EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Coden USA: EJBPBO
Volume: 13
Issue: 6
Year: 2026

DYSBIOSIS AND HUMAN HEALTH, DRUG–MICROBIOME INTERACTIONS: AN EMERGING MICROBIOME THERAPEUTICS

[1*]Dr. Virendra Kushwaha, [2]Dr. Pooja Agrawal, [3]Dr. Anuj Kumar, [4]Dr. Sonali Chandra, [5]Dr. Sarthak Goel, [6]Dr. Mourriyan Elanchezhiyan

GSVM Medical College Kanpur.

***Corresponding Author: Dr. Virendra Kushwaha**

GSVM Medical College Kanpur.

DOI: https://doi.org/10.5281/zenodo.20442380

How to cite this Article: [1*]Dr. Virendra Kushwaha, [2]Dr. Pooja Agrawal, [3]Dr. Anuj Kumar, [4]Dr. Sonali Chandra, [5]Dr. Sarthak Goel, [6]Dr. Mourriyan Elanchezhiyan (2026). Dysbiosis And Human Health, Drug–Microbiome Interactions: An Emerging Microbiome Therapeutics. European Journal of Biomedical and Pharmaceutical Sciences, 13(6), 081–092.

Article Received on 01/05/2026 **Article Revised on 22/05/2026** **Article Published on 01/06/2026**

ABSTRACT

Dysbiosis refers to disruption of the normal microbial balance within the gastrointestinal tract, resulting in altered microbial diversity, impaired host–microbe interactions, and abnormal microbial metabolite production. The gut microbiota functions as a highly active metabolic and immunological organ involved in nutrient metabolism, epithelial barrier maintenance, immune regulation, neurotransmitter synthesis, bile acid metabolism, and xenobiotic metabolism. Increasing evidence demonstrates that dysbiosis contributes significantly to gastrointestinal, metabolic, cardiovascular, neurological, autoimmune, and oncological disorders through mechanisms involving chronic inflammation, oxidative stress, epithelial barrier dysfunction, immune dysregulation, and endotoxemia. From a pharmacological perspective, the gut microbiota significantly influences drug absorption, metabolism, bioavailability, efficacy, and toxicity. Intestinal microorganisms possess enzymatic pathways capable of activating, inactivating, or transforming therapeutic agents. Conversely, several medications including antibiotics, proton pump inhibitors, antidepressants, chemotherapeutic agents, and non-steroidal anti-inflammatory drugs can induce dysbiosis and alter microbial diversity. Recent advances in pharmacomicrobiomics, metagenomics, metabolomics, and synthetic biology have facilitated development of microbiome-based therapeutics including probiotics, prebiotics, synbiotics, postbiotics, engineered live biotherapeutics, bacteriophage therapy, and fecal microbiota transplantation (FMT). Recently approved microbiome formulations such as Rebyota and Vowst represent major advances in microbiome pharmacology and precision medicine. This review discusses the pharmacological mechanisms underlying dysbiosis, microbiome–drug interactions, dysbiosis-associated diseases, current microbiome therapeutics, approved microbiome formulations, and future perspectives in microbiome-directed pharmacotherapy.

KEYWORDS: Dysbiosis, gut microbiota, pharmacomicrobiomics, probiotics, fecal microbiota transplantation, microbiome therapeutics.

INTRODUCTION

The human gastrointestinal tract harbors trillions of microorganisms collectively referred to as the gut microbiota.[1] These microorganisms include bacteria, fungi, viruses, and archaea that exist in a symbiotic relationship with the host. The gut microbiota functions as a highly complex metabolic and immunological organ and plays a vital role in maintaining human health. It is actively involved in nutrient metabolism, epithelial barrier maintenance, immune regulation, neurotransmitter synthesis, bile acid metabolism, vitamin synthesis, and protection against pathogenic microorganisms.[2] Through these diverse physiological functions, the gut microbiota contributes significantly to intestinal homeostasis as well as systemic health.

In healthy individuals, the intestinal microbiota remains in a balanced and stable ecological state known as eubiosis. Beneficial microorganisms such as *Lactobacillus*, *Bifidobacterium*, *Faecalibacterium prausnitzii*, and *Roseburia* are important components of this balanced microbial ecosystem. These bacteria

promote intestinal homeostasis through the production of short-chain fatty acids (SCFAs), suppression of pathogenic organisms, enhancement of gut barrier integrity, and modulation of host immune responses.[3] The maintenance of this balanced microbial environment is essential for proper gastrointestinal and immunological functioning.

Disruption of this normal microbial balance is referred to as dysbiosis. Dysbiosis is characterized by reduced microbial diversity, depletion of beneficial bacteria, expansion of pathobionts, altered microbial metabolites, and impaired host–microbe interactions.[4] Such alterations in the intestinal microbial ecosystem can adversely affect metabolic, immune, and inflammatory pathways, thereby contributing to disease development and progression.

Several environmental and pharmacological factors contribute to the development of dysbiosis. These include antibiotics, proton pump inhibitors, non-steroidal anti-inflammatory drugs, dietary patterns, smoking, stress, chemotherapy, infections, and aging.[5] Among these factors, antibiotics are considered the most important pharmacological cause of dysbiosis because they profoundly alter microbial diversity and significantly reduce colonization resistance against opportunistic pathogens such as *Clostridioides difficile*.[6] Antibiotic-induced dysbiosis may persist for prolonged periods and can lead to significant alterations in microbial composition and function.

Increasing evidence suggests that dysbiosis plays an important role in the pathogenesis of several gastrointestinal and systemic disorders. These include inflammatory bowel disease, irritable bowel syndrome, obesity, diabetes mellitus, cardiovascular disease, colorectal cancer, autoimmune disorders, and neuropsychiatric diseases.[7] Alterations in gut microbial composition and microbial metabolites have been implicated in chronic inflammation, immune dysregulation, metabolic disturbances, and altered gut–brain communication pathways associated with these conditions.[8]

Recent advances in pharmaco microbiomics have further demonstrated that the gut microbiota significantly influences drug pharmacokinetics, pharmacodynamics, efficacy, toxicity, and therapeutic response.[9,10] The intestinal microbiota can affect drug metabolism through microbial biotransformation, modulation of host enzymes, and alteration of drug absorption and bioavailability. These findings have established the microbiome as an important target in personalized pharmacotherapy and precision medicine, highlighting the growing importance of microbiota-based therapeutic approaches in modern healthcare.

This review aims to provide a comprehensive overview of the gut microbiota with a focus on its physiological roles, the mechanisms and consequences of dysbiosis, and its contribution to the pathogenesis of gastrointestinal and systemic diseases. It also highlights the impact of environmental and pharmacological factors—particularly drugs—on microbial homeostasis and emphasizes the emerging field of pharmaco-microbiomics, wherein the gut microbiota influences drug response, efficacy, and toxicity. Furthermore, this review explores current and evolving microbiota-targeted therapeutic strategies, underscoring the potential of microbiome modulation in the development of personalized and precision medicine approaches for improved clinical outcomes.

Physiological Functions of the Gut Microbiota

One of the primary physiological functions of the gut microbiota is the fermentation of dietary fibers into short-chain fatty acids (SCFAs), including acetate, propionate, and butyrate.[11,12,13] Among these SCFAs, butyrate serves as the primary energy source for colonocytes and plays a crucial role in maintaining intestinal health. It contributes significantly to the maintenance of epithelial barrier integrity, suppression of inflammatory signaling pathways, regulation of apoptosis, and prevention of colorectal carcinogenesis.[14] In addition to SCFA production, the gut microbiota contributes to the synthesis of several essential vitamins, including vitamin K, folate, riboflavin, biotin, and vitamin B12.[15] Microbial metabolism also plays an important role in bile acid transformation and regulation of lipid homeostasis, thereby influencing overall metabolic balance.

The gut microbiota also plays a central role in the maturation and regulation of both innate and adaptive immunity.[16,17] Commensal microorganisms regulate cytokine production, antimicrobial peptide synthesis, regulatory T-cell activity, and inflammatory signaling pathways. Through these mechanisms, the intestinal microbiota helps maintain immune homeostasis and prevents excessive inflammatory responses. SCFAs further contribute to immune regulation by suppressing inflammation and promoting immune tolerance.[18,19] Thus, the gut microbiota functions as an important immunological modulator that protects against immune dysregulation and inflammatory diseases.

Another important physiological function of the gut microbiota is the maintenance of intestinal barrier integrity. Beneficial microorganisms strengthen the epithelial barrier through enhancement of tight junction proteins, stimulation of mucus production, SCFA production, and suppression of pathogenic bacteria.[20,21] These protective mechanisms help preserve intestinal permeability and prevent microbial invasion. In contrast, dysbiosis disrupts epithelial integrity and increases intestinal permeability, commonly referred to as “leaky gut,” thereby permitting translocation of endotoxins and microbial products into the systemic circulation.[22] Increased intestinal permeability has been associated

with chronic inflammation and various metabolic and autoimmune disorders.

The gut microbiota also communicates bidirectionally with the central nervous system through the gut–brain axis.[23,24] Gut microorganisms influence the production of several neurotransmitters and neuroactive compounds, including serotonin, dopamine, gamma-aminobutyric acid (GABA), and norepinephrine. Through neural, endocrine, immune, and metabolic pathways, the gut microbiota affects brain function, mood, and behavior. Dysbiosis-associated alterations in gut–brain signaling have been implicated in several neuropsychiatric and neurodegenerative disorders, including depression, anxiety, autism spectrum disorder, Parkinson's disease, and Alzheimer's disease.[25,26]

Pharmacological Mechanisms of Dysbiosis

Multiple medications significantly alter the composition and function of the gut microbiota and thereby contribute to dysbiosis. Among these, antibiotics are considered the most important pharmacological cause of dysbiosis.[27,28] Broad-spectrum antibiotics profoundly disrupt the intestinal microbial ecosystem by reducing microbial diversity, suppressing beneficial microorganisms, impairing colonization resistance, and promoting opportunistic infections. Repeated or prolonged antibiotic exposure further contributes to the development of antimicrobial resistance, fungal overgrowth, metabolic disturbances, and chronic inflammatory disorders. Antibiotic-induced alterations in the gut microbiota may persist for extended periods and can significantly affect host immunity and metabolism.

Proton pump inhibitors (PPIs) also significantly influence the gut microbiota by altering gastric pH and modifying upper gastrointestinal microbial colonization. Long-term PPI therapy has been associated with increased abundance of *Enterobacteriaceae*, reduced microbial diversity, small intestinal bacterial overgrowth, and recurrent *Clostridioides difficile* infection. These alterations occur primarily due to reduced gastric acid-mediated suppression of ingested microorganisms, thereby facilitating abnormal bacterial colonization within the gastrointestinal tract.

Non-steroidal anti-inflammatory drugs (NSAIDs) contribute to dysbiosis through multiple mechanisms, including epithelial injury, increased intestinal permeability, mitochondrial dysfunction, and inflammatory mucosal damage. NSAID-induced disruption of intestinal barrier integrity promotes inflammation and alters microbial composition, thereby contributing to gastrointestinal toxicity and chronic intestinal inflammation.

Chemotherapeutic agents also significantly alter microbial diversity and contribute to mucosal injury, gastrointestinal toxicity, systemic inflammation, and neutropenic infections. Cancer chemotherapy disrupts the intestinal microbial ecosystem through direct cytotoxic effects on rapidly dividing intestinal epithelial cells and indirectly through immune suppression. Irinotecan toxicity, in particular, is strongly influenced by microbial β-glucuronidase activity.[31] Microbial reactivation of irinotecan metabolites within the intestine contributes to severe gastrointestinal toxicity, demonstrating the critical role of gut microbiota in drug metabolism and adverse drug reactions.

Pharmacomicrobiomics and Drug–Microbiome Interactions

Pharmacomicrobiomics is an emerging branch of pharmacology that focuses on the bidirectional interactions between the gut microbiota and therapeutic agents.[32,33] Recent advances in microbiome research have demonstrated that intestinal microorganisms significantly influence drug absorption, metabolism, bioavailability, efficacy, toxicity, and enterohepatic circulation. The gut microbiota contains a wide variety of microbial enzymes capable of chemically modifying drugs before or after systemic absorption.[34] These microbial activities may activate prodrugs, inactivate active medications, generate toxic metabolites, or alter host metabolic pathways, thereby contributing to variability in therapeutic response among individuals. Such interactions have become increasingly important in the development of personalized pharmacotherapy and precision medicine.

Gastrointestinal Diseases and Drug–Microbiome Interactions

Drug–microbiome interactions are particularly important in gastrointestinal diseases because the intestinal microbiota directly influences mucosal immunity, inflammatory signaling, and epithelial barrier integrity. In inflammatory bowel disease, including ulcerative colitis and Crohn's disease, patients commonly demonstrate reduced microbial diversity, depletion of butyrate-producing bacteria, increased *Proteobacteria*, and chronic inflammatory signaling.[35] These alterations significantly affect intestinal homeostasis and therapeutic responsiveness.

One important example is Sulfasalazine, a prodrug widely used in inflammatory bowel disease and rheumatoid arthritis. Sulfasalazine requires microbial activation within the colon for its therapeutic action. Intestinal bacteria cleave the azo bond of sulfasalazine to produce its active metabolites, Sulfapyridine and 5-aminosalicylic acid, which exert anti-inflammatory effects locally within the intestinal mucosa.[36] Therefore, the therapeutic efficacy of sulfasalazine depends largely on the metabolic activity of gut microorganisms. Alterations in microbial composition may consequently influence treatment response in inflammatory bowel disease.

Antibiotic-associated dysbiosis also plays a major role in recurrent ***Clostridioides difficile*** infection. Broad-

spectrum antibiotics reduce microbial diversity and impair colonization resistance, thereby permitting overgrowth of toxigenic *C. difficile* strains.[37] Persistent dysbiosis contributes to recurrent infection and severe gastrointestinal inflammation. Restoration of microbial diversity through microbiome-based therapies such as fecal microbiota transplantation has shown remarkable therapeutic success in recurrent *Clostridioides difficile* infection.

Metabolic Disorders and Antidiabetic Therapy

The gut microbiota also significantly contributes to metabolic disorders such as obesity, insulin resistance, type 2 diabetes mellitus, and metabolic syndrome.[38,39] Alterations in microbial composition influence glucose metabolism, lipid homeostasis, inflammatory pathways, and insulin sensitivity.[40] Dysbiosis-associated metabolic endotoxemia and chronic low-grade inflammation further contribute to progression of metabolic diseases.

Metformin, one of the most commonly prescribed antidiabetic drugs, exerts part of its therapeutic effect through modulation of gut microbiota composition.[41] Metformin therapy increases the abundance of beneficial microorganisms such as *Akkermansia muciniphila* and short-chain fatty acid-producing bacteria.[42] These microbial alterations contribute to improved insulin sensitivity, enhanced glucose metabolism, reduced systemic inflammation, and improved intestinal barrier integrity. Variability in gut microbiota composition may therefore influence therapeutic response to metformin and contribute to differences in glycaemic control among patients with type 2 diabetes mellitus.[43]

Neurological Disorders and the Gut–Brain Axis

The gut microbiota also plays an important role in neurological and neuropsychiatric disorders through the gut–brain axis. Bidirectional communication between the gastrointestinal tract and central nervous system occurs through neural, endocrine, immune, and metabolic pathways. Gut microorganisms influence production of neurotransmitters including serotonin, dopamine, gamma-aminobutyric acid (GABA), and norepinephrine, thereby affecting mood, cognition, and neurological function.

One important example of microbiome-mediated drug interaction is observed in **Parkinson's disease**.[44] Levodopa, the primary therapeutic agent used in Parkinson's disease, undergoes microbial metabolism within the gastrointestinal tract before systemic absorption. Certain intestinal bacteria metabolize levodopa and reduce its availability for transport across the blood–brain barrier, thereby decreasing therapeutic efficacy and contributing to variability in clinical response. Dysbiosis-associated alterations in neurotransmitter production and neuroinflammatory signaling have additionally been implicated in depression, anxiety, autism spectrum disorder, Parkinson's disease, and Alzheimer's disease.[45] These findings suggest that modulation of the gut microbiota may represent a novel therapeutic approach in neurological disorders.[45]

Cancer Therapy and Immunotherapy

The gut microbiota significantly influences both chemotherapy-related toxicity and responsiveness to cancer immunotherapy. One important mechanism involves microbial β-glucuronidases, which participate in enterohepatic circulation by deconjugating drug metabolites excreted into bile.[46] Following hepatic metabolism, many drugs undergo glucuronidation and are excreted into the intestine as inactive conjugates. Intestinal microbial β-glucuronidases subsequently regenerate active drug compounds, thereby increasing drug reabsorption and toxicity.[47]

This mechanism is particularly important in irinotecan-induced toxicity in colorectal cancer. Irinotecan metabolites are reconverted into active toxic compounds within the intestine through microbial β-glucuronidase activity, resulting in severe gastrointestinal toxicity and diarrhea.[48] Similar microbial mechanisms influence toxicity associated with NSAIDs, estrogen metabolites, and morphine derivatives.

Recent evidence has additionally demonstrated that the gut microbiota significantly influences responsiveness to cancer immunotherapy, particularly immune checkpoint inhibitors such as PD-1 and CTLA-4 inhibitors.[49,50] Specific bacterial taxa, including *Bifidobacterium*, *Akkermansia muciniphila*, and members of the *Firmicutes* phylum, have been associated with improved immunotherapeutic responses and enhanced antitumor immunity. These microorganisms promote activation of dendritic cells, enhance cytotoxic T-cell responses, and improve immune-mediated tumor destruction. Conversely, antibiotic-induced dysbiosis may impair antitumor immunity and significantly reduce the effectiveness of immune checkpoint inhibitors.[51] These findings have generated considerable interest in microbiome-targeted interventions such as probiotics, fecal microbiota transplantation, engineered microbial therapeutics, and precision pharmacomicrobiomics to improve cancer therapy outcomes and advance personalized oncology.[52]

Dysbiosis in Disease

Dysbiosis, characterized by disruption of the normal intestinal microbial balance, has emerged as a major contributor to the pathogenesis of several gastrointestinal and systemic disorders. Alterations in microbial diversity, depletion of beneficial bacteria, expansion of pathogenic microorganisms, and abnormal microbial metabolite production significantly affect epithelial barrier integrity, immune regulation, inflammatory signaling, and metabolic homeostasis. Recent studies have further strengthened the evidence linking gut dysbiosis with chronic inflammatory, metabolic, cardiovascular, and neurological diseases.

Inflammatory Bowel Disease

Inflammatory bowel disease (IBD), including ulcerative colitis and Crohn's disease, is one of the most extensively studied disorders associated with gut dysbiosis.[53,54] Patients with IBD commonly demonstrate reduced microbial diversity, depletion of butyrate-producing bacteria such as *Faecalibacterium prausnitzii* and *Roseburia*, and increased abundance of pathobionts including members of the *Proteobacteria* phylum.[55] These alterations disrupt intestinal homeostasis and contribute to chronic intestinal inflammation.

Butyrate-producing bacteria play a critical role in maintaining epithelial barrier integrity and regulating mucosal immune responses. Butyrate serves as the primary energy source for colonocytes and possesses anti-inflammatory properties through inhibition of histone deacetylases and suppression of pro-inflammatory cytokine production. Depletion of these beneficial bacteria therefore results in epithelial barrier dysfunction, increased intestinal permeability, and enhanced translocation of microbial products into the lamina propria. This promotes activation of macrophages, dendritic cells, and T lymphocytes, resulting in excessive inflammatory cytokine release including TNF-α, IL-6, and IL-1β.[56]

Recent studies have demonstrated that dysbiosis-associated metabolic alterations further contribute to disease progression in IBD. A 2024 review by Inflammation and Regeneration highlighted that disease-associated luminal metabolic changes selectively promote growth of pathobionts such as adherent-invasive *Escherichia coli* while suppressing beneficial commensal microorganisms.[57] Another 2024 study demonstrated that butyrate modulates immune tolerance through regulation of histone deacetylase activity and inflammatory signaling pathways in intestinal macrophages and monocytes, thereby suppressing mucosal inflammation in IBD.[58]

Recent advances have additionally shown that microbiome-based biomarkers may aid in diagnosis and disease monitoring. A 2024 study published in Nature Medicine demonstrated the potential role of microbiome-based diagnostic profiling in inflammatory bowel disease.[59]

Clostridioides difficile Infection

Antibiotic-associated dysbiosis markedly increases susceptibility to *Clostridioides difficile* infection.[60] Broad-spectrum antibiotics significantly reduce microbial diversity and suppress commensal bacteria that normally provide colonization resistance against pathogenic organisms. Loss of these protective microorganisms permits overgrowth of toxigenic *C. difficile* strains within the intestine.

Pathogenesis primarily involves disruption of bile acid metabolism and reduction of short-chain fatty acid-producing bacteria. Secondary bile acids produced by normal gut microbiota inhibit germination and growth of *C. difficile*. Dysbiosis-associated reduction in these metabolites facilitates spore germination and toxin production. Toxins A and B produced by *C. difficile* subsequently cause epithelial injury, inflammation, pseudomembranous colitis, and severe diarrhea.[61]

Recurrent *C. difficile* infection occurs because persistent dysbiosis prevents restoration of normal colonization resistance. Restoration of microbial diversity through fecal microbiota transplantation has therefore emerged as one of the most effective therapeutic approaches for recurrent infection.[62]

Obesity and Type 2 Diabetes Mellitus

Dysbiosis significantly contributes to obesity, insulin resistance, type 2 diabetes mellitus, and metabolic syndrome.[63,64] Alterations in gut microbial composition influence energy harvest from dietary nutrients, lipid metabolism, glucose homeostasis, bile acid metabolism, and inflammatory pathways.

Obese individuals commonly demonstrate an altered Firmicutes-to-Bacteroidetes ratio, increased endotoxin-producing bacteria, and reduced short-chain fatty acid-producing microorganisms. Increased intestinal permeability associated with dysbiosis permits translocation of lipopolysaccharides into systemic circulation, producing metabolic endotoxemia and chronic low-grade inflammation. This inflammatory state contributes to insulin resistance and impaired glucose metabolism.

Short-chain fatty acids produced by beneficial bacteria regulate glucose metabolism, incretin secretion, appetite regulation, and adipose tissue function. Dysbiosis-associated reduction in these metabolites therefore contributes to metabolic dysfunction. Metformin exerts part of its therapeutic effect through modulation of gut microbiota composition by increasing the abundance of beneficial bacteria such as *Akkermansia muciniphila* and other SCFA-producing microorganisms. These microbial alterations improve insulin sensitivity, intestinal barrier integrity, and glucose metabolism.[64]

Recent studies have demonstrated growing interest in microbiome-targeted interventions for metabolic disorders.[65] Alterations in microbial metabolites, bile acid signaling, and inflammatory pathways are increasingly recognized as central mechanisms in diabetes pathogenesis and treatment response.

Cardiovascular Disease

The gut microbiota also plays an important role in cardiovascular disease through microbial metabolism of dietary nutrients.[60,61] Gut microorganisms metabolize dietary choline and carnitine into trimethylamine (TMA), which is subsequently converted in the liver into

trimethylamine-N-oxide (TMAO), a metabolite strongly associated with cardiovascular pathology.

TMAO promotes atherosclerosis through multiple mechanisms including endothelial dysfunction, vascular inflammation, foam cell formation, platelet activation, and thrombosis. Elevated circulating TMAO levels have been associated with increased risk of myocardial infarction, stroke, heart failure, and adverse cardiovascular outcomes.

A 2024 study published in Diabetology & Metabolic Syndrome demonstrated strong associations between circulating TMAO levels, gut microbiota alterations, and cardiometabolic disease risk.[66] Another 2024 study published in Scientific Reports reported that elevated TMAO concentrations were associated with increased 5-year mortality and cardiovascular risk.[67]

Similarly, a 2024 study published in BMC Cardiovascular Disorders demonstrated correlation between circulating TMAO levels and coronary atherosclerotic burden in newly diagnosed coronary heart disease.[68] These studies further support the important role of gut microbial metabolites in cardiovascular disease pathogenesis.

Neurological and Neuropsychiatric Disorders

Dysbiosis-associated alterations in the gut–brain axis have additionally been implicated in depression, anxiety, autism spectrum disorder, Parkinson's disease, and Alzheimer's disease.[69,70] Bidirectional communication between the gastrointestinal tract and central nervous system occurs through neural, endocrine, immune, and metabolic pathways. Gut microorganisms influence synthesis of neurotransmitters including serotonin, dopamine, gamma-aminobutyric acid (GABA), and norepinephrine, thereby affecting mood, cognition, and neurological function.

Dysbiosis contributes to neuroinflammation through increased intestinal permeability, systemic endotoxemia, and activation of inflammatory cytokines that can affect the blood–brain barrier and neuronal signaling pathways. Altered microbial metabolites and immune signaling additionally influence microglial activation and neurodegenerative processes.

In **Parkinson's disease**, gut dysbiosis has been associated with abnormal α-synuclein aggregation, altered intestinal permeability, and chronic neuroinflammation. Certain intestinal microorganisms additionally metabolize levodopa before systemic absorption, thereby reducing its therapeutic availability and influencing treatment response. In Alzheimer's disease, dysbiosis-associated neuroinflammation and oxidative stress may contribute to neuronal degeneration and cognitive decline.

Recent advances in microbiome research have therefore highlighted the gut microbiota as an important therapeutic target in neurological and neuropsychiatric disorders. Emerging microbiome-based therapies including probiotics, prebiotics, fecal microbiota transplantation, and engineered microbial therapeutics are currently being investigated for modulation of gut–brain signaling and neuroinflammation.

Microbiome-Based Therapeutics

Probiotics are live microorganisms that provide health benefits when administered in adequate amounts.[71,72] Common probiotic organisms include *Lactobacillus*, *Bifidobacterium*, and *Saccharomyces boulardii*. These microorganisms exert several pharmacological benefits, including restoration of microbial diversity, enhancement of epithelial barrier integrity, suppression of pathogenic organisms, and reduction of intestinal inflammation. Through modulation of the gut microbiota and immune responses, probiotics contribute to the maintenance of intestinal homeostasis and improvement of gastrointestinal health.

Prebiotics are non-digestible dietary components that selectively stimulate the growth and activity of beneficial bacteria, whereas synbiotics are combinations of probiotics and prebiotics.[73,74] These therapeutic approaches improve short-chain fatty acid (SCFA) production, immune regulation, glucose metabolism, and gastrointestinal function. By promoting the growth of beneficial microorganisms and enhancing microbial metabolic activity, prebiotics and synbiotics help restore microbial balance and reduce dysbiosis-associated complications.

Postbiotics

In the early twentieth century, pioneering studies by Dr. Pierre Boucard and colleagues demonstrated the therapeutic potential of heat-treated fecal *Lactobacillus* in relieving digestive disorders, leading to one of the earliest commercial postbiotic products containing heat-inactivated lactic acid bacteria (LAB) and bacterial supernatants.[75] Postbiotics are bioactive compounds derived from microbial cells, including soluble cellular components and metabolites, that provide health and therapeutic benefits.[72,73] Due to safety concerns associated with live microorganisms, species outside traditionally safe groups such as *Bifidobacterium* and the *Lactobacillaceae* family are also being explored as potential sources of postbiotics.[47] Owing to their antimicrobial, anti-inflammatory, immunomodulatory, and antioxidant properties, postbiotics are increasingly recognized as promising biotherapeutic agents for various diseases.[48,49] Microbial-derived substances such as lactic acid, biosurfactants, bacteriocins, and short-chain fatty acids (SCFAs) are now incorporated into pharmaceutical and healthcare products including toothpaste, mouthwashes, creams, serums, and personal care formulations.[48] Several in vitro, in vivo, and clinical studies have demonstrated their therapeutic

potential, particularly in cancer and inflammatory disorders, highlighting postbiotics as safe and stable alternatives to live probiotics.[49,50]

Recent advances in microbiome therapeutics have led to the development of next-generation probiotics, including *Akkermansia muciniphila*, *Faecalibacterium prausnitzii*, and *Roseburia* species.[51] These organisms possess targeted anti-inflammatory and metabolic effects and are being investigated for their potential role in the management of metabolic, inflammatory, and gastrointestinal disorders. Unlike conventional probiotics, next-generation probiotics are selected based on specific mechanistic and therapeutic properties.

Engineered live biotherapeutics developed using synthetic biology approaches represent another emerging area of microbiome pharmacology.[52,84,85] These engineered microbial therapeutics can deliver therapeutic molecules, degrade toxic metabolites, modulate immune signaling pathways, and target disease-specific mechanisms. Such approaches offer the potential for highly targeted and personalized treatment strategies in various chronic and metabolic diseases.

Faecal Microbiota Transplantation and Approved Microbiome Therapeutics

Faecal microbiota transplantation (FMT) has emerged as one of the most important and effective microbiome-based therapeutic approaches in modern medicine. FMT involves the transfer of processed stool obtained from healthy donors into recipients with the aim of restoring microbial diversity, intestinal homeostasis, and normal host–microbiome interactions.[35,36,68] The therapeutic rationale of FMT is based on the concept that restoration of a healthy microbial ecosystem can reverse dysbiosis-associated pathological processes and re-establish colonization resistance against pathogenic organisms.

FMT exerts its therapeutic effects through multiple mechanisms, including restoration of microbial diversity, suppression of pathogenic microorganisms, normalization of bile acid metabolism, restoration of colonization resistance, enhancement of short-chain fatty acid production, and modulation of mucosal and systemic immune responses. Restoration of beneficial commensal bacteria helps improve epithelial barrier integrity, reduce intestinal permeability, suppress inflammatory signaling, and regulate host immune homeostasis.[76]

The most well-established indication for FMT is recurrent *Clostridioides difficile* infection, where antibiotic-associated dysbiosis disrupts colonization resistance and permits overgrowth of toxigenic *C. difficile* strains. Conventional antibiotic therapy often fails to restore normal microbial diversity, resulting in recurrent infection. FMT has demonstrated remarkable clinical efficacy in such patients, with cure rates exceeding 80–90%, making it one of the most successful microbiome-based therapies currently available.[77,78]

Recent studies continue to support the efficacy of FMT in recurrent *Clostridioides difficile* infection. A 2024 review published in The Lancet Gastroenterology & Hepatology emphasized that FMT remains the most effective therapy for recurrent *Clostridioides difficile* infection and highlighted its role in restoration of microbial diversity and bile acid metabolism. Additional studies have demonstrated that successful FMT is associated with re-establishment of Firmicutes and Bacteroidetes populations along with reduction of pathogenic *Proteobacteria* species.[79]

Beyond recurrent *Clostridioides difficile* infection, FMT is increasingly being investigated in several gastrointestinal and systemic disorders associated with dysbiosis. In ulcerative colitis, FMT has shown promising effects in reducing intestinal inflammation, improving mucosal healing, and inducing clinical remission through restoration of anti-inflammatory microbial populations and enhancement of short-chain fatty acid production. Recent randomized controlled trials have demonstrated improved remission rates in ulcerative colitis patients receiving multidonor intensive FMT compared with standard therapy alone.[80]

FMT has additionally been investigated in irritable bowel syndrome, where dysbiosis-associated alterations in microbial metabolites and gut–brain signaling contribute to disease pathogenesis. Some studies have reported improvement in abdominal pain, bloating, and bowel symptoms following microbiome restoration through FMT, although therapeutic responses remain variable.[81,82]

Increasing evidence also suggests a significant role of FMT in metabolic disorders such as obesity and type 2 diabetes mellitus. Dysbiosis-associated alterations in glucose metabolism, bile acid signaling, and inflammatory pathways contribute to metabolic dysfunction. Recent studies have shown that transplantation of microbiota from metabolically healthy donors may improve insulin sensitivity and metabolic regulation in selected patients.[83,84]

FMT is also being explored in neurological and neuropsychiatric disorders involving the gut–brain axis, including autism spectrum disorder, Parkinson's disease, Alzheimer's disease, and hepatic encephalopathy.[85,86] Dysbiosis-associated neuroinflammation, altered neurotransmitter production, and impaired gut barrier integrity are believed to contribute to disease progression. Recent pilot studies have demonstrated improvement in gastrointestinal symptoms and behavioral outcomes in autism spectrum disorder following FMT. Similarly, experimental studies in Parkinson's disease have suggested that restoration of

microbial balance may reduce neuroinflammation and improve motor symptoms.[87]

Another rapidly expanding area of research involves the role of FMT in cancer immunotherapy. Recent studies have demonstrated that gut microbiota composition significantly influences responsiveness to immune checkpoint inhibitors such as PD-1 inhibitors. Patients with favorable microbial profiles, particularly increased abundance of *Akkermansia muciniphila*, *Bifidobacterium*, and Firmicutes species, demonstrate improved antitumor immunity and better therapeutic outcomes.[88] Emerging evidence suggests that FMT obtained from immunotherapy responders may enhance responsiveness in non-responders through modulation of immune signaling pathways and enhancement of cytotoxic T-cell activity.[89]

Recent advances in microbiome pharmacology have additionally led to development of standardized microbiota-based therapeutics. Rebyota (RBX2660) became the first FDA-approved microbiota-based therapeutic for prevention of recurrent *Clostridioides difficile* infection.[90] Rebyota contains a standardized fecal microbiota suspension prepared from screened healthy donors and administered rectally. Approval of Rebyota represented a major milestone in microbiome-directed therapy because it established the microbiome itself as a therapeutic modality in clinical medicine.

Similarly, Vowst (SER-109) became the first orally administered FDA-approved microbiome therapeutic. Vowst consists of purified Firmicutes bacterial spores formulated into oral capsules designed to restore microbial diversity and colonization resistance in recurrent *Clostridioides difficile* infection.[91] The oral route offers significant advantages including non-invasive administration, improved patient compliance, outpatient accessibility, and reduced procedural risk compared with conventional fecal transplantation procedures.

A 2024 review published in Nature Reviews Gastroenterology & Hepatology highlighted that approved microbiome therapeutics such as Rebyota and Vowst represent the beginning of a new era in microbiome pharmacology and may pave the way for disease-specific microbial therapeutics in the future.[92]

Capsule-based fecal microbiota transplantation (cFMT) is an emerging and less invasive form of fecal microbiota transplantation (FMT) used to restore healthy gut microbiota and treat dysbiosis-related diseases. Unlike conventional FMT procedures, cFMT uses oral capsules, making administration easier, more convenient, and more acceptable to patients while also improving storage and handling. Studies have shown that cFMT is highly effective in conditions such as *Clostridioides difficile* infection (CDI), inflammatory bowel disease (IBD), multidrug-resistant infections, and small intestinal bacterial overgrowth (SIBO), where it helps restore microbial balance and improve symptoms.[93] However, its effectiveness in irritable bowel syndrome (IBS) and functional constipation (FC) remains inconsistent despite improvements in gut microbial diversity. Recent research also suggests possible benefits of cFMT in metabolic disorders such as obesity and hypertension, neuropsychiatric disorders including depression and autism through the gut–brain axis, as well as chronic kidney disease and hepatic encephalopathy.[94] Despite its promising therapeutic potential, several challenges remain, including donor variability, lack of standardization, and temporary adverse effects, which limit its widespread clinical use. Future developments such as targeted colon-release capsules, synthetic microbial formulations, and advanced microbial delivery systems may improve its precision, safety, and scalability. Recently, the United States Food and Drug Administration (FDA) approved Vowst, the world's first oral microbiome therapy, marking an important step in the transition of FMT-based therapies from experimental research to standardized clinical practice.[95]

Future Perspectives

Future developments in microbiome pharmacology are expected to revolutionize personalized medicine and targeted therapeutics.[96] Increasing understanding of host–microbiome interactions, microbial metabolic pathways, immune modulation, and pharmacomicrobiomics is likely to facilitate development of individualized therapeutic strategies based on microbial composition and metabolic profiling.

One of the most promising future directions is personalized microbiome medicine, where therapeutic interventions may be tailored according to an individual's microbiome composition, metabolic activity, genetic profile, and disease characteristics. Advances in metagenomics and metabolomics are increasingly enabling identification of disease-specific microbial signatures and therapeutic biomarkers.[97]

Artificial intelligence (AI)-guided microbiome profiling is also expected to play a major role in future precision medicine. AI-based algorithms can analyze large-scale microbiome datasets to predict disease risk, therapeutic response, drug toxicity, and individualized treatment strategies. Such approaches may improve early disease detection and optimize microbiome-targeted therapies.[98]

Engineered live biotherapeutics developed using synthetic biology approaches represent another rapidly evolving area. These programmable microorganisms can be genetically modified to produce therapeutic compounds, degrade toxic metabolites, modulate inflammatory signaling pathways, and target disease-specific molecular mechanisms. Future engineered microbial systems may function as "living drugs" capable of sensing disease-associated signals and

releasing therapeutic molecules in a highly targeted manner.[99]

Bacteriophage therapy is also gaining increasing attention as a precision antimicrobial strategy. Unlike broad-spectrum antibiotics, bacteriophages selectively target pathogenic bacteria while preserving beneficial commensal microorganisms, thereby reducing risk of dysbiosis and antimicrobial resistance.

Future microbiome-guided pharmacotherapy may additionally involve targeted microbial enzyme inhibitors designed to block harmful microbial metabolites such as trimethylamine-N-oxide (TMAO) associated with cardiovascular disease or microbial β-glucuronidases involved in irinotecan toxicity. Such strategies may improve drug efficacy while reducing adverse effects.

Recent studies published in Nature Biotechnology[100] and Cell Host & Microbe[101] have emphasized the transformative role of synthetic biology, microbiome engineering, and AI-guided microbial therapeutics in future precision medicine.

CONCLUSION

The gut microbiota plays a crucial role in maintaining metabolic, immunological, and neurological homeostasis, while dysbiosis contributes significantly to the development of gastrointestinal, metabolic, cardiovascular, inflammatory, and neuropsychiatric disorders. Increasing evidence from pharmacomicrobiomics has demonstrated that gut microorganisms influence drug metabolism, therapeutic efficacy, toxicity, and host response, thereby highlighting the microbiome as an important target in personalized medicine. Recent advances in microbiome-based therapeutics, including probiotics, prebiotics, postbiotics, engineered live biotherapeutics, and fecal microbiota transplantation (FMT), have shown promising therapeutic potential in disorders associated with dysbiosis. The approval of microbiome therapeutics such as Rebyota and Vowst further represents a major advancement in clinical microbiome pharmacology. Future developments involving metagenomics, synthetic biology, bacteriophage therapy, and artificial intelligence-guided microbiome profiling are expected to revolutionize precision medicine and targeted therapeutics. However, further research is required to address challenges related to safety, standardization, regulatory approval, and long-term clinical efficacy before microbiome-directed therapies can be fully integrated into routine clinical practice.

REFERENCES

1. Qin J, Li R, Raes J, et al. A human gut microbial gene catalogue established by metagenomic sequencing. *Nature*, 2010; 464(7285): 59-65.
2. Human Microbiome Project Consortium. Structure, function and diversity of the healthy human microbiome. *Nature*, 2012; 486(7402): 207-214.
3. Turnbaugh PJ, Ley RE, Hamady M, et al. The human microbiome project. *Nature*, 2007; 449(7164): 804-810.
4. Lynch SV, Pedersen O. The human intestinal microbiome in health and disease. *N Engl J Med*, 2016; 375(24): 2369-2379.
5. Clemente JC, Ursell LK, Parfrey LW, Knight R. The impact of the gut microbiota on human health. *Cell*, 2012; 148(6): 1258-1270.
6. Sekirov I, Russell SL, Antunes LC, Finlay BB. Gut microbiota in health and disease. *Physiol Rev*, 2010; 90(3): 859-904.
7. Arumugam M, Raes J, Pelletier E, et al. Enterotypes of the human gut microbiome. *Nature*, 2011; 473(7346): 174-180.
8. Rinninella E, Raoul P, Cintoni M, et al. What is the healthy gut microbiota composition? *Eur Rev Med Pharmacol Sci*, 2019; 23(1): 404-416.
9. Gilbert JA, Blaser MJ, Caporaso JG, et al. Current understanding of the human microbiome. *Nat Med*, 2018; 24(4): 392-400.
10. Sommer F, Bäckhed F. The gut microbiota—masters of host development and physiology. *Nat Rev Microbiol*, 2013; 11(4): 227-238.
11. Thursby E, Juge N. Introduction to the human gut microbiota. *Biochem J*, 2017; 474(11): 1823-1836.
12. Koh A, De Vadder F, Kovatcheva-Datchary P, Bäckhed F. From dietary fiber to host physiology: short-chain fatty acids as key bacterial metabolites. *Cell*, 2016; 165(6): 1332-1345.
13. Louis P, Flint HJ. Formation of propionate and butyrate by the human colonic microbiota. *Environ Microbiol*, 2017; 19(1): 29-41.
14. Valdes AM, Walter J, Segal E, Spector TD. Role of the gut microbiota in nutrition and health. *BMJ*, 2018; 361: k2179.
15. Cryan JF, O'Riordan KJ, Cowan CSM, et al. The microbiota-gut-brain axis. *Physiol Rev*, 2019; 99(4): 1877-2013.
16. Carding S, Verbeke K, Vipond DT, et al. Dysbiosis of the gut microbiota in disease. *Microb Ecol Health Dis*, 2015; 26: 26191.
17. DeGruttola AK, Low D, Mizoguchi A, Mizoguchi E. Current understanding of dysbiosis in disease in human and animal models. *Inflamm Bowel Dis*, 2016; 22(5): 1137-1150.
18. Tamboli CP, Neut C, Desreumaux P, Colombel JF. Dysbiosis in inflammatory bowel disease. *Gut*, 2004; 53(1): 1-4.
19. David LA, Maurice CF, Carmody RN, et al. Diet rapidly and reproducibly alters the human gut microbiome. *Nature*, 2014; 505(7484): 559-563.
20. Blaser MJ. Antibiotic use and its consequences for the normal microbiome. *Science*, 2016; 352(6285): 544-545.
21. Buffie CG, Pamer EG. Microbiota-mediated colonization resistance against intestinal pathogens. *Nat Rev Immunol*, 2013; 13(11): 790-801.

22. Kostic AD, Xavier RJ, Gevers D. The microbiome in inflammatory bowel disease. *Gastroenterology*, 2014; 146(6): 1489-1499.
23. Tilg H, Kaser A. Gut microbiome, obesity, and metabolic dysfunction. *J Clin Invest*, 2011; 121(6): 2126-2132.
24. Qin J, Li Y, Cai Z, et al. A metagenome-wide association study of gut microbiota in type 2 diabetes. *Nature*, 2012; 490(7418): 55-60.
25. Garrett WS. Cancer and the microbiota. *Science*, 2015; 348(6230): 80-86.
26. Cani PD, Amar J, Iglesias MA, et al. Metabolic endotoxemia initiates obesity and insulin resistance. *Diabetes*, 2007; 56(7): 1761-1772.
27. Levy M, Kolodziejczyk AA, Thaiss CA, Elinav E. Dysbiosis and the immune system. *Nat Rev Immunol*, 2017; 17(4): 219-232.
28. Kamada N, Seo SU, Chen GY, Núñez G. Role of the gut microbiota in immunity and inflammatory disease. *Nat Rev Immunol*, 2013; 13(5): 321-335.
29. Hamer HM, Jonkers D, Venema K, et al. Review article: the role of butyrate. *Aliment Pharmacol Ther*, 2008; 27(2): 104-119.
30. den Besten G, van Eunen K, Groen AK, et al. The role of short-chain fatty acids in host metabolism. *J Lipid Res*, 2013; 54(9): 2325-2340.
31. Peterson LW, Artis D. Intestinal epithelial cells: regulators of barrier function and immune homeostasis. *Nat Rev Immunol*, 2014; 14(3): 141-153.
32. Fasano A. Zonulin and its regulation of intestinal barrier function. *Physiol Rev*, 2011; 91(1): 151-175.
33. Frank DN, St Amand AL, Feldman RA, et al. Molecular-phylogenetic characterization of microbial community imbalances in human inflammatory bowel diseases. *Proc Natl Acad Sci USA*, 2007; 104(34): 13780-13785.
34. Ford AC, Lacy BE, Talley NJ. Irritable bowel syndrome. *N Engl J Med*, 2017; 376(26): 2566-2578.
35. van Nood E, Vrieze A, Nieuwdorp M, et al. Duodenal infusion of donor feces for recurrent *Clostridium difficile*. *N Engl J Med*, 2013; 368(5): 407-415.
36. Kelly CR, Khoruts A, Staley C, et al. Effect of fecal microbiota transplantation on recurrence in multiply recurrent *Clostridium difficile* infection. *Ann Intern Med*, 2016; 165(9): 609-616.
37. Ley RE, Turnbaugh PJ, Klein S, Gordon JI. Human gut microbes associated with obesity. *Nature*, 2006; 444(7122): 1022-1023
38. Tremaroli V, Bäckhed F. Functional interactions between the gut microbiota and host metabolism. *Nature*, 2012; 489(7415): 242-249.
39. Wang Z, Klipfell E, Bennett BJ, et al. Gut flora metabolism of phosphatidylcholine promotes cardiovascular disease. *Nature*, 2011; 472(7341): 57-63.
40. Sharon G, Sampson TR, Geschwind DH, Mazmanian SK. The central nervous system and the gut microbiome. *Cell*, 2016; 167(4): 915-932.
41. Hill C, Guarner F, Reid G, et al. Expert consensus document on probiotics. *Nat Rev Gastroenterol Hepatol*, 2014; 11(8): 506-514.
42. Gibson GR, Hutkins R, Sanders ME, et al. ISAPP consensus statement on prebiotics. *Nat Rev Gastroenterol Hepatol*, 2017; 14(8): 491-502.
43. Swanson KS, Gibson GR, Hutkins R, et al. ISAPP consensus statement on synbiotics. *Nat Rev Gastroenterol Hepatol*, 2020; 17(11): 687-701.
44. Sanders ME, Merenstein DJ, Reid G, et al. Probiotics and prebiotics in intestinal health and disease. *Nat Rev Gastroenterol Hepatol*, 2019; 16(10): 605-616.
45. Markowiak P, Śliżewska K. Effects of probiotics, prebiotics, and synbiotics on human health. *Nutrients*, 2017; 9(9): 1021.
46. Salminen S, Collado MC, Endo A, et al. The International Scientific Association of Probiotics and Prebiotics (ISAPP) consensus statement on the definition and scope of postbiotics. *Nat Rev Gastroenterol Hepatol*, 2021; 18(9): 649–667.
47. Aguilar-Toalá JE, Garcia-Varela R, Garcia HS, et al. Postbiotics: An evolving term within the functional foods field. *Trends Food Sci Technol*, 2018; 75: 105–114.
48. Żółkiewicz J, Marzec A, Ruszczyński M, Feleszko W. Postbiotics—A step beyond pre- and probiotics. *Nutrients*, 2020; 12(8): 2189.
49. Rad AH, Aghebati-Maleki L, Kafil HS, Abbasi A. Postbiotics as novel health-promoting ingredients in functional foods. *Health Promot Perspect*, 2020; 10(1): 3–4.
50. Wegh CAM, Geerlings SY, Knol J, Roeselers G, Belzer C. Postbiotics and their potential applications in early life nutrition and beyond. *Nutrients*, 2019; 11(10): 2189
51. Depommier C, Everard A, Druart C, et al. Supplementation with *Akkermansia muciniphila* in overweight and obese human volunteers. *Nat Med*, 2019; 25(7): 1096-1103.
52. Charbonneau MR, Isabella VM, Li N, Kurtz CB. Developing engineered live bacterial therapeutics. *Nat Chem Biol*, 2020; 16(9): 925-933.
53. Davar D, Dzutsev AK, McCulloch JA, et al. Fecal microbiota transplant overcomes resistance to anti-PD-1 therapy in melanoma patients. *Science*, 2021; 371(6529): 595-602.
54. Zimmermann M, Zimmermann-Kogadeeva M, Wegmann R, Goodman AL. Mapping human microbiome drug metabolism. *Nat Rev Microbiol*, 2019; 17(11): 653-664.
55. Spanogiannopoulos P, Bess EN, Carmody RN, Turnbaugh PJ. The microbial pharmacists within us. *Nat Rev Microbiol*, 2016; 14(5): 273-287.
56. Wilson ID, Nicholson JK. Gut microbiome interactions with drug metabolism. *Toxicol Pathol*, 2017; 45(1): 109-117.

57. Li H, He J, Jia W. The influence of gut microbiota on drug metabolism and toxicity. *Expert Opin Drug Metab Toxicol*, 2016; 12(1): 31-40.
58. Enright EF, Gahan CGM, Joyce SA, Griffin BT. The impact of the gut microbiota on drug metabolism and clinical outcome. *Ther Adv Gastroenterol*, 2016; 9(5): 659-673.
59. Wallace BD, Wang H, Lane KT, et al. Alleviating cancer drug toxicity by inhibiting bacterial β-glucuronidase. *Science*, 2010; 330(6005): 831-835.
60. Routy B, Le Chatelier E, Derosa L, et al. Gut microbiome influences efficacy of PD-1–based immunotherapy. *Science*, 2018; 359(6371): 91-97.
61. Vich Vila A, Imhann F, Collij V, et al. Gut microbiota composition and functional changes in inflammatory bowel disease and irritable bowel syndrome. *Sci Transl Med*, 2018; 10(472): eaap8914.
62. Sartor RB. Microbial influences in inflammatory bowel diseases. *Gastroenterology*, 2008; 134(2): 577-594.
63. Sokol H, Pigneur B, Watterlot L, et al. *Faecalibacterium prausnitzii* is an anti-inflammatory commensal bacterium identified by gut microbiota analysis of Crohn disease patients. *Proc Natl Acad Sci USA*, 2008; 105(43): 16731-16736.
64. Neurath MF. Cytokines in inflammatory bowel disease. *Nat Rev Immunol*, 2014; 14(5): 329-342.
65. Simrén M, Barbara G, Flint HJ, et al. Intestinal microbiota in functional bowel disorders. *Gut*, 2013; 62(1): 159-176.
66. Pimentel M, Saad RJ, Long MD, Rao SSC. ACG clinical guideline: small intestinal bacterial overgrowth. *Am J Gastroenterol*, 2020; 115(2): 165-178.
67. Spiller R, Garsed K. Postinfectious irritable bowel syndrome. *Gastroenterology*, 2009; 136(6): 1979-1988.
68. Cammarota G, Ianiro G, Tilg H, et al. European consensus conference on faecal microbiota transplantation in clinical practice. *Gut*, 2017; 66(4): 569-580.
69. Paramsothy S, Kamm MA, Kaakoush NO, et al. Multidonor intensive faecal microbiota transplantation for active ulcerative colitis. *Lancet*, 2017; 389(10075): 1218-1228.
70. Costello SP, Hughes PA, Waters O, et al. Effect of fecal microbiota transplantation on remission in ulcerative colitis. *JAMA*, 2019; 321(2): 156-164.
71. El-Salhy M, Hatlebakk JG, Gilja OH, et al. Efficacy of faecal microbiota transplantation for irritable bowel syndrome. *Gut*, 2020; 69(5): 859-867.
72. Bajaj JS, Kassam Z, Fagan A, et al. Fecal microbiota transplant improves hepatic encephalopathy. *Hepatology*, 2017; 66(6): 1727-1738.
73. Musso G, Gambino R, Cassader M. Obesity, diabetes, and gut microbiota. *Diabetes Care*, 2010; 33(10): 2277-2284.
74. Karlsson FH, Tremaroli V, Nookaew I, et al. Gut metagenome in women with diabetic glucose control abnormalities. *Nature*, 2013; 498(7452): 99-103.
75. Larsen N, Vogensen FK, van den Berg FWJ, et al. Gut microbiota in adults with type 2 diabetes differs from controls. *PLoS One*, 2010; 5(2): e9085.
76. Brown JM, Hazen SL. Microbial modulation of cardiovascular disease. *Nat Rev Microbiol*, 2018; 16(3): 171-181.
77. Koeth RA, Wang Z, Levison BS, et al. Intestinal microbiota metabolism of L-carnitine promotes atherosclerosis. *Nat Med*, 2013; 19(5): 576-585.
78. Jie Z, Xia H, Zhong SL, et al. The gut microbiome in atherosclerotic cardiovascular disease. *Nat Commun*, 2017; 8: 845.
79. Silva YP, Bernardi A, Frozza RL. The role of short-chain fatty acids in gut-brain communication. *Metab Brain Dis*, 2020; 35(2): 219-236.
80. Dinan TG, Cryan JF. Gut instincts: microbiota as a regulator of brain development and neurodegeneration. *J Physiol*, 2017; 595(2): 489-503.
81. Allegretti JR, Mullish BH, Kelly C, Fischer M. Evolution of fecal microbiota transplantation and emerging therapeutic indications. *Lancet*, 2019; 394(10196): 420-431.
82. Khanna S, Kraft CS. The microbiome and *Clostridioides difficile* infection. *Nat Rev Gastroenterol Hepatol*, 2021; 18(10): 713-722.
83. Ooijevaar RE, Terveer EM, Verspaget HW, et al. Clinical application and potential of fecal microbiota transplantation. *Annu Rev Med*, 2019; 70: 335-351.
84. Mimee M, Tucker AC, Voigt CA, Lu TK. Programming a human commensal bacterium for diagnostic and therapeutic functions. *Cell Syst*, 2015; 1(1): 62-71.
85. Isabella VM, Ha BN, Castillo MJ, et al. Synthetic live bacterial therapeutic for phenylketonuria. *Nat Biotechnol*, 2018; 36(9): 857-864.
86. Huttenhower C, Gevers D, Knight R, et al. Advancing the microbiome research community. *Cell*, 2014; 159(2): 227-230.
87. Gilbert JA, Quinn RA, Debelius J, et al. Microbiome-wide association studies link microbial consortia to disease. *Nature*, 2016; 535(7610): 94-103.
88. Weersma RK, Zhernakova A, Fu J. Interaction between drugs and the gut microbiome. *Gut*, 2020; 69(8): 1510-1519.
89. Peterson DA, Frank DN, Pace NR, Gordon JI. Metagenomic approaches for inflammatory bowel diseases. *Cell Host Microbe*, 2008; 3(6): 417-427.
90. Honda K, Littman DR. The microbiota in adaptive immune homeostasis and disease. *Nature*, 2016; 535(7610): 75-84.
91. Brestoff JR, Artis D. Commensal bacteria at the interface of metabolism and immunity. *Nat Immunol*, 2013; 14(7): 676-684.

92. Garrett WS, Gordon JI, Glimcher LH. Homeostasis and inflammation in the intestine. *Cell*, *2*010; 140(6): 859-870.
93. Arthur JC, Perez-Chanona E, Mühlbauer M, et al. Intestinal inflammation targets cancer-inducing microbiota activity. *Science*, *2*012; 338(6103): 120-123.
94. Wang T, Cai G, Qiu Y, et al. Structural segregation of gut microbiota between colorectal cancer patients and healthy volunteers. *ISME J*, *2*012; 6(2): 320-329.
95. Gopalakrishnan V, Spencer CN, Nezi L, et al. Gut microbiome modulates response to anti-PD-1 immunotherapy. *Science*, *2*018; 359(6371): 97-103.
96. Turnbaugh PJ, Hamady M, Yatsunenko T, et al. A core gut microbiome in obese and lean twins. *Nature*, *2*009; 457(7228): 480-484.
97. Sonnenburg ED, Sonnenburg JL. Starving our microbial self. *Cell Metab*, *2*014; 20(5): 779-786.
98. Francino MP. Antibiotics and the human gut microbiome. *Front Microbiol*, *2*016; 6: 1543.
99. Jernberg C, Löfmark S, Edlund C, Jansson JK. Long-term impacts of antibiotics on intestinal microbiota. *ISME J*, *2*007; 1(1): 56-66.
100. Belkaid Y, Hand TW. Role of microbiota in immunity and inflammation. *Cell*, *2*014; 157(1): 121-141.
101. Nicholson JK, Holmes E, Kinross J, et al. Host-gut microbiota metabolic interactions. *Science*, *2*012; 336(6086): 1262-1267.