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Correlation between oral-gut microbiome laboratory findings and oral health in clinical dentistry-An Updated Review for Laboratory Professionals, Dentists, and Health Administrators

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Abstract

Background: The oral and gut microbiomes constitute the two largest microbial ecosystems in the human body and are closely interconnected through microbial translocation, immune signaling, and metabolic interactions. Alterations in either ecosystem lead to microbial dysbiosis associated with systemic inflammatory, metabolic, and neoplastic diseases.

Aim: This review aims to summarize current evidence on the bidirectional relationship between oral and gut microbiomes, highlight mechanisms underlying microbial transfer, and evaluate their relevance to disease progression and therapeutic strategies.

Methods: A comprehensive literature-based synthesis was conducted focusing on microbial composition, dysbiosis patterns, cross-ecosystem microbial migration, and mechanistic pathways involving bacteria, fungi, and viruses. The review further integrates findings from human studies and experimental animal models.

Results: The oral microbiome influences gut microbial diversity through translocation of pathogenic species such as *Porphyromonas gingivalis* and *Streptococcus mitis*, leading to reduced gut microbial richness and increased inflammatory taxa. Conversely, gut dysbiosis in inflammatory bowel disease and colorectal cancer induces significant shifts in oral microbial composition, enriching taxa such as *Streptococcus* and *Actinomyces*. Fungal and viral communities also exhibit cross-site transmission, contributing to disease-associated microbial remodeling and epithelial barrier disruption. Mechanistic pathways include direct microbial translocation, systemic dissemination, immune modulation, and metabolic reprogramming.

Conclusion: Oral–gut microbial interaction plays a central role in systemic health, contributing to inflammatory, metabolic, and neoplastic diseases. Understanding these mechanisms is essential for developing targeted interventions including periodontal therapy, probiotics, dietary optimization, and microbiome-based diagnostics.

Keywords: Oral microbiome, gut microbiome, dysbiosis, microbial translocation, periodontitis, inflammatory bowel disease, colorectal cancer, virome, mycobiome.

Introduction

The human body represents a complex ecological system inhabited by a vast and diverse population of microorganisms that collectively form what is known as the human microbiota. It is estimated that the number of microbial cells associated with the human body exceeds the number of human cells by at least an order of magnitude, with a commonly cited ratio of approximately ten microbial cells for every one human cell (1). These microorganisms are not merely passive colonizers but instead play essential roles in maintaining physiological homeostasis, contributing to metabolic processes, immune modulation, epithelial integrity, and protection against pathogenic invasion. Within this extensive microbial ecosystem, the oral cavity and the gastrointestinal tract constitute the two largest and most densely populated microbial habitats in the human body, each hosting highly complex and dynamic microbial communities (1). Data derived from the Human Microbiome Project have significantly advanced the understanding of microbial distribution across different anatomical sites. According to its findings, a substantial proportion of the body's total bacterial population resides primarily in two anatomical regions, with approximately 26 percent located in the oral cavity and around 29 percent in the gastrointestinal tract (1). These two microbial niches are not isolated systems but are instead interconnected through continuous biological

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and physiological exchange processes. The oral cavity, as the initial segment of the digestive system, serves as a critical gateway through which microorganisms can enter the gastrointestinal tract. Consequently, the phenomenon of microbial dissemination from the oral cavity to the gut is not only common but also biologically significant in shaping gut microbial composition under both physiological and pathological conditions (2).

Recent scientific attention has increasingly focused on the bidirectional relationship between the oral and gut microbiomes, highlighting their functional and ecological interdependence. Evidence suggests that microbial populations originating in the oral cavity can colonize the intestinal environment, thereby influencing the overall diversity and stability of the gut microbiota. This microbial exchange is supported by findings from large-scale microbiome analyses, which demonstrate substantial overlap between oral and intestinal bacterial communities. In a study involving more than 200 healthy adult individuals, approximately 45 percent of bacterial taxa were found to be shared between oral and fecal samples, indicating a considerable degree of microbial continuity along the gastrointestinal tract (1). This overlap challenges the traditional view of the gut microbiome as an entirely distinct ecosystem and instead supports a model of dynamic microbial interconnectivity between anatomical sites. The clinical implications of oral-gut microbial interactions have become increasingly evident through epidemiological and experimental research. Alterations in the composition and diversity of the oral microbiota, particularly those associated with oral diseases such as periodontitis and dental caries, have been linked to concurrent changes in gut microbial communities. These microbial shifts are often characterized by dysbiosis, a condition defined by the disruption of normal microbial equilibrium and the proliferation of pathogenic or opportunistic species. Clinical studies have demonstrated that individuals suffering from chronic oral conditions exhibit a higher prevalence of gastrointestinal disorders, suggesting a potential causal or contributory relationship between oral microbial imbalance and intestinal disease development.

Among the most well-documented associations is the link between periodontal disease and inflammatory bowel disease (IBD). Epidemiological evidence indicates that individuals with periodontal disease, particularly those with severe manifestations such as tooth loss and advanced periodontitis, are at increased risk of developing IBD-related complications and functional impairment (3). This relationship highlights the systemic impact of oral inflammation and its potential role in modulating intestinal immune responses. Furthermore, periodontal disease has also been associated with an elevated risk of colorectal cancer (CRC). Comparative studies have shown that individuals with periodontal disease experience a 21 percent increased risk of developing CRC compared with those maintaining good oral health (4). These findings suggest that chronic oral infection and inflammation may contribute to carcinogenic processes in the gastrointestinal tract, possibly through microbial translocation, immune activation, or metabolic byproducts that influence epithelial integrity. The relationship between oral and intestinal health is further supported by evidence indicating that oral lesions and periodontal pathology may function not only as initiating factors in gut microbial dysbiosis but also as potential clinical indicators of underlying intestinal disease. For instance, periodontal disease has been found to occur with significantly higher prevalence among patients diagnosed with inflammatory bowel disease, with more severe periodontal manifestations observed in this population (5). This bidirectional association suggests that systemic inflammatory processes may simultaneously affect both oral and intestinal tissues, reinforcing the concept of a shared pathophysiological axis between these two microbial ecosystems.

Experimental animal models have provided additional insights into the mechanistic links between oral and gut microbiota. Studies involving murine models of intestinal inflammation, particularly those induced by Dextran Sulfate Sodium (DSS), have demonstrated that colitis can exacerbate periodontal tissue damage, including increased alveolar bone resorption (6). These findings indicate that intestinal inflammation is capable of influencing distant oral tissues, thereby reinforcing the concept of a bidirectional relationship between gut pathology and oral health. Such observations support the hypothesis that systemic inflammatory mediators and microbial metabolites may circulate between anatomical sites, contributing to reciprocal tissue damage and microbial imbalance. Despite the growing body of evidence supporting oral-gut microbial interactions, current research remains predominantly focused on the effects of gut microbiota alterations following oral microbial translocation. In other words, most existing studies emphasize how oral bacteria influence intestinal health after migration to the gut environment. However, the reverse mechanisms, particularly the pathways through which oral microbiota actively contribute to gut dysbiosis and systemic disease progression, remain insufficiently understood. The molecular, immunological, and ecological mechanisms underlying these interactions require further elucidation to fully characterize the functional relationship between oral and gut microbial ecosystems. Addressing this gap in knowledge is essential for developing a more comprehensive understanding of human microbial ecology and for identifying potential therapeutic

targets aimed at restoring microbial balance and preventing disease progression across multiple organ systems.

The oral microbiome: functions, dysbiosis, and its impact on gut microbiome

The oral cavity represents the initial anatomical segment of the gastrointestinal tract and constitutes one of the most densely populated microbial ecosystems in the human body. It harbors the second largest microbial community after the gut, with more than 700 bacterial species identified within its ecological niche (7). This microbial community is highly diverse and structured, encompassing multiple dominant bacterial phyla, including Firmicutes, Bacteroidetes, Proteobacteria, Actinobacteria, Fusobacteria, and Neisseria (8). At the genus level, the oral microbiota is predominantly composed of Streptococcus, Gemella, Veillonella, Haemophilus, Porphyromonas, Fusobacterium, Actinomyces, and Prevotella, which collectively contribute to a dynamic and functionally active microbial environment (7). Under physiological conditions, these microorganisms coexist in a finely balanced symbiotic relationship with the host, contributing to essential biological processes that extend beyond oral health and influence systemic physiological function. The functional roles of the oral microbiome can be broadly categorized into metabolic activity, microbial defense, modulation of host behavior, and systemic physiological regulation. From a metabolic perspective, specific anaerobic bacteria such as Fusobacterium and Peptostreptococcus demonstrate aminopeptidase activity, enabling the breakdown of amino acids into short-chain fatty acids and other low-molecular-weight metabolites that are essential for microbial survival and ecological stability within the oral biofilm (9). These metabolic products not only support microbial community maintenance but also contribute to local environmental regulation within the oral cavity.

In addition to metabolic functions, the oral microbiota plays a critical role in microbial defense mechanisms that protect both the host and the microbial community from pathogenic invasion. Streptococcus dentisani is a notable example of a beneficial oral bacterium that exerts protective effects by inhibiting the growth of Streptococcus mutans, a key cariogenic pathogen. It achieves this through the production of hydrogen peroxide and the neutralization of acidic conditions within dental plaque, thereby maintaining biofilm stability and reducing the risk of dental caries (10). This competitive inhibition highlights the importance of microbial equilibrium in preventing dysbiotic shifts that may lead to oral disease. The oral microbiome also appears to influence host dietary behavior through its interaction with sensory and metabolic pathways. Certain microbial taxa, including members of Clostridia and Prevotella, have been associated with modulation of taste perception thresholds, which may subsequently influence dietary preferences and food intake patterns (11). Such interactions suggest a complex bidirectional relationship in which microbial composition can influence host behavior in ways that promote microbial persistence and ecological stability within the oral environment. Beyond local effects, the oral microbiome exerts systemic physiological influence, particularly through its involvement in the nitrate-nitrite-nitric oxide pathway. Oral bacteria are capable of reducing dietary nitrate to nitrite, which is subsequently absorbed into the systemic circulation and converted into nitric oxide, a key signaling molecule involved in vascular homeostasis. This pathway contributes to the regulation of vascular tone, maintenance of endothelial function, and prevention of hypertension-related vascular dysfunction (12). This demonstrates that the oral microbiome plays an integral role in cardiovascular regulation and systemic metabolic processes.

Maintenance of microbial balance within the oral cavity is essential for preserving oral and systemic health. Disruption of this equilibrium, commonly referred to as dysbiosis, is strongly associated with the development of oral diseases. Dental caries represents one of the most well-characterized consequences of microbial imbalance, characterized by an increased prevalence of acidogenic and aciduric bacteria such as Streptococcus, Lactobacillus, and Bifidobacterium. These organisms metabolize dietary carbohydrates, producing organic acids that progressively demineralize enamel and dentin, ultimately leading to structural tooth damage (13, 14). Periodontitis, a chronic inflammatory disease affecting the supporting structures of the teeth, is also strongly linked to oral microbial dysbiosis. This condition is characterized by a shift in microbial composition toward pathogenic anaerobic species, particularly those belonging to the red complex group, including Porphyromonas gingivalis, Tannerella forsythia, and Treponema denticola. These bacteria are highly virulent and contribute to tissue destruction through the production of proteolytic enzymes, inflammatory mediators, and immune-modulating factors. Concurrently, beneficial commensal species such as Streptococcus salivarius are significantly reduced during disease progression, further contributing to microbial imbalance and disease exacerbation (15, 16). Emerging evidence suggests that oral dysbiosis extends its pathological influence beyond the oral cavity and significantly impacts the composition and function of the gut microbiome. Clinical studies in patients with periodontitis have demonstrated a reduction in gut microbial alpha diversity, indicating a loss of microbial richness and ecological stability. This is accompanied by an increased abundance of pathogenic taxa such as Porphyromonadaceae, Tannerella, and Treponema, alongside a reduction in beneficial bacterial families including

Streptococcaceae, Pasteurellaceae, and Veillonellaceae (17, 18). These findings suggest that oral microbial disturbances may contribute to systemic microbial alterations through translocation and colonization of the gastrointestinal tract.

Experimental animal studies further support the concept of oral-gut microbial transmission and its pathological consequences. In murine models, ligature-induced periodontitis has been shown to result in reduced gut microbial diversity, along with an increased abundance of Firmicutes at the phylum level and genera such as Barnesiella and Akkermansia (19). These microbial changes are often associated with low-grade intestinal inflammation, indicating a functional impact on gut immune homeostasis. Additional studies have demonstrated that oral administration of saliva derived from periodontitis patients leads to significant disruption of cecal microbiota composition in mice, characterized by increased abundance of Porphyromonadaceae and Fusobacterium and a concurrent decrease in Akkermansia, a genus commonly associated with gut barrier integrity and metabolic health (20, 18). Specific oral pathogens have been identified as key mediators in the induction of gut dysbiosis. Porphyromonas gingivalis, in particular, has been extensively studied for its systemic effects. Oral administration of this pathogen in experimental models has been associated with increased abundance of bacterial families such as Lachnospiraceae, Acetatifactor, and Acholeplasmataceae, while control groups exhibit higher levels of Rikenellaceae and Mycoplasmataceae (21, 22). These findings indicate that P. gingivalis can significantly alter gut microbial ecology, potentially through immune modulation, epithelial barrier disruption, and microbial competition. In addition to P. gingivalis, other oral bacteria also contribute to gut microbial imbalance. Streptococcus mitis, when introduced orally in experimental models, has been shown to promote the expansion of multiple gut bacterial taxa, including Lactobacillus, Bacteroides, Staphylococcus, Clostridium, and Jeotgalicoccus, thereby further illustrating the capacity of oral microorganisms to reshape intestinal microbial communities (23). Collectively, these findings highlight the significant role of the oral microbiome in influencing gut microbial composition and function. Identification of key pathogenic oral species and elucidation of the mechanisms underlying their translocation and activity in the gut are essential for advancing therapeutic strategies. Such interventions may include targeted antimicrobial approaches aimed at suppressing pathogenic oral bacteria, as well as microbiome modulation strategies involving the introduction of beneficial or antagonistic bacterial strains. These approaches hold potential for restoring microbial equilibrium, improving gut health, and reducing the systemic impact of oral dysbiosis, thereby reinforcing the importance of integrated oral and systemic microbiome research.

The gut microbiome: functions, dysbiosis, and its impact on oral microbiome

The human gut microbiome represents the most extensive and metabolically active microbial ecosystem within the human body, comprising trillions of microbial cells that collectively exceed all other body-associated microbial communities in both density and functional complexity (24). This ecosystem is dominated by a limited number of major bacterial phyla, specifically Firmicutes, Bacteroidetes, Actinobacteria, Fusobacteria, Proteobacteria, and Verrucomicrobia, which together form a highly structured and interactive microbial network. Among these, Firmicutes and Bacteroidetes constitute the predominant proportion, accounting for more than ninety percent of the total microbial population within the gastrointestinal tract (25). This dominance reflects their central role in maintaining metabolic equilibrium, ecological stability, and host–microbe interactions. The functional significance of the gut microbiota extends across multiple physiological domains, including metabolism, host defense, immune system development, and neuroregulation. In metabolic processes, members of the Firmicutes and Bacteroidetes phyla collaborate in the enzymatic breakdown of indigestible dietary polysaccharides that are resistant to host digestive enzymes. Through this process, they generate short-chain fatty acids, which serve as critical energy substrates for colonic epithelial cells and play essential roles in regulating metabolic homeostasis, inflammation, and epithelial integrity (26). Beyond metabolic contributions, the gut microbiota plays a fundamental role in protecting the host against pathogenic colonization. This protective effect is achieved through competitive exclusion, whereby commensal microorganisms outcompete pathogenic species for nutrients and ecological niches, thereby limiting pathogen proliferation (27). In addition, the gut microbiota produces a variety of antimicrobial compounds, including short-chain fatty acids, bile acid derivatives, and bacteriocins, all of which contribute to the suppression of pathogenic bacterial growth and the maintenance of intestinal microbial balance (28). These mechanisms collectively establish a robust barrier function that is essential for gastrointestinal health.

The gut microbiome is also indispensable for the proper development and maturation of the host immune system. Experimental evidence derived from germ-free animal models has demonstrated profound immunological deficiencies in the absence of gut microbiota. Germ-free mice exhibit impaired development of mesenteric lymph nodes and Peyer's patches, both of which are critical components of gut-associated lymphoid tissue. Furthermore, these

animals display significantly reduced populations of CD4+ and CD8+ T lymphocytes, as well as regulatory T cells expressing Foxp3, indicating widespread immune dysregulation. In addition, decreased production of secretory immunoglobulin A by B cells has been observed, leading to compromised mucosal immunity and increased susceptibility to enteric pathogens such as Shigella flexneri and Salmonella typhimurium (29). These findings underscore the essential role of the gut microbiota in shaping both innate and adaptive immune responses. In addition to metabolic and immunological functions, the gut microbiome is increasingly recognized as a key regulator of neurophysiological processes through its involvement in the gut–brain axis. Gut microbial communities are capable of producing and modulating a range of endocrine and neuroactive compounds that influence neurotransmitter synthesis and signaling pathways. These microbial-derived signals facilitate bidirectional communication between the gastrointestinal tract and the central nervous system, thereby contributing to the regulation of mood, behavior, and cognitive function (30). This neuroregulatory capacity highlights the systemic influence of the gut microbiota beyond the confines of the intestinal environment.

Under healthy conditions, the gut microbiota exists in a state of dynamic equilibrium with the host, characterized by mutualistic interactions that support physiological stability and homeostasis. However, disruption of this balance, commonly referred to as dysbiosis, is strongly associated with a range of gastrointestinal disorders, including irritable bowel syndrome, inflammatory bowel disease, and colorectal cancer. In irritable bowel syndrome, microbial diversity is frequently reduced, accompanied by an increase in Proteobacteria, Lactobacillaceae, Enterobacteriaceae, and certain species within Clostridium and Ruminococcus, alongside a decrease in beneficial taxa such as Faecalibacterium, Bifidobacterium, and Bacteroides (31, 32). These alterations suggest a shift toward a pro-inflammatory and less metabolically stable microbial environment. Similar patterns of dysbiosis are observed in inflammatory bowel disease, where there is a notable enrichment of Veillonellaceae, Enterobacteriaceae, and Fusobacteriaceae, coupled with a reduction in Firmicutes and Bifidobacterium populations (9, 33, 34). This microbial imbalance is closely associated with chronic intestinal inflammation, epithelial barrier disruption, and immune dysregulation. In colorectal cancer, dysbiosis is characterized by a reduction in overall microbial diversity and richness, alongside the selective enrichment of pathogenic species such as Fusobacterium nucleatum, Escherichia coli, and enterotoxigenic Bacteroides fragilis, all of which have been implicated in tumor initiation and progression through mechanisms involving inflammation, genotoxicity, and modulation of host immune responses (35, 36).

Emerging evidence indicates that gut microbial dysbiosis is not confined to the intestinal environment but may also exert significant influence on the oral microbiome. Clinical studies involving patients with inflammatory bowel disease have demonstrated measurable alterations in salivary microbial composition. These changes include an increase in the abundance of Actinobacteria and Proteobacteria at the phylum level, a decrease in Bacteroidetes, and elevated representation of genera such as Streptococcus, Rothia, and Actinomyces (37). These findings suggest that systemic inflammatory conditions associated with gut dysbiosis can extend their effects to the oral cavity, potentially through immune-mediated mechanisms or microbial translocation. Experimental models further support this bidirectional relationship. In animal studies involving colitis induced by Citrobacter rodentium infection or dextran sulfate sodium treatment, similar alterations in the oral microbiome have been observed, including increased salivary abundance of Betaproteobacteria, Lactobacillus, and Spirochetes (38). These findings reinforce the concept that intestinal inflammation can induce measurable shifts in oral microbial communities, indicating systemic microbial interconnectivity. Changes in the oral microbiome are also evident in patients with colorectal neoplasia. Individuals diagnosed with colorectal cancer exhibit increased oral microbial diversity alongside significant alterations in taxonomic composition. At the phylum level, there is an observed increase in Fusobacteria, Bacteroidetes, and Firmicutes, accompanied by a reduction in Absconditabacteria and Proteobacteria (39, 40). At the genus level, enrichment of Bacteroides, Streptococcus, and Desulfovibrio has been reported, while reductions in Porphyromonas and Prevotella are also observed (40). These microbial signatures suggest a complex restructuring of the oral ecosystem in response to underlying intestinal pathology. Consistent findings have been reported in colorectal cancer animal models, where increased oral alpha diversity and decreased abundance of genera such as Bacteroides, Gemella, and Streptococcus have been documented (41). Although these alterations in oral microbial composition are strongly associated with intestinal disease states, the causal direction of this relationship remains uncertain. It is not yet fully understood whether oral microbiome changes contribute to the initiation and progression of gut pathology or whether they arise as a secondary consequence of systemic disease processes. Clarifying this relationship is of significant clinical importance, as it may enable the development of salivary microbiota profiles as non-invasive predictive biomarkers for gastrointestinal disorders, thereby enhancing early diagnosis and disease monitoring strategies.

The connection between the oral and gut microbiomes

Bacteria

The human oral and gut microbiomes are increasingly recognized as interconnected microbial ecosystems that share notable taxonomic and functional similarities, despite being anatomically distinct. At the broad taxonomic level, both microbial communities are composed of several dominant bacterial phyla, including Firmicutes, Fusobacteria, Proteobacteria, Bacteroidetes, and Actinobacteria (8, 42). This shared phylogenetic structure reflects common evolutionary adaptations that allow these microorganisms to survive and thrive in mucosal environments characterized by fluctuating nutrient availability, host immune surveillance, and complex microbial competition. At a more refined taxonomic resolution, both the oral cavity and the gastrointestinal tract harbor overlapping bacterial genera, including Streptococcus, Veillonella, Actinomyces, and Haemophilus. Comparative microbiome analyses have identified as many as 125 bacterial species that are common to both sites, highlighting a substantial degree of microbial overlap between these two ecosystems (2). This overlap supports the concept of microbial continuity along the gastrointestinal tract, beginning in the oral cavity and extending to the distal gut. However, despite these shared taxonomic features, the relative abundance and ecological dominance of specific microbial taxa differ significantly between the two environments. The oral microbiome is characterized by a higher level of alpha diversity compared with fecal microbial communities, reflecting the greater environmental heterogeneity and continuous exposure to external factors such as food intake, saliva flow, and oxygen availability (43).

The presence of shared microbial taxa between the oral cavity and the gut is partly explained by the continuous microbial translocation that occurs under physiological conditions. Swallowed saliva and ingested oral bacteria regularly enter the gastrointestinal tract, where only a subset of these microorganisms are able to survive and integrate into the existing gut microbial ecosystem. Despite this continuous microbial influx, the overall contribution of oral-origin bacteria to the stable gut microbiota in healthy individuals remains relatively limited. Quantitative analyses have demonstrated that bacteria originating from the oral cavity constitute approximately 0.0 to 9.37 percent of the rectal microbiota in healthy subjects (44). This proportion suggests that while microbial passage from the oral cavity to the gut is frequent, successful colonization and long-term persistence are restricted by the competitive and selective environment of the intestinal microbiome. Among the oral-derived species detected in the gut, Streptococcus salivarius, Fusobacterium nucleatum subspecies vincentii, Streptococcus parasanguinis, and Fusobacterium nucleatum subspecies animalis have been identified as notable representatives (44). These findings indicate that only specific taxa with adaptive capabilities are able to transition between these ecological niches. The dynamics of oral-to-gut microbial transfer become significantly altered in pathological conditions, particularly in gastrointestinal diseases such as irritable bowel syndrome, inflammatory bowel disease, and colorectal cancer. In these disease states, the gut microbial ecosystem undergoes structural disruption, creating ecological niches that may facilitate colonization by oral-derived bacteria. Comparative microbiome studies have shown that in patients with ulcerative colitis and Crohn's disease, the gut microbiota exhibits a compositional shift toward an oral-like microbial profile. This includes increased abundances of Enterobacteriaceae, Fusobacteriaceae, Gemellaceae, Neisseriaceae, Proteobacteria, and Veillonellaceae, alongside a reduction in typically dominant gut-associated taxa such as Bacteroidales, Eubacterium, Firmicutes, and Lactobacillus (45). This transition reflects a loss of gut microbial stability and an increased presence of facultative anaerobes and inflammation-associated bacterial groups.

Further evidence supporting enhanced oral microbial colonization in intestinal disease is derived from analyses of colon tissue samples, which reveal an increased presence of pathogenic oral bacteria in diseased individuals compared with healthy controls. These oral-associated taxa include Aggregatibacter, Corynebacterium, Eubacterium, Fusobacterium, Gemella, Lactobacillus, Porphyromonas, Pseudomonas, Staphylococcus, Streptococcus, and Veillonella (46). The detection of these organisms within colonic tissue suggests not only transient passage but also potential tissue-level colonization or enrichment under disease conditions. This phenomenon may be facilitated by compromised intestinal barrier function, altered immune responses, and changes in the local microenvironment that favor the survival of oral-derived bacteria. A similar pattern of microbial enrichment is observed in colorectal cancer, where multiple oral taxa have been identified within tumor-associated microbiomes. Intratumoral microbial profiling has revealed significant enrichment of oral pathobionts, including Leptotrichia buccalis and Filifactor alocis, which have been associated with increased mortality risk in affected patients (47). The presence of these organisms within tumor tissue suggests a potential role in modulating tumor biology, either through direct interactions with epithelial cells, induction of inflammatory pathways, or alteration of local microbial ecology. Collectively, these findings provide strong evidence that ectopic colonization of oral bacteria within the gut increases significantly in

the context of inflammatory and neoplastic intestinal diseases. While in healthy individuals the contribution of oral microbiota to gut composition remains limited and tightly regulated, disease-associated disruption of gut homeostasis appears to facilitate microbial migration, survival, and proliferation of oral-origin taxa within intestinal and even tumor tissues. This altered microbial landscape may play an active role in disease progression by exacerbating inflammation, disrupting epithelial integrity, and modifying host immune responses. However, further research is required to determine the precise mechanistic pathways governing oral-to-gut bacterial translocation and to clarify whether these microbial changes represent causal drivers of disease or secondary consequences of an already disrupted intestinal environment.

Fungal microbiome

Fungi constitute a relatively minor yet functionally significant component of the human microbiome when compared with bacterial populations. In the oral cavity of healthy individuals, the fungal community, or mycobiota, is predominantly dominated by the genus Candida, which accounts for approximately seventy five percent of the total fungal population (48). Alongside Candida, other fungal genera commonly detected in the oral environment include Cladosporium, Aureobasidium, Saccharomyces, Aspergillus, Fusarium, and Cryptococcus, reflecting a diverse but low-abundance fungal ecosystem (48). Despite their limited numerical representation, these organisms contribute to ecological balance and microbial interactions within the oral niche. In disease conditions, the composition and diversity of the fungal microbiome undergo significant alterations in both the oral and intestinal environments. In the oral cavity, a reduction in fungal diversity has been observed alongside an increased abundance of the genus Pichia, which correlates with the severity of oral lesions (49). Patients with periodontitis exhibit an expanded range of fungal species in saliva, including opportunistic pathogens such as Candida parapsilosis and Candida zeylanoides, which are typically absent or present in minimal quantities in healthy individuals (50). Elevated levels of Candida species are associated with altered oral ecological conditions, particularly reduced pH, which contributes to the development and progression of dental caries by promoting enamel demineralization (49). Fungal organisms also interact closely with bacterial communities, contributing to microbial imbalance and disease progression through synergistic mechanisms. A notable example is the interaction between Candida albicans and Streptococcus oralis in the oral cavity, where their co-existence enhances biofilm formation, disrupts epithelial tight junction integrity, and increases tissue invasion capacity (51). These interactions illustrate the importance of inter-kingdom communication in shaping disease-associated microbial communities.

In the gut, fungal populations are primarily composed of members of the phyla Ascomycota and Basidiomycota, with Saccharomycetes and Saccharomycetales representing dominant taxonomic groups at class and order levels respectively (52). In inflammatory bowel disease, significant fungal dysbiosis is observed, characterized by an increased Basidiomycota to Ascomycota ratio, reduced abundance of Saccharomyces cerevisiae, and increased presence of pathogenic Candida species such as C. albicans, C. glabrata, and C. tropicalis (53). The abundance of C. albicans has been linked to both disease remission and relapse patterns, while C. tropicalis is associated with immune responses involving anti Saccharomyces cerevisiae antibodies, a recognized biomarker of Crohn's disease (49). Certain fungi may directly exacerbate intestinal inflammation through host immune interactions, as demonstrated by Candida famata, which impairs mucosal healing and aggravates inflammatory bowel disease via activation of the myeloid cell specific type I interferon CCL5 signaling axis (54). In colorectal cancer, alterations in gut mycobiota composition include depletion of Aspergillus kawachii and enrichment of species such as Aspergillus rambellii, Erysiphe pulchra, and Moniliophthora perniciosa (55). Under physiological conditions resembling the healthy distal gut environment, characterized by low oxygen tension, limited simple sugars, and a complex bacterial ecosystem, most fungal species are unable to establish stable long term colonization. The majority of intestinal fungi are transient and are introduced through dietary intake or salivary transfer (56). For example, Saccharomyces species may become undetectable in fecal samples when dietary sources are eliminated, highlighting their transient nature in the gut ecosystem (56). Oral fungi can significantly influence gut microbial balance, particularly under conditions of dysbiosis. Candida albicans has been shown to inhibit the growth of other fungal taxa, including Aspergillus, Cladosporium, and Bipolaris within the intestinal environment (57). In immunosuppressed murine models, C. albicans infection suppresses commensal saprophytic fungi such as Rhizopus, Mucor, and Penicillium, thereby further disrupting fungal homeostasis (58). Additionally, Aspergillus rambellii has been observed to co-enrich with pro tumorigenic bacterial species including Fusobacterium nucleatum, Parvimonas micra, and Gemella morbillorum, suggesting a synergistic role in carcinogenesis (48). Oral hygiene practices also influence fungal load, as increased frequency of tooth cleaning has been associated with significantly reduced levels of Candida albicans in stool samples (56). These findings highlight the dynamic relationship between oral and gut fungal communities and underscore the

need for further investigation into fungal mediated microbial interactions and their therapeutic potential. The viral component of the human microbiome, known as the virome, has received comparatively less scientific attention due to methodological challenges in detection and characterization. The virome is primarily composed of bacteriophages, which infect bacterial hosts, alongside a smaller proportion of eukaryotic viruses. In the oral cavity, particularly within subgingival plaque and saliva, the dominant viral families include Siphoviridae, Myoviridae, Podoviridae, and Herpesviridae (59). In contrast, the fecal virome is commonly dominated by bacteriophage families such as Podoviridae, Myoviridae, Siphoviridae, Autographiviridae, and Ackermannviridae (59).

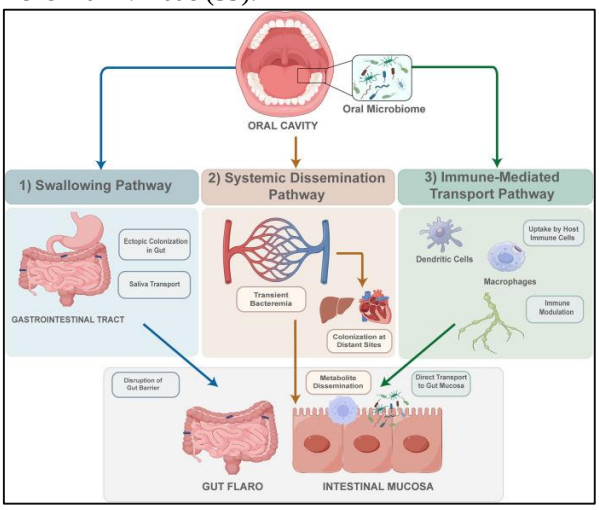

Fig. 1: Oral Microbiome migration mechanisms.

Virome

These viral populations play a critical role in regulating bacterial abundance, influencing microbial community structure, and modulating host physiological responses through indirect mechanisms. Evidence from experimental models suggests that viruses can significantly influence host immunity even in the absence of overt disease symptoms. Studies involving murine norovirus demonstrate that enteric viruses are capable of modulating immune responses without inducing gastrointestinal pathology such as diarrhea, indicating a regulatory role in immune homeostasis (60). Although the existence of a universally defined "healthy virome" remains under investigation, it is increasingly recognized that viral nucleic acid sensing contributes to intestinal immune balance and supports epithelial barrier integrity under physiological conditions. Alterations in virome composition are associated with both oral and intestinal diseases. In periodontitis, increased levels of Epstein Barr virus and cytomegalovirus have been observed, alongside a reduction in Siphoviridae within subgingival plaque communities (61). In inflammatory bowel disease, bacteriophages associated with Bacteroides fragilis are more prevalent, while ulcerative colitis is characterized by an enrichment of Caudovirales bacteriophages within the mucosal virome (54). In colorectal cancer and premalignant adenomas, viral communities show increased abundance of families such as Microviridae, Podoviridae crAss like, and Quimbyviridae, suggesting a potential association between viral dysbiosis and tumorigenesis (62).

Although direct evidence linking the oral and gut viromes remains limited, several studies indicate potential viral translocation and shared viral signatures between these anatomical sites. Increased prevalence of human polyomavirus has been associated with adenomatous polyposis, while elevated rates of beta human papillomavirus infections, including oncogenic genotypes such as HPV5, have been detected in colorectal cancer patients (63). These findings suggest possible oral to gut viral migration or shared susceptibility factors influencing viral colonization. In healthy individuals, certain phage families such as HB1 and HB2, associated with Firmicutes, are detected in both oral and fecal samples (64). During periodontitis, Pepyhexavirus has been observed to translocate from subgingival plaque to the gut environment, while parallel trends in viral abundance, including Alphabaculovirus, Marseillevirus, and Emaravirus, have been documented in both oral and intestinal niches (59). Correlation analyses further demonstrate associations between specific oral and gut viral taxa, such as a positive relationship between Bingvirus in the gut and Cheoctovirus in oral samples, alongside negative associations involving Pamexvirus, Kenoshavirus, and Pepyhexavirus (59). Bacteriophages play a central role in regulating microbial ecology through direct infection and modulation of bacterial populations. During disease states, the complexity of phage bacterial interaction networks is reduced in both oral and gut environments (65). Certain viral taxa in saliva, including Torbevirus, Cafeteriavirus, Emaravirus, Karamvirus, and Mufasoctovirus, show positive correlations with red complex bacterial genera, suggesting a role in periodontal pathogenicity (59). Experimental studies have demonstrated that phage mediated genetic modulation in bacteria, such as the CLB_P3 phage interaction with Escherichia coli, can influence biofilm formation and gene expression changes relevant to inflammatory bowel disease (66). In colorectal cancer, bacteriophages targeting Bacteroidaceae are enriched, whereas those infecting Bifidobacteriaceae are reduced, indicating selective viral pressure on bacterial communities (62). Overall, viral communities are not primary pathogens in most oral or gastrointestinal diseases, yet their composition and functional interactions shift significantly under pathological conditions. These changes suggest a regulatory role for the virome in shaping bacterial ecosystems and influencing disease progression.

Further research is required to elucidate the mechanistic pathways linking oral and gut viromes and to clarify their potential as diagnostic or therapeutic targets in microbiome related diseases.

Mechanisms

The oral and gut microbiomes interact through multiple biological routes that allow microbial transfer, signaling, and systemic effects. One primary mechanism is direct translocation of oral microorganisms into the gastrointestinal tract through swallowing. Saliva continuously introduces oral bacteria, fungi, and viral particles into the gut, where they may temporarily survive or integrate into existing microbial communities. A second route involves systemic dissemination. Inflammatory conditions in the oral cavity can disrupt epithelial integrity and permit oral microbes or microbial fragments to enter the bloodstream, producing transient bacteremia and enabling distant seeding to intestinal tissues. A third mechanism is immune cell–mediated transport. Oral pathogens can be internalized by dendritic cells and macrophages, which migrate through mucosal immune networks and deliver microbial antigens or viable organisms to the intestinal mucosa without requiring free circulation in blood. Once in the gut environment, oral microbes influence microbial ecology through ecological remodeling and metabolic reprogramming. They establish new microbial networks by integrating into biofilms and interacting with resident gut bacteria, which alters nutrient availability, oxygen gradients, and metabolic outputs. These interactions reshape fermentation pathways, including carbohydrate breakdown and short-chain fatty acid production, and modify nitrate, sulfur, and lipid metabolism. Oral-derived organisms also alter microbial competition by producing acids and antimicrobial compounds, favoring acid-tolerant and inflammation-adapted taxa. In parallel, phage and fungal interactions contribute to horizontal gene transfer, spreading virulence and antibiotic resistance traits across microbial populations. Immune modulation represents another central mechanism. Oral pathogens activate innate immune receptors such as Toll-like receptors and NOD-like receptors, triggering cytokine cascades and recruitment of neutrophils and T cells. This drives imbalance between pro-inflammatory and regulatory immune responses, particularly affecting Th17 and Treg equilibrium. Excess inflammatory signaling increases epithelial stress, promotes antimicrobial peptide release, and shifts microbial selection toward pathobionts that thrive under inflammatory conditions. Immune activation also enhances oxidative stress and neutrophil extracellular trap formation, further damaging microbial and epithelial balance. Barrier disruption is a fourth mechanism. Oral pathogens and their metabolites directly impair intestinal epithelial tight junctions, reduce mucus integrity, and degrade protective proteins such as mucins and antimicrobial peptides. This increases intestinal permeability and facilitates microbial invasion. In addition, secreted virulence factors such as proteases, toxins, extracellular vesicles, and cell wall components amplify tissue injury and systemic inflammation. These molecules can act independently of live bacteria, allowing distal effects even when microbial translocation is limited (67,68).

Treatment and Biomarkers:

Therapeutic strategies targeting the oral–gut microbial axis aim to restore microbial equilibrium, reduce inflammation, and reinforce barrier integrity. One of the most direct approaches is periodontal and oral hygiene intervention. Mechanical debridement, scaling, and periodontal therapy reduce the oral burden of pathogenic species and limit their migration to the gut. Clinical and experimental evidence shows that improving oral health can restore gut microbial diversity, increase beneficial short-chain fatty acid–producing bacteria, and reduce intestinal colonization by oral-origin pathogens. Antimicrobial therapy represents another intervention, although it requires careful application. Systemic or dental antibiotics may reduce pathogenic load in oral and intestinal environments, but they also risk disrupting commensal communities and promoting opportunistic infections. This is particularly relevant in individuals with pre-existing intestinal inflammation, where antibiotic exposure may trigger microbial imbalance and secondary complications. Probiotic and dietary interventions provide a non-invasive strategy to modulate both microbiomes. Probiotic organisms such as Lactobacillus and Bifidobacterium can compete with pathogenic species, restore metabolic balance, and enhance mucosal barrier function. Fermented foods and probiotic-rich diets support microbial diversity and reduce inflammatory signaling. Dietary regulation, particularly reduction of refined sugars and inflammatory substrates, limits the expansion of cariogenic and pro-inflammatory microbial taxa in both oral and intestinal ecosystems. Adjunctive approaches include modulation of microbial metabolites and host immunity. Targeting short-chain fatty acid imbalance, nitrate metabolism, and sulfur metabolism may help restore ecological stability. Immunomodulatory strategies aim to correct Th17 and Treg imbalance, reduce excessive cytokine release, and enhance regulatory immune responses. Strengthening mucosal immunity through IgA support and epithelial protection also helps maintain microbial containment at barrier sites. Emerging approaches focus on microbiome-based biomarkers and precision medicine. Salivary microbial signatures and metabolic profiles may be used for early detection of intestinal diseases and monitoring of treatment response. This allows non-invasive assessment and longitudinal tracking of disease activity. Future strategies may combine oral microbiome modulation with gut-targeted therapies

to achieve synchronized control of both ecosystems and reduce systemic inflammatory burden (69,70).

Conclusion:

The growing body of evidence demonstrates that the oral and gut microbiomes function as interconnected ecosystems whose balance is essential for systemic health. Disruption of the oral microbiota, particularly in conditions such as dental caries and periodontitis, contributes to gut dysbiosis by introducing pathogenic bacteria, fungi, and viruses that alter intestinal diversity, metabolic pathways, and immune responses. Conversely, gastrointestinal diseases such as inflammatory bowel disease and colorectal cancer exert measurable effects on oral microbial structure, reinforcing a bidirectional pathological axis. Mechanistic links involve microbial migration, epithelial barrier impairment, immune activation, and metabolic remodeling. Therapeutic interventions targeting oral hygiene, dietary modulation, probiotics, and immunoregulation show promise in restoring microbial equilibrium across both sites. Future research should prioritize precision microbiome therapies and biomarker development to enhance early disease detection, improve treatment outcomes, and support integrated oral–systemic health strategies.

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