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# The Role of the Human Microbiome from Symbiosis to Dysbiosis

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# دَوْرُ الميكروبيوم البَشَرِيّ مِنَ التَّعَاشُرِ إِلَى الاخْتِلَالِ

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## ABSTRACT

**Background:** The Human microbiome is a complex symbiotic ecosystem, which is crucial to human health, and which plays vital roles in metabolism and immunity. Its disturbance, which is called dysbiosis, is progressively involved in a variety of chronic diseases.
**Objective:** This review synthesizes evidence on the microbiome's dual role in health and disease, examining the mechanisms of homeostasis maintenance by a balanced microbiota and the contribution of dysbiosis to several disorders.
**Methods:** A scientific literature narrative review was carried out, which incorporated results of human cohort studies, animal models, and mechanistic in vitro research to explain the most important microbial functions, host-microbe interactions, and inter-organ communication pathways.
**Results:** Commensal microbes play an important role in the production of metabolites, training of the immune system, and colonization resistance. Diversity loss, pathobiont growth, and metabolite shift are caused by dysbiosis as a result of antibiotics and diet. This disturbance is associated with disorders such as IBD, diabetes, and neurodegenerative diseases. Microbial metabolites and components are two sided swords, mediating their systemic effects via gut-brain, gut-lung and gut-skin axes through immune, neural and metabolic pathways.
**Conclusion:** Microbial harmony is essential in health, and its imbalance is the cause of chronic illness, so the microbiome is an ideal candidate of new diagnostics, therapeutics, and personal approaches to its recovery.

**Keywords: Microbiome, Gut–immune axis, Dysbiosis, Secretory IgA, Regulatory T cells**



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## INTRODUCTION

Microbial communities are intricate human-body-wide populations of microbes known as the microbiome in nearly all natural habitats, such as the gut, skin, mouth, lungs, and the urogenital tract [1]. These communities include bacteria, archaea, viruses, fungi and phages with bacteria being the most common and functionally important [2]. Although traditionally considered to be passive participants, commensal microorganisms play a role in host physiology, immunity and metabolism [3]. Nevertheless, in some circumstances, the same organisms may be a source of or directly cause a disease duality which is the conceptualization of their role in human health and pathology. The Microbiome is not a fixed community of microbes but a very dynamic and active ecosystem encompassing host genetics, environmental exposures, diet, age, and lifestyle [4]. Microbial colonization commences in utero at the earliest stages of life and during birth and infancy, colonization is highly determined by maternal microbiota, mode of delivery, type of feeding, and exposure to antibiotics. Within the initial two years of life, the microbiome evolves into a site-specific, functionally steady community that is very important in immune responses development, metabolic programming and barrier integrity [5]. Some of the mechanisms through which communication takes place in this ecosystem include quorum sensing which facilitates intra-species and interspecies coordination that aids in biofilm formation, nutrient sharing, and collective defense. One of the characteristics of a healthy microbiome is that it is resilient and can control homeostasis, but perturbations known as dysbiosis may cause this to break down resulting in pathology [6]. Dysbiosis can be either in the form of changes in the relative abundance of major phyla (especially Firmicutes and Bacteroidetes of the gut), loss of keystone species, or excessive growth of opportunistic pathogens [7]. Significantly, the microbiome cannot work alone: there is emerging evidence to suggest that there exist inter-organ communication axes in which microbial metabolites, immune signals and neural pathways can connect far apart sites [8]. As an illustration, short-chain fatty acids produced by the gut regulate lung immunity, whereas bacterial bile acid synthesis has an impact on systemic inflammation and neural activity. Microbiome dysbiosis has been linked to such a wide range of diseases as inflammatory bowel disease, type 2 diabetes, psoriasis, asthma, Parkinson's disease, and even Alzheimer, which highlights the systemic effect of microbiome dysbiosis. In this way, the human microbiome is not just a localized symbiont but a regulatory system in its entirety, with a dynamic equilibrium that is fundamental to health and the failure of which is becoming a key determinant of the pathogenesis of chronic and inflammatory diseases [9].

### Beneficial Roles of the Commensal Microbiota

Commensal microbiota is crucial to human health by their roles in digestion, immune system development, metabolic regulation and colonization resistance to pathogens [10]. In the gut, resident bacteria such as Bifidobacterium and Bacteroides species metabolize complex dietary substrates including human milk oligosaccharides in infants and plant-derived polysaccharides like xyloglucans in adults producing essential nutrients and bioactive metabolites that the host cannot generate independently [11]. A major class of these metabolites, short-chain fatty acids (SCFAs) such as butyrate, propionate, and acetate, are derived from microbial fermentation of dietary fiber and serve as energy sources for colonocytes, modulators of immune function, and regulators of systemic inflammation [12]. Commensal microbes also actively shape the development and function of the host immune system: for instance, specific clusters of Clostridioides species induce colonic regulatory T cells (Tregs) that express the transcription factor RORγ+, thereby promoting

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immune tolerance and preventing inappropriate inflammatory responses [13]. Moreover, the gut microbiota participates in the biotransformation of host-derived compounds, notably bile acids; by deconjugating primary bile acids via bile salt hydrolases, commensal bacteria enable the formation of secondary bile acids that act as signaling molecules influencing host metabolism, glucose homeostasis, and antimicrobial defense. In other niches, such as the oral cavity Streptococcus mitis and the skin Staphylococcus epidermidis, commensals occupying a certain niche provide stability to the ecosystem by interacting with other species, which includes communicating to build protective biofilms and preventing the overgrowth of pathogens by competition or antimicrobial product production [14]. All of these roles highlighted by the commensal microbiota are not those of inert observers but, on the contrary, active participants in the maintenance of physiological homeostasis, and their advantageous functions are a vital basis of host resistance to disease.

## Nutrient Metabolism and Digestion

The commensal gut microbiota has a central and essential role in nutrient metabolism and digestion as it increases the biochemical capacities of the host to harvest energy and essential building blocks in both dietary and endogenous sources that cannot be converted by the human enzymes alone [15]. The most prominent among them are intricate dietary carbohydrates especially non-digestible fibers and resistant starches that are not digested in the proximal gastrointestinal system and are the major precursors of microbial fermentation in the colon [15]. Such activities are driven by short-chain fatty-acid (SCFAs) end-products, which are mainly acetate, propionate and butyrate, as a result of this saccharolytic activity and are carried out by specialized bacterial taxa, including Faecalibacterium prausnitzii, Roseburia spp., and Bacteroides spp. Butyrate is the major energy source of the colonocytes, has anti-inflammatory and anti-carcinogenic effects by inhibiting histone deacetylase and inducing apoptosis in transformed cells [15]. Propionate is delivered to the liver, where it helps in gluconeogenesis and satiety regulation by G protein-coupled receptors (GPR41/FFAR3 and GPR43/FFAR2), whereas acetate is used peripherally in lipogenesis, cholesterol synthesis and it has recently been demonstrated to stimulate central appetite regulation. In a condition of low fermentable carbohydrates, the microbiota is replaced by proteolytic fermentation, which breaks down dietary and endogenous proteins into amino acids and derivatives like branched-chain fatty acids and indoles processes, ammonia and hydrogen sulfide processes which under different circumstances may be useful or detrimental depending on the availability of the substrates and the microorganismal balance [16]. Notably, aromatic amino acids like tryptophan, tyrosine, and phenylalanine are converted into bioactive phenylpropanoid metabolites (e.g., phenylacetic acid, 4-hydroxyphenylacetic acid), which overlap with metabolites derived from plant polyphenol degradation. Beyond macronutrient metabolism, the gut microbiota synthesizes essential micronutrients, including vitamin K and several B vitamins (e.g., biotin, folate, riboflavin, cobalamin), with metagenomic analyses estimating that microbially produced B vitamins may contribute over 25% of the recommended daily intake for several of these cofactors; moreover, colonic epithelial cells express specific transporters capable of absorbing these microbially derived vitamins [17]. The microbiota also critically modify host-derived compounds, particularly bile acids: primary bile acids (cholic acid and chenodeoxycholic acid) synthesized in the liver are conjugated to glycine or taurine and secreted into the intestine, where bacterial bile salt hydrolases (BSH) widely distributed across Bacteroides, Lactobacillus, Bifidobacterium, and Clostridium deconjugate them, enabling further microbial transformation into secondary bile acids (e.g., deoxycholic acid, lithocholic acid) [18]. These second messenger bile acids are signaling molecules, which bind receptors including FXR and TGR5, host lipid and

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glucose metabolism, energy homeostasis and antimicrobial defense. The targeted bacteria like the Bifidobacterium species ferment the human milk oligosaccharides complex glycans that are highly concentrated in the breast milk and which cannot be digested by the infant hence facilitating the establishment of microbial colonies in the gut, maturation of gut barriers and the development of immune system in infants. Taken together, all these various metabolic activities demonstrate that the commensal microbiota are not passive residents but rather active metabolic companions, which in essence determine the digestive physiology, nutritional condition and overall wellness of the host [15, 18].

## Immune System Development and Regulation

Commensal microbiota plays a vital role in the normal development, education, and control of the host immune system since early life to adulthood [19]. The gut microbiome is a leading initiator of maturing both the innate and adaptive immune system, the first two years of life when microbial colonization are observed to overlap with immune programming critical periods [19]. Germ free animal models have played a significant role in proving that lack of exposure to microbes causes severe immunological defects, such as underdeveloped gut-associated lymphoid tissue (GALT) decreased Peyer patches and mesenteric lymph nodes, reduced secretory IgA, and a loss of barrier function of the epithelium caused by a thinner mucus layer [20]. There is a mutual relationship between the gut microbiota and the host immune system; commensal bacteria promote immune development and functioning and the adaptive immune system, especially via IgA and regulatory T cells, influences and stabilize microbial composition [21]. The commensals largely induce secretory IgA (SIgA) that in turn coats intestinal bacteria to regulate their proliferation, localization and limit systemic immune response. Lacking of IgA (e.g., in AID- or pIgR-deficient mice) causes dysbiosis, which is an overgrowth of anaerobes, such as segmented filamentous bacteria (SFB), and loss of microbial diversity. Diversification and affinity maturation of IgA in germinal centers (GCs) in Peyer patches is essential in keeping microbial homeostasis; a defective somatic hypermutation leads to disproportionate microbiota (e.g. Proteobacteria proliferation). T follicular helper (Tfh) and T follicular regulatory (Tfr) cells closely control the IgA selection in GCs and that PD-1 and Foxp3 are important checkpoints. Deficiency PD-1 interferes with the quality of IgA, decreasing beneficial bacteria (e.g., Bifidobacterium), and entering into pro-inflammatory Enterobacteriaceae, which causes hyperactivation of the systemic immune. Foxp3+ regulatory T cells and in particular the ones induced by Clostridia clusters IV and XIVa, enhance microbial diversity and are necessary to sustain Clostridia populations themselves. This TregIgA axis is mutualistic: Foxp3+ T cell transfer does not recapitulate microbiota in AID-deficient hosts devoid of IgA. Finally, a complete adaptive immune system is not only required to protect us against pathogens, but also to maintain a symbiont, diverse, and spatially structured gut microbiota that is necessary to balance immune homeostasis in the system [21, 22].

Bile Acid Modification and Host Signaling

Intestinal microbes that are commensal are important in the biotransformation of host-derived bile acids, thus regulating major cellular metabolic and immune signaling pathways [23]. In the liver cholesterol is converted into primary bile acids cholic acid (CA) and chenodeoxycholic acid (CDCA) by the rate-limiting enzyme CYP7A1 and conjugated to either glycine or taurine to increase their detergent properties and solubility. When they are released in the duodenum during the digestive process, the conjugated bile acids help in the absorption of the lipids and fat-soluble vitamins present in the diet. Most of them are reabsorbed in the terminal ileum and are recycled by the enterohepatic circulation, although a small proportion (15-5 percent) is not reabsorbed and

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get released to the colon where they are utilized by microorganisms. Intestinal bacteria especially Bacteroides, Lactobacillus, Bifidobacterium, Clostridium, and Listeria express the bile salt hydrolase (BSH) enzymes to deconjugate primary bile acids to free glycine or taurine. This deconjugation does not only lower the bile acid toxicity of the microbes, it is also a source of carbon, nitrogen and sulfur. More to the point, it allows further microbial conversions, such as 7alpha-dehydroxylation of CA and CDCA to the secondary bile acids deoxycholic acid (DCA) and lithocholic acid (LCA) by species such as Clostridium scindens. These microbially modified bile acids are highly potent signalling molecules which activate host receptors especially the nuclear farnesoid X receptor (FXR) and the membrane-bound G protein-coupled bile acid receptor TGR5 (or M-BAR). The activation of FXR in the ileum leads to the secretion of fibroblast growth factor 19 (FGF19), which circulates to the liver to inhibit the expression of CYP7A1 and prevent the de novo synthesis of bile acids, and stimulate the synthesis of glycogen and reduce gluconeogenesis [24]. Intestinal L-cells activated by TGR5 promote the release of glucagon-like peptide- 1 (GLP-1), which enhances the insulin release during glucose dependence and increases glucose homeostasis in the body. In addition to metabolism, the immune functions are regulated by bile acid signaling: secondary bile acids affect the macrophage polarization, dendritic cell activity, as well as epithelial barrier integrity, and the dysregulation of this axis is associated with chronic inflammation. The composition and size of the bile acid pool is disturbed by administration of antibiotics, dietary changes, or dysbiosis, and disrupts these regulatory circuits. The range of pathologies is linked to such disruptions, and they are inflammatory bowel disease (IBD), Crohn disease, small intestinal bacterial overgrowth (SIBO), obesity, non-alcoholic fatty liver disease, cirrhosis, and hepatocellular carcinoma. As an example, patients with hepatitis B virus (HBV)-related cirrhosis have a significant gut dysbiosis with a decreased proportion of Bifidobacterium and Lactobacillus and an increase in Enterococcus and Enterobacteriaceae abundance and correlates with aberrant bile acid profile and pathogenesis [8]. On the other hand, low bile acid levels have the potential to increase the number of bacteria in the small intestine, whereas alterations in the composition of bile acid pools can in turn change the composition of the microbes, thereby establishing a vicious circle of homeostasis or pathogenesis. Therefore, a role of the commensal microbiota in the bile acid modification is a highly important biochemical interface wherein the microbial activity directly regulates host physiology, immunity and disease susceptibility [8, 24].

## Pathogenic Potential of Commensal Bacteria: From Symbiosis to Dysbiosis

### Dysbiosis and Disease Pathogenesis

Alteration of homeostasis of microbes known as dysbiosis is gradually being identified as a primary cause of pathogenesis of a broad range of human diseases [25]. Dysbiosis, which is the disturbance of a normal composition, diversity or functional balance of commensal microbial communities, indicates transition of symbiosis to pathobiont state, which is caused by exposure to antibiotics, dietary alterations, immune disease or genetic predisposition. This disbalance is normally characterized by a shift in microbial diversity toward decreased diversity (e.g., Faecalibacterium prausnitzii, Akkermansia muciniphila, Bifidobacterium and Ruminococcus), and an increase in proinflammatory or opportunistic organisms [26]. Inflammatory bowel disease (IBD) is an example, where dysbiosis can be typified by a loss of obligate anaerobes and an increase in facultative anaerobes e.g., adherent-invasive Escherichia coli which colonizes the ileal mucosa and provokes inflammation [27]. Likewise, in type 2 diabetes and obesity, a high Firmicutes to Bacteroidetes ratio is associated with the improvement of energy harvesting,

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intestinal permeability, and low-grade inflammation in the body [28]. Extra-intestinal pathologies are also based on dysbiosis: in psoriasis and atopic dermatitis, the microbiota of the skin changes to be dominated by Staphylococcus aureus [29]; in asthma and cystic fibrosis, the lung microbiome becomes less diverse and richer in pathogenic genera such as Pseudomonas and Haemophiles [30]. More importantly, there has been increasing evidence to suggest gut dysbiosis as the pathogenesis of neurodegenerative diseases, especially Alzheimer. Microbial imbalances in AD such as reduced Faecalibacterium, Bifidobacterium and Eubacterium rectale and increased Escherichia/Shigella and Bacteroides destroy intestinal barrier integrity, permitting microbial products such as lipopolysaccharide (LPS) to enter the systemic circulation [8, 31]. LPS is capable of bypassing the impaired blood-brain barrier (BBB), microglia-TLR2/4 activation, and activating neuroinflammatory cascades through NF-kB signaling, which results in increased proinflammatory cytokines (e.g., IL-1 2, TNF- 2) and NLRP3 inflammasome activation. At the same time, dysbiosis suppresses the generation of protective short-chain fatty acids (SCFA) that helps to increase BBB integrity, neuroinflammation, and microglial maturation [32]. Other processes involve increased levels of circulating trimethylamine N-oxide (TMAO) that enhances amyloid-beta (A3) aggregation and tau hyperphosphorylation and bacterial amyloids (e.g., curli in E. coli) that might cross-seed host A3 through molecular mimicry [33]. These interrelated pathways that include microbial translocation, systemic and neuroinflammation, oxidative stress, metabolic dysregulation, and protein misfolding make gut dysbiosis not only an outcome but also a contributor to the pathogenesis of AD. Importantly, fecal microbiota transfer research shows that diseased-dysbiotic microbiomes of diseased donors can be able to cause inflammation and pathological phenotypes in healthy recipients and this proves a causal role. Therefore, the evolution of symbiosis into dysbiosis is a critical process in a variety of clinical settings, and the microbiome is a biomarker and a potential therapeutic agent in chronic inflammatory, metabolic, and neurodegenerative conditions [8].

## Context-Dependent Virulence

Commensal bacteria are frequently context-dependent in their virulence, meaning that their pathogenic capacity is not inherent but arises upon a certain host, microbial or environmental signal. One major example is Streptococcus agalactiae (Group B Streptococci), which may be a normal flora of the vagina in up to 36 percent of healthy women, but in pregnant women, vertically transmitted to the baby, this organism may cause sepsis, pneumonia, or meningitis [34]. The transition to virulent phenotype is associated with the expression of special virulence factors like the polysaccharide capsule coded by cps gene and surface proteins such as Rib and C 2 whose regulation is affected by host factors which are not fully known. Likewise, adherent-invasive Escherichia coli (AIEC), which is not present in healthy guts and is not frequently present in enteropathology, proliferates during intestinal dysbiosis and leads to the pathogenesis of Crohn's disease by invading ileal epithelial cells and surviving in the macrophage. Host factors that promote this pathobiont behavior would include impaired autophagy or mutations in immune sensors like NOD2 which would alter the mucosal environment and allow bacterial overgrowth. Moreover, quorum-sensing pathways, e.g., QseBC two-component regulator in E. coli, allow bacteria to detect host stress conditions (e.g., catecholamines) and respond by increasing motility and virulence gene expression [8]. These examples emphasize that virulence does not always represent the fixed characteristic of a microbe but represents a dynamic process that is determined by the interactions among microbial genetics, host immunity and ecological perturbation of the microbiome.

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## Microbial Metabolites as Double-Edged Swords

Microbial metabolites are important hosts microbiome crosstalk mediators that are both protective and pathogenic in context-dependent, concentration-dependent, and host relevant per context differences. There are notable examples of this duality in short-chain fatty acids (SCFA) butyrate, propionate and acetate that are the products of bacterial fermentation of dietary fiber [35]. When the environment is homeostatic, SCFAs feed on colonocytes, stabilize epithelial barrier integrity, induce regulatory T-cell (Treg) differentiation through histone deacetylase (HDAC) inhibition and G protein-coupled receptor (GPR43/GPR109A) stimulation and inhibit neuroinflammation. This protective effect is however abrogated in the case of Alzheimer disease (AD): high concentrations of butyrate, propionate, acetate, and valerate in blood and brain are strongly linked to increased deposition of amyloid-beta (A 2) tissue as shown in PET scans of human cohorts. Mechanistically, although physiological concentrations of the SCFA block the process of A1000 cell aggregation dose-dependently (best at a 4:1 ratio of SCFA/ A1000), persistent production could promote pathological aggregates and microglial priming. Here, similarly in tuberculosis, Mycobacterium tuberculosis would harness host-derived sources of SCFAs during its persistent phase as a gained carbon source, and convert a host-based anti-inflammatory signal into a means of pathogen survival. This dual nature is also seen through the commensal bacteria generation of secondary bile acids as a result of deconjugation and 7alpha-dehydroxylation of primary bile acids. As ligands to the nuclear farnesoid X receptor (FXR) and the TGR5 that is a membrane-bound molecule, they coordinate glucose homeostasis, energy expenditure, and anti-inflammatory mechanisms. However, in dysbiotic conditions (e.g., Crohn's disease, cirrhosis, or hepatitis B virus infection) that cause a disturbance in balance between bile acid pools (e.g., decreased deoxycholic acid, increased toxic intermediates), FXR signaling is impaired, and cholesterol metabolism is disrupted, which favor carcinogenesis [36]. Further evidence of this context dependency is found in other metabolites: histamine released by Morganella morganii can inhibit eosinophilia of the lung in experimental animals through immunomodulation, but excessive production in an asthmatic would worsen the situation [37]. Similarly, lipopolysaccharide, an endotoxin of gram-negative bacteria, is released into the body and can reach the brain in conditions such as Alzheimer's disease, where the protective lining of the gut and the blood-brain barrier are progressively weakened. There, it activates specific signaling systems (TLR2/4 and NF-κB pathways) within the brain's immune cells, called microglia. This induces a chronic inflammatory state in the brain and leads to the deleterious modification of tau proteins. Overall, these examples emphasize that microbial metabolites are not inherently beneficial or harmful. Rather, their biological impact is determined by the host's ecological and immunological context, making them true double-edged swords in human health and disease [8, 37].

## Gut–Brain Axis: Gut dysbiosis is implicated in neurodegenerative disorders:

Gut dysbiosis is increasingly implicated in the pathogenesis of neurodegenerative disorders, particularly Alzheimer's disease (AD) and Parkinson's disease (PD), through bidirectional communication along the gut–brain axis [38]. In PD, clinical and epidemiological evidence supports a strong link between gut microbial alterations and disease severity [8]. Infection with the gastric pathobiont Helicobacter pylori is associated with worse motor symptoms in PD patients, and its eradication significantly improves levodopa absorption and increases daily "on" time, indicating that gut microbial status directly modulates neurological outcomes. Population-based

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studies further reveal that individuals who underwent truncal vagotomy a surgical severing of the vagus nerve have a markedly reduced risk of developing PD over two decades, strongly suggesting that pathological signals originating in the gut propagate to the brain via the vagus nerve. At the microbial level, PD is characterized by a depletion of beneficial, mucin- and fiber-fermenting taxa such as Prevotellaceae and butyrate producers (Faecalibacterium, Roseburia, Coprococcus, Blautia), alongside an expansion of proinflammatory genera like Enterobacteriaceae and Ralstonia[8]. This dysbiosis impairs the integrity of intestinal barriers, increases systemic lipopolysaccharide (LPS), and allows the misfolding of alpha -synuclein and neuroinflammation of the substantia nigra. Gut dysbiosis has been observed in AD as an abnormal Firmicutes/Bacteroidetes ratio followed by profound depletion of anti-inflammatory, SCFA-producing species (Ruminococcus, Bifidobacterium, Faecalibacterium, and Eubacterium rectale) and increases in proinflammatory taxa (Escherichia/ Shigella, Bacteroides, and Rikenella [8, 39]). Importantly, microbial metabolites pass through the damaged gut barrier and have an effect on brain pathology: high plasma concentrations of LPS and short-chain fatty acids (SCFA), in particular butyrate, acetate, and valerate, are strongly linked to amyloid- β (A 2) deposits in various regions of the brain, which is verified by PET imaging. Although the physiological SCFAs have neuroprotective action, chronic up-regulation of SCFA during dysbiosis might encourage dose-dependent A -oilmerization[40]. Besides, LPS of such species as Bacteroides fragilis destabilizes intestinal and blood brain barrier, induces microglia stimulation through TLR2/4NF-KB signaling, and leads to neuroinflammation and tau hyperphosphorylation [41]. Other neurotoxic metabolites which increase the brain oxidative stress include cyanobacterial excitotoxin 2-phenanthrenedicarboxyl (2-PDC). When combined, these data would lend credence to a single model where gastrointestinal unbalancedness caused by age or disease suppressed the microbial environment results in leaky gut, systemic translocation of microbial products, chronic neuroinflammation, reduced autophagy and pathological protein fibril formation all ultimately contribute to the development of the pathological hallmarks and clinical course of neurodegenerative diseases [42, 43].

## Gut–Lung Axis: Altered gut microbiota affects respiratory health

The gut-ling axis is one of the paramount bidirectional communication systems in which the gut microbiota regulates immune and inflammatory responses throughout the respiratory system, and this has far reached consequences of respiratory health both in the old-age and premature infancy groups [44]. Gut dysbiosis, particularly at the most sensitive stages of immune maturation in infancy, or as part of age-associated surfaces immunosenescence and malnutrition, disrupts local and systemic immunity, making to the vulnerability of acute and chronic respiratory illnesses, including asthma, cystic fibrosis (CF), chronic obstructive pulmonary disease (COPD), influenza, and tuberculosis [45]. In CF, extensive depleted beneficial gut bacteria such as Bacteroides vulgatus, Bacteroides uniformis, Faecalibacterium prausnitzii and Bifidobacterium species coincide with pathogenic changes in the lung microbiome, indicating that the dysbiosis is co-ordinated in the mucosal sites so distant [44]. Likewise, gut microbial imbalances like reduced Lachnospiraceae abundance and an increased Clostridioides are antecedents of clinical disease progression and can be attributed to defective immune responses in pediatric asthma. Metagenomic studies of adult asthmatics report depletion of butyrate generating bacteriophages such as F. prausnitzii and Coprococcus eutactus, and enrichment of proinflammatory bacteria such as Clostridium bolteae and Eggerthella lenta. The key points in this axis include microbial metabolites acetate, propionate, and butyrate ensuing bacterial fermentation of dietary fiber [44].

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SCFAs improve the activity of the alveolar macrophages, differentiate regulatory T -cells, decrease proinflammatory cytokine concentrations (e.g., TNF- 2, IL-1, IL-17), and strengthen antiviral interferon reactions [46]. An example is that acetate counters the effect of influenza on the impairment of the activity of alveolar macrophage in the killing of bacteria and increases the survival rate in secondary bacterial pneumonia. In tuberculosis, on the other hand, Mycobacterium tuberculosis takes advantage of gut-derived SCFAs as carbon sources in its persistent phase and patients show increased abundance of SCFA-producing gut bacteria (Faecalibacterium, Roseburia) and decrease of non-SCFA producers (Prevotella, Lachnospira), and reflects the duality of these metabolites depending on its particular context. Also, bacterial histamine of organisms such as Morganella morganii is also increased in severe asthma and can potentially worsen the airway inflammation. Imperatively, respiratory infections per se may also reciprocally change gut microbiota composition either by systemic inflammation or anorexia, or daily changes on a vicious cycle making one vulnerable to secondary infections [8, 47]. As they age, even more of the gut and lung epithelia become permeable to further enhance the unfiltered exchange of microbes and metabolic products, destabilize compartmentalization, and deteriorate the barrier functionality. These results highlight the importance of gut microbiome not only in local intestinal immunity but also a systemic effect on respiratory disease, which places the gut-lung axis at the forefront of nutritional, prebiotic, probiotic, and microbiota-regulated therapeutic interventions especially in the most susceptible groups of patients including the old and children [8].

## Gut–Skin Axis

The gut microbiome regulates the homeostasis of the skin, immune, and inflammatory response of the skin by a bidirectional communication system known as the gut-skin axis. Thought to be the case already but hard data were provided by work that revealed that oral supplementation with certain gut commensals including Lactobacillus paracasei and Lactobacillus pentosus GMNL-77 can promote a change in skin phenotype in both mice and humans, which decreases transepidermal water loss, fortifies epidermal barrier function, and subsequently blocks Th17-mediated inflammation [48]. Microbial metabolites, immune cells, and inflammatory mediators mediate this systemic effect, which occurs as the gut microbial products go to remote locations, such as the skin. A unique instance of systemic inflammatory disease in psoriasis, prototypical systemic inflammatory disease metagenomic studies show a considerable level of functional dysbiosis in spite of a can often relatively small alteration in total microbial diversity. Among the main changes are an increase in the synthesis of lipopolysaccharides (LPS), the secretion systems of bacteria, and fructose/mannose metabolism, as well as a decrease in anti-inflammatory processes, including WNT signaling and the sulfur metabolism [8]. LPS, a strong endotoxin of Gram-negative bacteria, crosses a weakened intestinal barrier (the leaky gut) and enters the blood, where it triggers TLR /NF-KB signaling, Th17/Treg imbalance, and IL-23/ IL-17 inflammatory axis that is critical in plaque development in psoriasis. In a regular theme, increased amounts of antiinflammatory genera including Faecalibacterium prausnitzii and Akkgermansia muciniphila and decreased amounts of proinflammatory genera such as Ruminococcus gnavus and Escherichia/ Shigella are more regularly shown to appear in psoriasis patients. On the same note, gut dysbiosis may run ahead, or coincide, with skin lesionation in atopic dermatitis, where the lack of microbial diversity and proliferation of Staphylococcus aureus on lesional skin, which is not usually a dominant microbe of healthy skin but is promoted by a systemic immune environment biased towards Th2 responses and structural barrier defectiveness, is found. [49]. Gut-derived metabolites further shape cutaneous immunity: short-chain fatty acids (SCFAs) such as butyrate and propionate

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promote Treg differentiation and suppress inflammation, while phenolic compounds like p-cresol (produced by Clostridioides difficile) impair epidermal differentiation and keratinization. Tryptophan derivatives and other microbial ligands also modulate aryl hydrocarbon receptor (AhR) signaling, influencing Langerhans cell function and IL-22 production. Collectively, these findings support the concept that disturbances in the gut microbiome propagate inflammatory and metabolic signals that disrupt cutaneous homeostasis, positioning the gut–skin axis as a critical target for therapeutic interventions including probiotics, prebiotics, and dietary modulation in inflammatory skin disorders such as psoriasis, atopic dermatitis, and acne [48, 50].

## Conflict of interests.

There are non-conflicts of interest.

## References

[1] A. A. Al-Judaibi, "Microbiota and their Influence in the Human Body," Journal of Pure & Applied Microbiology, vol. 15, no. 1, 2021.

[2] J. M. Leonard, and D. D. Toro, "Defining the microbiome components (bacteria, viruses, fungi) and microbiome geodiversity," Surgical infections, vol. 24, no. 3, pp. 208-212, 2023.

[3] E. M. Brown, J. Clardy, and R. J. Xavier, "Gut microbiome lipid metabolism and its impact on host physiology," Cell host & microbe, vol. 31, no. 2, pp. 173-186, 2023.

[4] B. Strasser, M. Wolters, C. Weyh et al., "The effects of lifestyle and diet on gut microbiota composition, inflammation and muscle performance in our aging society," Nutrients, vol. 13, no. 6, pp. 2045, 2021.

[5] S. Pedroza Matute, and S. Iyavoo, "Exploring the gut microbiota: lifestyle choices, disease associations, and personal genomics," Frontiers in Nutrition, vol. 10, pp. 1225120, 2023.

[6] Y. Belkaid, and O. J. Harrison, "Homeostatic immunity and the microbiota," Immunity, vol. 46, no. 4, pp. 562-576, 2017.

[7] H. Brüssow, "Problems with the concept of gut microbiota dysbiosis," Microbial biotechnology, vol. 13, no. 2, pp. 423-434, 2020.

[8] J. Manos, "The human microbiome in disease and pathology," Apmis, vol. 130, no. 12, pp. 690-705, 2022.

[9] M. A. O'Malley, "The concept of balance in microbiome research," Bioessays, vol. 46, no. 8, pp. 2400050, 2024.

[10] P. Dey, and S. Ray Chaudhuri, "The opportunistic nature of gut commensal microbiota," Critical reviews in microbiology, vol. 49, no. 6, pp. 739-763, 2023.

[11] S. M. Jandhyala, R. Talukdar, C. Subramanyam et al., "Role of the normal gut microbiota," World journal of gastroenterology: WJG, vol. 21, no. 29, pp. 8787, 2015.

[12] J. G. LeBlanc, F. Chain, R. Martín et al., "Beneficial effects on host energy metabolism of short-chain fatty acids and vitamins produced by commensal and probiotic bacteria," Microbial cell factories, vol. 16, no. 1, pp. 79, 2017.

[13] E. Cremonesi, V. Governa, J. F. G. Garzon et al., "Gut microbiota modulate T cell trafficking into human colorectal cancer," Gut, vol. 67, no. 11, pp. 1984-1994, 2018.

[14] N. Okahashi, M. Nakata, H. Kuwata et al., "Oral mitis group streptococci: A silent majority in our oral cavity," Microbiology and Immunology, vol. 66, no. 12, pp. 539-551, 2022.

[15] I. Rowland, G. Gibson, A. Heinken et al., "Gut microbiota functions: metabolism of nutrients and other food components," European journal of nutrition, vol. 57, no. 1, pp. 1-24, 2018.
[16] J. Miyamoto, S. Hasegawa, M. Kasubuchi et al., "Nutritional signaling via free fatty acid receptors," International journal of molecular sciences, vol. 17, no. 4, pp. 450, 2016.
[17] S.-R. Ma, J.-B. Yu, J. Fu et al., "Determination and application of nineteen monoamines in the gut microbiota targeting phenylalanine, tryptophan, and glutamic acid metabolic pathways," Molecules, vol. 26, no. 5, pp. 1377, 2021.
[18] M. Bourgin, A. Kriaa, H. Mkaouar et al., "Bile salt hydrolases: at the crossroads of microbiota and human health," Microorganisms, vol. 9, no. 6, pp. 1122, 2021.
[19] M. G. Rooks, and W. S. Garrett, "Gut microbiota, metabolites and host immunity," Nature reviews immunology, vol. 16, no. 6, pp. 341-352, 2016.
[20] T. Uzbay, "Germ-free animal experiments in the gut microbiota studies," Current Opinion in Pharmacology, vol. 49, pp. 6-10, 2019.
[21] L. M. Kato, S. Kawamoto, M. Maruya et al., "The role of the adaptive immune system in regulation of gut microbiota," Immunological reviews, vol. 260, no. 1, pp. 67-75, 2014.
[22] A. Borrego-Ruiz, and J. J. Borrego, "Human gut microbiome, diet, and mental disorders," International Microbiology, vol. 28, no. 1, pp. 1-15, 2025.
[23] J. A. González-Regueiro, L. Moreno-Castañeda, M. Uribe et al., "The role of bile acids in glucose metabolism and their relation with diabetes," Annals of hepatology, vol. 16, no. 1, pp. 15-20, 2018.
[24] P. Portincasa, A. Di Ciaula, G. Garruti et al., "Bile acids and GPBAR-1: dynamic interaction involving genes, environment and gut microbiome," Nutrients, vol. 12, no. 12, pp. 3709, 2020.
[25] A. K. DeGruttola, D. Low, A. Mizoguchi et al., "Current understanding of dysbiosis in disease in human and animal models," Inflammatory bowel diseases, vol. 22, no. 5, pp. 1137-1150, 2016.
[26] R. M. R. A. Effendi, M. Anshory, H. Kalim et al., "*Akkermansia muciniphila* and *Faecalibacterium prausnitzii* in immune-related diseases," Microorganisms, vol. 10, no. 12, pp. 2382, 2022.
[27] J. Halfvarson, C. J. Brislawn, R. Lamendella et al., "Dynamics of the human gut microbiome in inflammatory bowel disease," Nature microbiology, vol. 2, no. 5, pp. 1-7, 2017.
[28] K. Ahmed, H.-N. Choi, S.-R. Cho et al., "Association of firmicutes/bacteroidetes ratio with body mass index in Korean type 2 diabetes mellitus patients," Metabolites, vol. 14, no. 10, pp. 518, 2024.
[29] R. Bjerre, J. Bandier, L. Skov et al., "The role of the skin microbiome in atopic dermatitis: a systematic review," British Journal of Dermatology, vol. 177, no. 5, pp. 1272-1278, 2017.
[30] K. Hufnagl, I. Pali-Schöll, F. Roth-Walter et al., "Dysbiosis of the gut and lung microbiome has a role in asthma." pp. 75-93, 2020.
[31] S. Liu, J. Gao, M. Zhu et al., "Gut microbiota and dysbiosis in Alzheimer's disease: implications for pathogenesis and treatment," Molecular neurobiology, vol. 57, no. 12, pp. 5026-5043, 2020.
[32] Y. Lu, X. Li, S. Liu et al., "Toll-like receptors and inflammatory bowel disease," Frontiers in immunology, vol. 9, pp. 72, 2018.
[33] M. E. Macpherson, J. R. Hov, T. Ueland et al., "Gut microbiota-dependent trimethylamine N-oxide associates with inflammation in common variable immunodeficiency," Frontiers in immunology, vol. 11, pp. 574500, 2020.
[34] M. Bayo, M. Berlanga, and M. Agut, "Vaginal microbiota in healthy pregnant women and prenatal screening of group B streptococci (GBS)," International Microbiology, vol. 5, no. 2, pp. 87-90, 2002.
[35] R. Mirzaei, B. Bouzari, S. R. Hosseini-Fard et al., "Role of microbiota-derived short-chain fatty acids in nervous system disorders," Biomedicine & Pharmacotherapy, vol. 139, pp. 111661, 2021.

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[36] C. Tamboli, C. Neut, P. Desreumaux et al., "Dysbiosis as a prerequisite for IBD," Gut, vol. 53, no. 7, pp. 1057-1057, 2004.
[37] P. Losol, M. Wolska, T. P. Wypych et al., "A cross talk between microbial metabolites and host immunity: Its relevance for allergic diseases," Clinical and Translational Allergy, vol. 14, no. 2, pp. e12339, 2024.
[38] Y. Zheng, L. Bonfili, T. Wei et al., "Understanding the gut–brain axis and its therapeutic implications for neurodegenerative disorders," Nutrients, vol. 15, no. 21, pp. 4631, 2023.
[39] B. J. Verhaar, H. M. Hendriksen, F. A. de Leeuw et al., "Gut microbiota composition is related to AD pathology," Frontiers in immunology, vol. 12, pp. 794519, 2022.
[40] M. Marizzoni, A. Cattaneo, P. Mirabelli et al., "Short-chain fatty acids and lipopolysaccharide as mediators between gut dysbiosis and amyloid pathology in Alzheimer's disease," Journal of Alzheimer's Disease, vol. 78, no. 2, pp. 683-697, 2020.
[41] W. J. Lukiw, "*Bacteroides fragilis* lipopolysaccharide and inflammatory signaling in Alzheimer's disease," Frontiers in microbiology, vol. 7, pp. 1544, 2016.
[42] A. Lee, R. Henderson, J. Aylward et al., "Gut symptoms, gut dysbiosis and gut-derived toxins in ALS," International Journal of Molecular Sciences, vol. 25, no. 3, pp. 1871, 2024.
[43] D. F. Silva, E. Candeias, A. R. Esteves et al., "Microbial BMAA elicits mitochondrial dysfunction, innate immunity activation, and Alzheimer's disease features in cortical neurons," Journal of Neuroinflammation, vol. 17, no. 1, pp. 332, 2020.
[44] V. Saint-Criq, G. Lugo-Villarino, and M. Thomas, "Dysbiosis, malnutrition and enhanced gut-lung axis contribute to age-related respiratory diseases," Ageing research reviews, vol. 66, pp. 101235, 2021.
[45] H. Ullah, "Gut-vitamin D interplay: key to mitigating immunosenescence and promoting healthy ageing," Immunity & Ageing, vol. 22, no. 1, pp. 20, 2025.
[46] Z. Chen, Y. Liu, and W. Huang, "Alveolar macrophage modulation via the gut–lung axis in lung diseases," Frontiers in Immunology, vol. 14, pp. 1279677, 2023.
[47] G. Precup, and D.-C. Vodnar, "Gut Prevotella as a possible biomarker of diet and its eubiotic versus dysbiotic roles: a comprehensive literature review," British Journal of Nutrition, vol. 122, no. 2, pp. 131-140, 2019.
[48] A. Y.-K. Thye, Y.-R. Bah, J. W.-F. Law et al., "Gut–skin axis: Unravelling the connection between the gut microbiome and psoriasis," Biomedicines, vol. 10, no. 5, pp. 1037, 2022.
[49] M. Jimenez-Sanchez, L. S. Celiberto, H. Yang et al., "The gut-skin axis: a bi-directional, microbiota-driven relationship with therapeutic potential," Gut Microbes, vol. 17, no. 1, pp. 2473524, 2025.
[50] R. Iizuka, "Gut bacteria and skin health," Handbook of diet, nutrition and the skin, pp. 25-43: Wageningen Academic, 2012.

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## الخلاصة

الخلفية: الميكروبيوم البشري هو نظام بيئي معقد يعتمد على التكافل، وهو ضروري لصحة الإنسان، ويلعب أدوارًا حيوية في التمثيل الغذائي والمناعة. واضطرابه، الذي يُسمى خلل التوازن البكتيري، يُشارك بشكل متزايد في مجموعة متنوعة من الأمراض المزمنة.

الهدف: تجمع هذه المراجعة الأدلة حول الدور المزدوج للميكروبيوم في الصحة والمرض، وتفحص آليات الحفاظ على الاستتباب بواسطة ميكروبيوتا متوازنة ومساهمة خلل التوازن البكتيري في عدة اضطرابات.

الطرق: تم إجراء مراجعة سردية للأدبيات العلمية، وشملت نتائج دراسات الأتراب البشرية، ونماذج الحيوانات، والأبحاث الميكانيكية في المختبر لتوضيح أهم الوظائف الميكروبية، وتفاعلات المضيف والميكروب، ومسارات التواصل بين الأعضاء.

النتائج: تلعب الميكروبات المتعايشة دورًا مهمًا في إنتاج المستقلبات، وتدريب الجهاز المناعي، ومقاومة الاستعمار. ينتج عن خلل التوازن البكتيري الناجم عن المضادات الحيوية والنظام الغذائي فقدان التنوع، ونمو الميكروبات المرضية، وتغير المستقلبات. ويرتبط هذا الاضطراب باضطرابات مثل مرض التهاب الأمعاء، والسكري، والأمراض التنكسية العصبية. المستقلبات والمكونات الميكروبية هي سيف ذو حدين، تنقل تأثيراتها الجهوية عبر محاور القناة الهضمية والدماغ، والرئة، والجلد من خلال المسارات المناعية، والعصبية، والتمثيل الغذائي.

الخاتمة: الانسجام الميكروبي ضروري للصحة، واختلال توازنه هو سبب المرض المزمن، لذلك يمثل الميكروبيوم مرشحًا مثاليًا للتشخيصات والعلاجات الجديدة، والنهج الشخصية لاستعادته.

الكلمات المفتاحية: ميكروبيوم، محور الأمعاء والمناعة، خلل التوازن البكتيري، الغلوبولين المناعي الإفرازي أ، الخلايا التائية التنظيمية.