling [25]. GPR43 activation mediated via short-chain fatty acids in fat cells inhibits insulin signaling by inhibiting Akt phosphorylation, reducing fat accumulation [26]. Evidence suggests that increasing short-chain fatty acids in the body is metabolically beneficial. In addition to the ingestion of non-digestible polysaccharides, the production of Short-Chain Fatty acids (SCFAs) has been attributed to physical activity [27,28]. Injections of Short-Chain Fatty acids as acetate, butyrate, and propionate, into the distal colon increased fasting fat oxidation, resting energy expenditure, and PYYS concentrations in men [29].

3.1FXR/TGR5/bile acids

The FXR receptor (NR1H4) (nuclear receptors) acts as a transcription factor in the cell [30]. It plays a main role in regulating the metabolism of glucose, bile acids, and lipids [31]. FXR, a group of genes that regulate metabolic processes, which is interestingly associated with intestinal microbiome (gut flora), has an influential role in this process. By reducing the concentration of muricoli acid, it is

one of the FXR inhibitors, leading to changes in the receptor's activity and metabolism of its effects [30,31]. Mice that lack the FXR receptor show a disorder in blood lipid metabolism (dyslipidemia), which indicates a role for FXR in maintaining metabolic balance [30,31]. On the other hand, activating FXR using substances or increasing it through genetic engineering led to an improvement in the metabolic index in mouse models in which FXR was disabled; mice showed improvement in a high-fat diet and increased secretion of the hormone GLP, which is concerned with regulating sugar. In addition, studies have indicated that the use of a selective and effective inhibitor such as glutathione Glycine led to a significant improvement in obesity, insulin resistance, and fatty liver[30,31].TGR5 receptor is a membrane receptor on the cell surface that is activated by bile acids and belongs to the class of G protein-coupled receptors found in many tissues of the body, including the liver, lung, intestine, spleen, and central nervous system[32]. When bile acids activate TGR5 receptor, the secretion of intestinal hormones is stimulated, which play a major role in regulating blood sugar levels and appetite, as GLp works to secrete insulin, while PYY an appetite suppressant by affecting the central nervous system, activating the TGR5 receptor in brown adipose tissue leads to increased energy consumption by stimulating the production of an enzyme known as D2, which is responsible for activating thyroid hormones within cells, which enhances the metabolism process. Thus, the interaction between bile acids and the TGR5 and FXR receptors shows the complexity of the regulatory network of the metabolism process [30,32]. The effect of bile acids on metabolic health does not stop at the liver or intestines only, but extends to include the regulation of appetite hormones, energy consumption, and even endocrine activity. Understanding these pathways helps in finding solutions to obesity, diabetes, and fatty liver. [30, 31, 32, 33].

Reduce endoplasmic reticulum stress as a result of bile acids, a cellular condition that increases in obesity and is closely linked to insulin resistance [34]. This type of stress disrupts insulin signaling by activating a specific enzyme that affects insulin. This step interferes with the normal insulin signaling pathway and thus contributes to pancreatic beta-adrenergic dysfunction and the onset of diabetes [33,34,35]. Administering oxydeoxycholic acid, a type of bile acid, reduces endoplasmic reticulum stress in helia transplanted into live animals. When administered to mice with obesity and diabetes, significant improvement in metabolic status, leading to an increase in beneficial bacteria, Lactobacillus and Bifidobacterium, confirming that microbial balance plays a beneficial role in metabolic pathways [34].

3.2 Imidazole drug

The gut microbiome and its interactions with bile acids play a critical role in regulating metabolic and inflammatory responses may directly impact the efficacy of drugs used to treat metabolic diseases such as type 2 diabetes[35]. Chronic treatment with antibiotics as vancomycin or metronidazole, significantly alters bile acid composition due to the loss of intestinal bacteria that produce enzymes responsible for converting primary bile acids into secondary acids, which are often proinflammatory [36]. antibiotic-induced modification of bile acids reduced systemic inflammation induced by a high-fat diet in C57BL6 mice. However, this effect was not observed in other types of mice, such as 129S1 or 129S6; the host's genetic background plays a role in determining the response to these microbial and biliary changes [36,37]. Hence, it appears that modifying the microbiome using antibiotics could be an effective way to improve glucose metabolism and reduce inflammation, but it is not a universal approach; rather, it is influenced by genetic and environmental factors the potential role of some other microbial metabolites, such as imidazole propionate (ImP), a metabolite derived from the

amino acid histidine (His) and produced by gut microbes[36]. A European study conducted in 1990 observed elevated levels of ImP in the serum of individuals with prediabetes and type 2 diabetes; this increase was not related to the amount of histidine consumed in the diet, indicating that gut microbes are primarily responsible for the production of this metabolite [36]. Imidazole propionate has been shown to contribute to increased insulin resistance by activating the mTOR pathway and inhibiting insulin-related signaling, which may contribute to the development of metabolic disorders [35,36, 37]. Elevated ImP levels are closely associated with certain bacterial species, such as *Clostridium bolteae, Cenarchaeum symbiosum,* and *Ruminococcus gnavus*. Furthermore, a diet high in saturated fats and low in fiber and unsaturated fatty acids is associated with increased production of this metabolite. Importantly, elevated ImP levels not only promote insulin resistance but also impair the effectiveness of metformin, a key treatment for diabetes. A recent study demonstrated that ImP inhibits metformin's ability to lower blood sugar in mouse models by inhibiting AMPK phosphorylation in a p38γ-dependent manner. This suggests that metabolites produced by the gut microbiome not only influence metabolic signaling but can also interfere with the efficacy of drug therapies. Therefore, understanding the interaction between diet, the microbiome, and its resulting metabolites may open new avenues in personalized medicine for treating metabolic disorders such as diabetes, obesity, and fatty liver [35,36, 37].

4. Dysbiosis

A result of a microbiome imbalance (dysbiosis), which weakens the intestinal barrier due to decreased production of intestinal mucus and intercellular binding proteins that leads to increased intestinal permeability, allowing bacterial components such as endotoxin (LPS) to pass into the circulation, causing chronic inflammation via TLR4 activation, particularly in the liver and adipose tissue, and exacerbating obesity-related insulin resistance. Microbial interventions can correct this imbalance [38]. Probiotic *YBifidobacterium animalis* prevents JLPS leakage and improves metabolic and inflammatory status in obese mice [38,39]. In humans, supplements containing strains of Bacillus spp. reduced endotoxin levels by 42%. *Akkermansia muciniphila* is also considered a beneficial bacterium that maintains the integrity of the intestinal mucosa [38,39]. Its levels have been found to decrease in obesity and diabetes. However, increasing its levels through interventions such as metformin, cranberry extract, herbal supplements such as Bofutsushosan, or prebiotics leads to improvements in insulin resistance, intestinal inflammation, and intestinal barrier function. Giving pasteurized *A. muciniphila* to obese mice has been shown to reduce weight by increasing energy expenditure [39,40]. Pasteurized *A. muciniphila* was more effective than its live form in improving weight, cholesterol, and insulin resistance [38,39, 40].

4.1. Dysbiosis and Liver Diseases

A healthy intestinal barrier maintains its function and prevents the microbial flora of the gut from reaching the liver [41]. An unbalanced diet causes gastrointestinal bacteria, and their components may migrate to the barrier is compromised as a result of various environmental factors and pathogen recognition receptors as Toll-like receptors (TLRs) and inflammasomes, that identify bacterial antigens and stimulate pro-inflammatory cytokine production via activating hepatic macrophages and the immune response [41]. Dysbiosis is associated with pathological conditions in various liver diseases as non-alcoholic Gand alcoholic hepatitis fatty Liver disease (NAFLD), liver fibrosis, and hepatocellular carcinoma (HCC) [40,41]. Chronic alcohol intake has been reported to cause impaired intestinal barrier function in humans, as well as microbial imbalance [42, 43]. Patients with

alcoholicAhepatitis have increased levels of *Enterococcus faecalis*, which secretes Scytolysin enzyme that causes hepatocyte death and liver damage [44].

4.2 Dysbiosis and Metabolic Syndrome

Dysbiosis of bacterial communities in the patient's gut can result in many diseases as surgery and antibiotic treatment, causing *pseudomembranous colitis* as a result of toxin production by *Clostridium difficile* and sepsis of *E. coli. faecalis* and *En. faecium*, as well as intraabdominalشabscesses due to aA*Bacteroides fragilis*. Presence of pathogens or disruption of the native bacterial community of the intestine plays a role in the development of cancers, prostate cancer, and gastrointestinal cancer [45,46,47]. Commensalشbacteria wereAconsidered asAcofactors in carcinogenesis. It was reported that the gut flora bacteria in the gut can trigger macrophages to generate chromosome-breaking factors and diffusible clastogens, and mediate DNA damage with induced instability of chromosomes in neighboring cells. The composition of the bacterial community of the gut is different between healthy and CRC individuals. For example, two of the *Prevotella* species. Completely absent in CRC samples, analyzed, higher levels of *Prevotella* in the healthy group may reflect differences in intake of plant materials compared to the individuals with.CRC patients [47]. Increasing use of immunosuppressive drugs affects both acquired and innate immunity by minimizing phagocytosis. Cytotoxic, antineoplastic drugs influence dividing cells rapidly, such as cells of the gastrointestinal mucosa, bone marrow, making a barrier, and translocation that act as a source of bacterial infection in cancer patients [48,49,50].

5. Microbial Estrogen Metabolism

Beta-glucuronidases enzymes encoded by gut bacteria, which affect estrogen by reactive after menstruation in women, lead to metabolic mess, and the gut flora microbes play a main role in reproductive and endocrine systems throughout a woman's that theAenzyme β glucuronidases secreted from bacteriaAplay aArole inAregulating estrogen levels affect the body's balance, and once this balance is disturbed leads to diseases as cancers, the uterus, or breast & menopause syndrome. For this reason, the enzyme beta-glucuronidases secreted by bacteria become a potential biomarker for the early diagnosis of estrogen-related diseases [51,52].

6. Personalized Microbiome Therapies

Genetically engineered, including Bacterial-based interventions, probiotics, and fecal-microbiota-transplantation (FMT), are tested on human metabolic management [53]. The microbiome has gained significant attention in scientific research and has been characterized in human and animal hosts using advanced tools as high-throughput sequencing and artificial intelligence [54]. Therapeutic strategies are one of the tools' help explore complex interactions and develop modern detection, therapeutic, and analysis of data technologies [55]. The FMT (fecal transplantation) applied technology faces challenges, including targeted interventions that focus only on essential probiotics colonizing the gastrointestinal tract after birth, establishing a symbiotic relationship with the host, and the disease control effect of any imbalance of the bacterial flora has been associated with various conditions, Aas inflammatory bowel disease and cancers [56]. Another technology is omics provided a deeper understanding of the relationship between the gut flora and host health in 2013, the first trial of fecal microbiota transplantation for the treatment of recurrent *ClostridiumAdifficile* infection, fecal microbiota products began to be systematically and commercially used, prompting researchers to expand their use and clinical applications in cases of inflammatory bowel disease and cancers, but the challenge remained in disease conditions such as irritable bowel disease [53, 54, 55].

6.1. Modern technologies and therapies

Modern technologies, including omics, genomics, and metabolomics, along with data-driven artificial intelligence, have enabled the precise identification and selection of probiotics [55]. The probiotics platform provides rapid machine learning screening of probiotics, facilitating the development of more precise treatments compared to traditional microbiota cultivation [56]. Probiotics were used to treat clinical conditions such as chronic constipation, Crohn's disease, ulcerative colitis, depression, type 2 diabetes, and irritable bowel syndrome (IBS) using groups of bacteria that contribute to maintaining intestinal balance [57,58,59]. *Faecalibacterium*, which is associated with inflammatory bowel disease and its effects on the mucous membrane; *Akkremansia*, which is associated with obesity and metabolic syndrome; and Lactobacillus, which is associated with colitis and colorectal cancer [58, 59, 60, 61]

Lactobacillus casei, isolated from Chinese yogurt, slows kidney deterioration in patients with chronic kidney disease. *Lactobacillus reuteri* is used to treat gastroenteritis in children. When applied clinically, these treatments provide a clear mechanism of action for probiotics [61,62]. However, applications also face challenges, aboutAhow ensure the viability of each strain, how to culture them separately or together, and how to dynamically modify the strains. Looking ahead, to address the challenges that hinder the implementation of these experiments and their transfer to reliable clinical trials, alternatives to mice must be used [62,63]. Organ culture chips, organoid cells, 3D culture, and artificial intelligence models can be used to predict toxicity to confirm the effectiveness of strains more broadly [64,65]. It is also suggested that safer and more effectiveALBP products be designed after understanding the effects and dosage of each bacterial strain used [66]. The use of metabolic models and artificial intelligence models to predict and design combinations of two strains that are more beneficial for restoring a healthy intestinal system [67]. When producing an ABLP, efforts must be made to reduce the exposure of completely anaerobic bacteria to oxygen, determine growth media within physiological parameters ensure the strains' ability to survive and stabilize for a longer period. It must be taken into account that patients' response to probiotic treatment in the case of intestinal inflammation is relative, which requires identifying a biomarker related to the microbiome used for treatment. Testing of strains used in intestinal inflammation products should also be expanded to include strains that have 't yet been cultured [65,66,67].

Other Modern technologies as machine learning and artificial intelligence, have accelerated the identification and characterization of microbes and their functions in the gut. Computational tools have been used to predict interactions and optimize probiotic strain compositions. Innovative probiotic delivery systems, including microcapsules, targeted ananoparticles, and antibiotic agents, have shown a great potential to improve probiotic viability and stability, thus improving clinical outcomes [64,65]. Microbiome therapies are also being proposed to be used extensively in conjunction with other advanced technologies of CRISPR-Cas9 geneAediting and personalized nutrition. CRISPR-Cas9Acan precisely modify probiotic genomes to enhance beneficial properties or eliminate harmful ones [66]. Personalized nutrition can further support microbiome interventions by tailoring diets to suit an individual's microbiome profile, increasing treatment efficacy, and maintaining long-term microbial balance. Finally, clinical research must be coupled with proactive engagement with pharmaceutical regulatory bodies to produce disease-targeting LBPs based on meeting clinical application criteria. Supplemental butyrate therapy may improve the imbalance caused by drug therapies and improve the quality of life of ulcerative colitis patients. A Heat-

inactivatedALactobacillus plantarum L-137 can clinically enhance immunity and reduce inflammation [68, 69]. Thus, in future treatment regimens, probiotics and postbiotics may represent a model resembling the wings of a bird, representing two therapeutic approaches based on contemporary biotechnology and omics analysis. Thanks to this approach, researchers can use multi-omics analyses and big data mining to identify and cultivate microbes, making strain testing and selection safer and more accurate in clinical applications. Looking ahead, these technologies will bring about revolutionary innovations in major disease areas such as tumors, chronic inflammation, and immune imbalance, providing a promising treatment for precision medicine [70, 71,72, 73].

7. Conclusion

Dysbiosis of the gut microbiome plays a pivotal role in obesity & metabolic disorders as insulin resistance and type 2 diabetes. Therapeutic interventions targeting the modulation of the gut microbiome composition, whether by surgery a probiotics, or fecal transplants, have proven effective in improving metabolic health indicators. Modern techniques such as comprehensive genomic analysis (Metagenomics) and artificial intelligence-supported computational models have enhanced our understanding of the composition and function of gut microbes, allowing for the design of precise and effective therapeutic strategies. In this context, personalized microbial therapies represent a qualitative development in the field of precision medicine, as they include interventions based on genetically modified probiotics and fecal microbiota transplantation (FMT), in addition to the use of omics and artificial intelligence techniques to discover effective bacterial species and determine their therapeutic effects. *Akkermansia muciniphila, Faecalibacterium prausnitzii,* and *Lactobacillu*s play important roles in regulating immune and metabolic balance, and have been used in the treatment of conditions such as irritable bowel syndrome, Crohn's disease, diabetes, and even certain types of cancer. However, the application of these treatments faces several challenges, including maintaining the vitality of bacterial strains, determining the appropriate dosage, and understanding the mechanism of action of each bacterial type individually or in groups. Furthermore, the response to treatment varies from person to person, necessitating the development of biomarkers that help predict treatment outcomes and guide it more accurately. The combination of three-dimensional culture techniques, organ-on-chip models, and computational modeling provides a promising means to test the efficacy and safety of these treatments without fully relying on animal models. Advanced delivery systems, such as microcapsules and nanoparticles, enhance the stability of probiotics and their delivery to specific areas in the gastrointestinal tract. It is expected that technologies such as genetic modification using CRISPR and personalized nutrition will contribute to maximizing the effectiveness of these treatments by designing interventions that align with the microbial composition of each individual. In the near future, these innovations will lead to a revolution in treating complex diseases such as tumors, chronic infections, and immune disorders, making personalized microbiome medicine a pivotal tool in the precision medicine framework, and offering hope forAimproving theAquality of life forA patients through interventions based on the most intricate details of the interaction between humans and microbes.

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