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MICROBES IN YOUR MOUTH: THE HIDDEN PLAYERS IN HEALTH, SICKNESS, AND TOMORROW'S CURES

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ABSTRACT

Background: The oral microbiome holds a unique position among human microbial communities, featuring over 700 bacterial species along with fungi, viruses, archaea, and protozoa distributed across distinct ecological niches. Development begins prenatally and undergoes significant childhood transitions as tooth eruption creates new colonization sites. Multiple factors shape oral microbial communities, including host genetics, delivery mode, diet, smoking, oral hygiene, alcohol consumption, and antibiotic use.
Aim: This study aimed to comprehensively review the oral microbiome's complexity, development patterns, influencing factors, and associations with oral and systemic diseases.
Materials and Methods: A comprehensive literature review examined current evidence on oral microbiome composition, development, influencing factors, and disease associations.
Results: Oral microbiome dysbiosis manifests through reduced microbial diversity, depletion of beneficial organisms, and pathogenic species proliferation, contributing to dental caries, periodontal disease, and oropharyngeal cancers. Growing evidence links dysbiosis to systemic conditions including Alzheimer's disease, diabetes, cardiovascular diseases, and colorectal cancers through bacterial translocation and inflammatory pathways. The oral cavity's accessibility enables non-invasive sampling and development of microbial biomarkers for early disease detection.
Conclusions: This review highlights microbiome-focused interventions' potential to address disease at microbial roots rather than treating symptoms, creating cascading positive effects throughout the body. As the gateway to human health, the oral microbiome represents a critical frontier in modern medicine deserving increased research attention and investment.

KEYWORDS

Oral Microbiome, Dysbiosis, Oral Care, Oral Diseases, Periodontal Disease, Systemic Health

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1. Introduction:

In the late 1670s, Dutchman Antony van Leeuwenhoek used a handmade microscope to discover microbes in dental plaque, reporting their diversity to the British Royal Society. Fascinated by their movement, he noted individual differences in the oral microbiome that indicated their impact on oral health [1]. He has been called the father of microbiology and a pioneer who discovered both protists and bacteria [2]. However, it took hundreds of years after his discovery before we realized how essential the micro-organisms in our oral cavity are to our health. Furthermore, an imbalance in these microorganisms often leads to diseases of the mouth and other parts of the body.

The oral microbiome holds a distinctive position among human microbial communities due to several unique characteristics. Unlike other microbiomes, the oral cavity presents a series of highly specialized yet interconnected microbial habitats. As highlighted in the review by Baker et al. [3], the mouth contains remarkably diverse microenvironments - hard tooth surfaces both above and below the gumline, keratinized surfaces of the palate, gingiva and tongue papillae, and soft mucosal surfaces - each supporting distinct microbial communities. (**Fig. 1**) The normal temperature of the oral cavity on an average is 37°C without significant changes, which provides bacteria a stable environment to survive. Saliva also has a stable pH of 6.5–7, the favorable pH for most species of bacteria [4]. These areas stay wet due to saliva and, in some spots, gingival fluid, which supplies nutrients to the microorganisms living there. Teeth are particularly suited for the growth and development of complex biofilms. This biogeographical specialization is so pronounced that certain genera like Fusobacterium and Veillonella contain separate, distinct species that have evolved to specialize in either the tongue, dental plaque, or gums. Because of this environment the oral microbiome is highly diverse, featuring more than 700 bacterial species (Human Oral Microbiome Database), along with fungi, viruses, archaea, and protozoa [5].

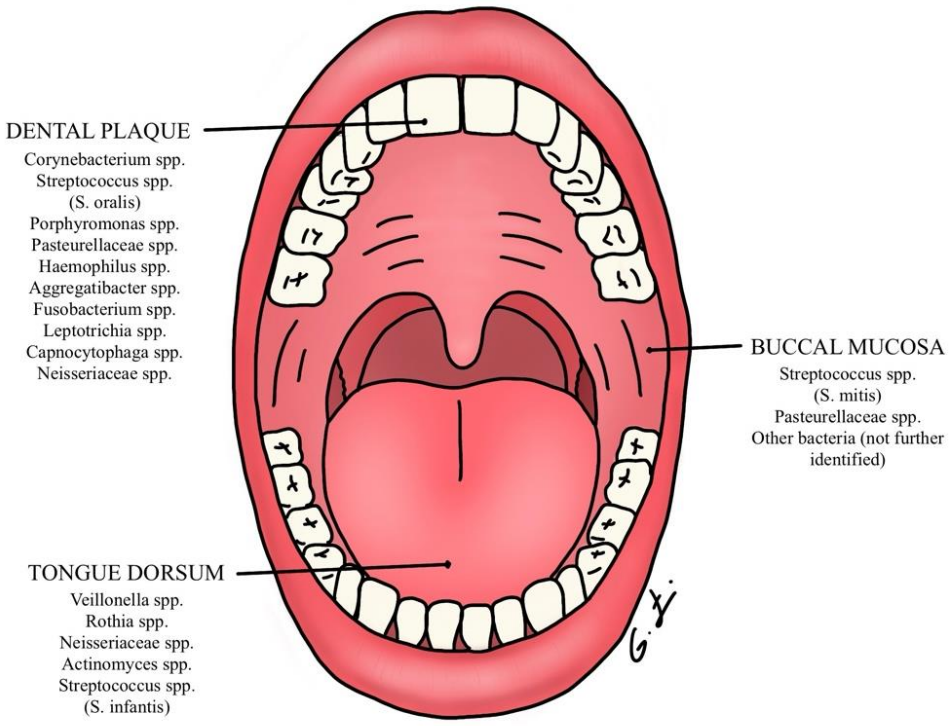

Fig. 1. *The oral microbiome exhibits remarkable biogeographical specialization, with specific bacterial taxa preferentially inhabiting distinct ecological niches. The figure highlights three primary habitats: dental plaque, buccal mucosa and tongue dorsum. [6, 7]*
Source: Author's own graphics, G.Łocik.

Recent metagenomic sequencing studies have revealed species-level distribution patterns that demonstrate remarkable site-specificity even among closely related bacteria. For example, different Streptococcus species show strong habitat preferences, with S. mitis predominantly found on buccal mucosa, S. oralis in dental plaque, and S. infantis on the tongue dorsum. [8] This biogeographical specialization reflects the different selective pressures, and nutritional environments present at each oral site, highlighting the complex ecological relationships within the oral microbiome.

In the past, scientists studied the oral microbiome using a method called 16S rRNA gene amplicon sequencing. This technique was great for finding bacteria but couldn't detect other types of microorganisms. Nowadays, thanks to technological advances - cheaper DNA sequencing, faster computers, and new bioinformatics tools - scientists can now use better methods like metagenomic sequencing and metatranscriptomic sequencing, which can find microorganisms that don't have 16S rRNA genes. This has opened the door to discovering much more about the oral microbiome [3].

Bacteria in the oral cavity are classified into several dozen genera, which are organized into seven major phyla: Actinomycetota (formerly Actinobacteria), Bacteroidota (Bacteroidetes), Bacillota (Firmicutes), Fusobacteriota (Fusobacteria), Pseudomonadota (Proteobacteria), Patescibacteria (Saccharibacteria, TM7), and Spirochaetota (Spirochaetes) (**Table 1**). This classification reflects the current taxonomic nomenclature, with former designations provided for clarity. The predominant bacterial species in the oral cavity are largely consistent across individuals. However, each person's oral microbiome exhibits unique characteristics due to several key factors: variations in relative abundance, strain-level differences and presence of rare species. These differences give rise to significant genetic diversity within the oral microbiome. Moreover, this unique microbial composition enables scientists to differentiate individuals based on their oral bacterial profiles [3].

In addition to bacteria, the oral microbiota encompasses a diverse array of microeukaryotes (fungi, amoebas, and flagellates), archaea, and viruses. Amplicon-based microbiome studies have identified over 100 genera of fungi in the oral cavity [3, 9-11], though far fewer are routinely detected [3, 9]. Individual oral

mycobiomes are typically dominated by either Candida [12-15] or Malassezia [9, 12, 16] species, which likely serve different ecological functions due to their distinct metabolic preferences—Candida primarily consuming sugars while Malassezia predominantly utilizes lipids [12].

Beyond fungi, the oral microbiome includes less-studied organisms. Archaea, amoeba and amitochondriate flagellates primarily inhabit periodontal pockets [3, 17-21]. Entamoeba gingivalis (amoeba) consumes live human cells, suggesting a direct pathological mechanism [17, 18]. Both amoebas and flagellates show strain-level variations affecting their disease potential [22]. Methanobrevibacter oralis is the predominant archaeal species in the oral cavity [23, 24]. Methanogenic archaea support fermentative bacteria by consuming hydrogen, potentially forming syntrophic relationships with Synergistes, Prevotella, and Veillonella [20]. Despite their lower abundance compared to bacteria, archaea and microeukaryotes likely have outsized ecological and pathogenic impacts due to their larger size and unique metabolic capabilities [3].

Most viruses in the oral microbiome are bacteriophages (phages) [3]. Recent advances in sequence databases, sequencing technology, and bioinformatics tools have dramatically expanded our understanding of oral phages, leading to the identification of more than 60,000 species-level groups in the oral microbiome [25]. Their influence is also evident through phage-targeting CRISPR spacer sequences found in oral bacterial genomes [26, 27]. A recent study of Porphyromonas gingivalis [28] revealed that many strains carry prophages (integrated phage genomes) in their DNA, while some P. gingivalis strains possess CRISPR spacers that likely protect against these same phages. This suggests phages play an important role in intraspecies competition within the oral microbiome. Limited studies indicate that oral phages can significantly impact overall community structure and interact with the human host [29, 30]. Beyond bacteriophages, research has identified viruses that target other microbiome members. The discovery of viruses infecting archaea [31], Entamoeba [32], Trichomonas [33] [34], and Malassezia [35] in other body sites suggests similar viruses likely exist for their oral counterparts. This has been confirmed with Redondoviridae [36], recently identified as viruses that infect Entamoeba gingivalis in the oral cavity [37]. Viruses can be also detected in saliva [38, 39]. Over 90% of people worldwide are chronically infected with Anelloviridae and Herpesviridae [40] viral families, which are commonly found in saliva [38, 41]. These persistent viral infections potentially influence overall immune function [40], emphasizing the importance of comprehensive approaches when studying how the oral microbiome impacts health, inflammatory processes, and disease development [3].

Table 1. This table presents a taxonomic organization of the major microorganisms found in the human oral microbiome, as compiled from the Human Oral Microbiome Database (HOMD v4). The data is structured hierarchically by phylum, genus, and representative species.

	Phylum	**Genus**	**Species**
1.	Actinomycetota	Actinomyces	graevenitzii massiliensis naeslundii oris sp. HMT-170
		Arachnia	rubra
		Corynebacterium	durum matruchotii
		Lancefieldella	parvula
		Peptidiphaga	sp. HMT-183
		Rothia	aeria dentocariosa mucilaginosa
		Schaalia	odontolytica sp. HMT-172 sp. HMT-240
2.	Bacteroidota	Alloprevotella	sp. HMT-473 tannerae
		Capnocytophaga	gingivalis leadbetteri ochracea sputigena
		Hoylesella	nanceiensis

		Porphyromonas	pasteri sp. HMT-930
		Prevotella	histicola intermedia jejuni melaninogenica pallens
		Riemerella	sp. HMT-322
3.	Bacillota	Gemella	haemolysans
		Granulicatella	elegans
		Megasphaera	micronuciformis
		Oribacterium	sinus
		Ruminococcaceae [G1]	bacterium HMT-075
		Streptococcus	australis gordonii infantis mitis oralis salivarius sanguinis
		Veillonella	atypica dispar parvula rogosae sp. HMT-779 sp. HMT-780
4.	Fusobacteriota	Fusobacterium	animalis periodonticum pseudoperiodonticum sp. HMT-248 vincentii
		Leptotrichia	sp. HMT-417
5.	Patescibacteria	Nanosynbacter	sp. HMT-352 sp. HMT-351
		Parvisynbacter	sp. HMT-348
		Saccharimonas	sp. HMT-346
6.	Pseudomonadota	Campylobacter	concisus
		Cardiobacterium	hominis
		Haemophilus	haemolyticus parainfluenzae sp. HMT-036
		Lautropia	dentalis mirabilis
		Neisseria	cinerea elongata flavescens mucosa perflava sicca subflava
7.	Spirochaetota	Treponema	denticola socranskii

2. Materials and methods:

We analyzed articles available in the published literature dealing with the topic of the oral microbiome. The most important issues concerning the development, dysbiosis and diseases associated with the oral microbiome are gathered and discussed below. We used AI tools to grammatically correct text.

3. Development of the oral microbiome

3.1. Oral bacterial community

The oral microbiome undergoes significant development from birth through early childhood. Pre-natal microbial exposure begins in the womb, with studies detecting oral microorganisms such as Streptococcus, Fusobacterium, Neisseria, Prevotella, and Porphyromonas in the human placenta [42-44]. At birth, initial colonization occurs through maternal transmission during childbirth, with the newborn's oral cavity acquiring microbes from the mother's vaginal, skin, and oral microbiomes. The earliest oral colonizers include Streptococcus (particularly S. epidermidis and S. salivarius), Staphylococcus, and Fusobacterium, followed by Gemella, Granulicatella, Haemophilus, and Rothia at 3-6 months [43, 45]. During the first few months of life, the mouth consists exclusively of mucosal surfaces for microbial colonization [46]. A major ecological shift occurs with the eruption of primary teeth, creating new binding sites and niches for microorganisms like Streptococcus mutans [47]. The emergence of these hard, non-shedding surfaces provides a unique environment in the body for microbial colonization and introduces another crucial habitat—the gingival crevice (where teeth emerge from the gums). This development also brings an additional nutrient source through gingival crevicular fluid (GCF). Unlike mucosal surfaces elsewhere in the body that undergo regular desquamation and maintain relatively light microbial loads, teeth allow the accumulation of large masses of microorganisms and their extracellular products, collectively termed dental plaque, especially at stagnant or retentive sites [46]. Post-tooth eruption, distinct communities form at different oral sites (tongue, gums, dental plaque), with microbial diversity steadily increasing throughout childhood [43, 47]. Ecological conditions within the mouth continue to be influenced by additional factors including the eruption and loss of teeth, dental treatments, insertion of prostheses, fluctuations in diet, antibiotic therapy, and variations in saliva composition and flow [46]. By age 7, nearly 550 operational taxonomic units can be identified in the oral cavity, demonstrating the remarkable complexity of this ecosystem that continues to develop throughout childhood [43, 45]. Despite these various transitions and perturbations, the composition of the microflora at each site generally remains relatively stable over time through microbial homeostasis [46].

3.2. Oral fungal community

The oral cavity harbors a complex fungal community (mycobiome) in addition to its bacterial inhabitants. Fungi, particularly Candida species, colonize the oral cavity of neonates from the first day of life, with colonization rates ranging from 40% to 82% during the first year depending on population characteristics and detection methodologies [43, 48]. Metagenomic analyses have expanded our understanding beyond Candida, with one seminal study identifying 74 cultivable and 11 uncultivable fungal genera in healthy adult oral cavities [11, 43]. While Candida remains predominant (detected in 75% of subjects), other fungi including Cladosporium (65%), Aureobasidium (50%), Saccharomycetales (50%), Aspergillus (35%), Fusarium (30%), and Cryptococcus (20%) demonstrate substantial prevalence [11, 43]. Recent amplicon sequencing of ITS2 regions has revealed that infant oral mycobiomes exhibit significantly lower alpha diversity compared to skin and anal mycobiomes, with notable intra-individual variability over time [43, 49]. The predominant taxa in infant oral cavities include C. parapsilosis, C. tropicalis, S. cerevisiae, C. orthopsilosis, and C. albicans. Despite these advances, the longitudinal development and functional significance of the oral mycobiome in early childhood remain underexplored, presenting a critical knowledge gap in our understanding of oral ecosystem dynamics [43].

3.3. Oral viral community

The oral virome represents an understudied yet integral component of the oral microbiome, with contemporary research indicating that each individual harbors between 300 and 2,000 viral genotypes within their oral cavity [43, 50]. Despite its significance, the characterization of the oral virome lags considerably behind bacterial and fungal community analyses, constituting a notable research disparity in oral microbial ecology. Metagenomic investigations have identified diverse viral populations including pathogenic viruses (rotavirus, norovirus, HIV, hepatitis C virus), herpesviruses (HSV1, HSV2, Epstein-Barr virus), and less

abundant constituents such as eukaryotic DNA viruses (herpesvirus HPV7, Anelloviruses) and RNA viruses [43, 51, 52]. In pediatric populations, viral manifestations demonstrate age-dependent clinical severity, with neonatal HSV infections occurring at rates of 1.6–33 per 100,000 live births and potentially resulting in severe outcomes due to immature immune function [43, 53, 54]. Additional viral agents that colonize the oral cavity during early childhood development include Coxsackie A virus, Morbillivirus, Rubulavirus, and human papillomavirus, each associated with distinct clinical presentations [43, 55]. Elucidating the temporal dynamics and functional implications of these viral communities remains a critical frontier in comprehensive oral microbiome research.

4. Factors shaping oral microbiome

The development and composition of the oral microbiome are influenced by multiple host and environmental factors. Host genetic determinants play a significant role, with genome-wide association studies identifying loci near genes such as IMMPL2 and INHBA-AS1 that influence microbial colonization patterns [43, 56]. Twin studies have demonstrated increased similarity in oral microbiota with shared host genotypes, with certain bacterial taxa showing heritable traits [43, 57]. Developmental factors also shape the oral microbiome, with differential colonization patterns observed between infants born via vaginal delivery versus cesarean section; the former resembling maternal vaginal communities (predominantly Lactobacillus, Prevotella, and Bacteroides), while the latter mirror maternal skin microbiota (predominantly Staphylococcus, Corynebacterium, and Propionibacterium) [43, 58]. Feeding methods further differentiate oral microbial communities, with breastfed infants exhibiting lower species richness at 4 months compared to formula-fed counterparts, though these differences often diminish by 12 months of age [43, 59]. Notably, maternal transmission represents a critical pathway for microbial acquisition, with studies indicating that approximately 95% of the infant's oral microbiome is shared with maternal microbiomes by day 3 of life [43, 60]. These maternal influences persist throughout early childhood development, though their impact gradually decreases following primary tooth eruption, suggesting that dental surfaces create new ecological niches for microbial colonization [43, 61].

5. The cause of oral microbial dysbiosis

Microbial dysbiosis manifests in three potential scenarios that can occur independently or in combination: reduced microbial diversity, depletion of beneficial microorganisms, and proliferation of pathogenic microorganisms [62]. The oral microbiome can be altered by numerous factors, including dietary patterns, tobacco use, areca nut chewing, alcohol consumption, inadequate oral hygiene, psychological stress, hormonal fluctuations, diabetes, and periodontitis [63]. Some of the major factors that contribute to oral microbiome dysbiosis are discussed in detail below, including their mechanisms of action and impact on microbial community structure and function.

5.1. Diet

Diet serves as a selective pressure on the oral microbiome, favoring the survival and replication of organisms best adapted to utilize specific food resources [64, 65]. The shift toward a "Westernized" dietary pattern characterized by farmed animal meats, high-sugar dairy products, refined vegetable oils, and processed grains has been accompanied by pathological changes in oral microbiota [64, 66, 67]. Specifically, consumption of refined carbohydrates promotes the growth of saccharolytic microbes like Streptococcus, Actinomyces, and Veillonella, which can cause demineralization of dental enamel through acid production [64, 68, 69]. As periodontal pockets deepen during disease progression, protein-rich environments create favorable conditions for proteolytic bacteria, further disrupting the microbiome balance and promoting inflammation [64, 70].

Research demonstrates that diet significantly impacts the oral microbiome composition beyond mere surface interactions [71]. Studies have shown that certain dietary components like medium chain fatty acids, omega-3 polyunsaturated fatty acids, and dietary fiber are associated with differences in oral bacterial diversity, community structure, and relative abundance of specific species [71]. The oral microbiota of vegans and omnivores differs significantly, with distinct operational taxonomic units (OTUs) present in each group, suggesting that long-term dietary patterns shape microbial communities in the mouth just as they do in the gut [72, 73]. Specifically, vegans tend to have higher abundance of upper respiratory tract commensals like Neisseria subflava, Haemophilus parainfluenzae, Rothia mucilaginosa, and Capnocytophaga spp., and Prevotella melaninogenica and Streptococcus spp. which were more abundant in omnivores. Campylobacter rectus and Porphyromonas endodontalis, species associated with periodontal disease, were also more abundant in vegans [71]. These differences extend to the genomic potential of the oral microbiome, with vegans showing enriched pathways for carbohydrate metabolism and short-chain fatty acid production compared to omnivores [71].

5.2. Smoking

Smoking alters the oral microbiome by depleting beneficial species and promoting pathogen colonization, ultimately leading to disease [74]. Studies show that smokers have less numerous Neisseria species or Branhamella compared to non-smokers, with distinct clustering of microbial communities based on smoking status [75, 76]. Smokers demonstrate a highly diverse, pathogen-rich, commensal-poor, anaerobic microbiome that is more closely aligned with disease-associated communities in clinically healthy individuals [77]. Research has found that processed tobacco leaves harbor diverse bacterial species including Agrobacterium, Arthrobacter, Bacillus, Klebsiella, Paenarthrobacter, Pseudomonas, and Pseudarthrobacter, which are introduced into the oral cavity during tobacco consumption and contribute to microbiota alterations [78]. Additionally, carcinogenic tobacco-specific nitrosamines present in tobacco products can significantly disrupt the normal microbial balance in a healthy oral environment [79]. Smoking contributes to oral dysbiosis through immunosuppression, oxygen deprivation, biofilm formation, and direct contact with microbes contained in tobacco products [80]. The altered oral microbiome in smokers is associated with increased risk of periodontitis [81] and may potentially be linked to systemic conditions like infective endocarditis [74, 82] and certain cancers [83-86].

5.3. Oral hygiene

Oral hygiene practices are probably the single greatest factor that has shaped the oral microbiome of modern human, with the goal of these procedures being to maintain plaque biofilm in an immature state with high proportions of early bacterial colonizers, which are mostly aerobic or facultative species [87]. The excessive proliferation of oral microbes due to poor oral hygiene can disturb the oral microbial ecology [88]. Different approaches to oral hygiene have been recommended, including prompt rinsing following food consumption, consistent flossing, and routine toothbrushing, nonetheless, traditional brushing with toothpaste remains the most strongly endorsed practice for oral health maintenance [89]. The balance of microorganisms in the oral cavity can be continuously preserved when cleaning techniques are executed comprehensively and according to proper timing schedules [90].

Studies have shown that certain mouthwashes like chlorhexidine can cause "dysbiosis" by killing beneficial bacteria such as Veillonella, Actinomyces, Haemophilus, Rothia, and Neisseria while allowing potentially harmful bacteria to predominate [91]. Research demonstrates that chlorhexidine decreases bacterial diversity in saliva and on the tongue, which may reduce the oral microbiome's ability to reduce dietary nitrates to nitrite, negatively impacting cardiovascular health [91]. Hydrogen peroxide slightly decreased plaque concentrations of obligate anaerobes associated with periodontal disease [92], but showed little antimicrobial action against Streptococcus mutans, the organism associated with dental caries [93]. Cetylpyridinium chloride was effective in reducing plaque and anaerobic species in plaque and saliva [94], with one study showing that it prevented increases in periodontal pathogens during experimental gingivitis [95]. Alcohol in mouthwashes can indiscriminately kill both beneficial and harmful bacteria, decreasing the abundance of commensal bacteria while increasing the abundance of certain genera containing oral pathogens [96].

5.4. Alcoholic beverage consumption

Research indicates that alcohol consumption significantly alters oral microbial communities, with heavy drinkers showing increased bacterial diversity and distinct community profiles compared to non-drinkers [96]. A large study of American adults found that alcohol consumption is associated with decreased abundance of beneficial Lactobacillales, which produce lactic acid and have antimicrobial properties, while potentially pathogenic bacteria including Actinomyces, Leptotrichia, Cardiobacterium, and Neisseria were enriched in drinkers [96]. Notably, Neisseria can convert ethanol to acetaldehyde, a known human carcinogen [97], while alcohol simultaneously reduces Lactobacillus bacteria that typically help metabolize acetaldehyde to less toxic compounds [98]. These alcohol-induced changes to the oral microbiome may contribute to alcohol-related diseases, including periodontitis, head and neck cancer, and digestive tract cancers. Different alcoholic beverages appear to affect the oral microbiome differently, with wine drinkers showing increased bacterial richness and altered microbial profiles compared to non-drinkers, while beer and liquor consumption were associated with different bacterial signatures.

In another study of Chinese individuals found that genus Prevotella and Moryella, and species Prevotella melaninogenica and Prevotella tannerae were significantly enriched in drinkers, while the genus Lautropia, Haemophilus and Porphyromonas, and species Haemophilus parainfluenzae were significantly depleted [99]. The study also revealed that alcohol drinking may affect metabolism pathways, with oxygen-independent

pathways (including galactose, fructose and mannose metabolism) [100] enriched in drinkers, while aerobic metabolism pathways like pyruvate metabolism [101] were decreased [99]. These findings suggest alcohol consumption may create an oxygen-starved environment in the oral cavity that favors the growth of certain potentially pathogenic bacteria [99].

5.5. Areca nut chewing

Based on Drucker and al. research [102], areca nut chewers show significant changes in their oral microbiome compared to non-chewers. The areca nut contains several alkaloids, including arecoline, arecaidine, guvacine, and guvacoline [103]. When chewed, these undergo nitrosation to form N-nitrosamine, which is cytotoxic [104]. There's a notable reduction in beneficial Streptococcus bacteria in chewers, while potentially harmful bacteria like Rothia dentocariosa, Actinomyces, and Prevotella show higher prevalence [102]. These microbiome shifts lead to less similarity between oral microbiomes of different betel nut chewers compared to the more uniform microbiomes of non-chewers.

5.6. Antibiotics

Antibiotics have profound and often long-lasting effects on the oral microbiome through several mechanisms. Antibiotics cause immediate disruption to the microbial community by selectively killing susceptible bacteria while allowing resistant species to flourish. As shown in Petersen & Round review [62], different antibiotics target specific bacterial populations. For example, amoxicillin significantly reduces diversity of Bifidobacterium species [105] and causes loss of Lactobacillus, Enterococcus and Enterobacteriaceae communities [106], while vancomycin causes widespread reduction to the microbiota [107], loss of Lactobacillus, Enterococcus, and Group D Streptococcus communities [108], and expansion of Enterobacteriaceae species [108]. Studies have shown that antibiotics often lead to fungal overgrowth, particularly Candida species, since fungi are not susceptible to antibacterial agents [62, 109]. Research by Gomez-Arango et al. [110] demonstrates that even maternal intrapartum antibiotics can shape the initial oral microbiome of neonates, with exposed infants showing higher abundance of potentially pathogenic Proteobacteria and decreased levels of beneficial bacteria like Streptococcaceae and Gemellaceae.

6. Diseases

6.1. Dental caries

Dental caries results from dysbiosis of the oral microbiome characterized by biofilm-forming, acid-producing, and acid-tolerant species [3], though contrary to historical belief, Streptococcus mutans is not required for caries development but contributes significantly when present due to its ability to generate extracellular glucans from sucrose [111-113]. Modern microbiome analysis has revealed a more complex ecological understanding, identifying other contributors like lactobacilli, Veillonella species [114], Candida albicans, Epstein-Barr virus, and Prevotella species in caries pathogenesis [113, 115].Conversely, nitrate-reducing bacteria (Rothia, Neisseria, and Haemophilus) are associated with good dental health [113, 116, 117], leading to exploration of nitrate and these bacteria as potential prebiotics and probiotics for caries prevention [117-119]. As dental caries remains the most common chronic infectious disease globally, these ecological insights could lead to new preventive approaches that complement traditional oral hygiene and fluoride treatments [67, 111].

6.2. Periodontal disease

Periodontal disease represents an inflammatory disruption in host-microbial homeostasis of the periodontal pocket, where healthy homeostasis is maintained through an active inflammatory surveillance state balancing subgingival microorganisms with host immune responses [120]. If this balance is disrupted, it can progress from gingivitis (a reversible condition) to periodontitis (characterized by irreversible bone resorption) [121], with modern single-cell RNAseq approaches identifying specific inflammatory host cell populations that enhance neutrophil recruitment and antimicrobial defenses [122]. Recent microbiome analyses have expanded our understanding beyond canonical periodontal pathogens (Porphyromonas, Treponema, and Tannerella species) to include potential new pathogens like Filifactor alocis, Peptoanaerobacter stomatis, and Saccharibacteria [123], while also revealing novel species correlations and the role of the virome [124, 125]. The experimental gingivitis model serves as a unique human model for studying microbially induced inflammation, allowing researchers to observe the transition from health to disease and back. A landmark study

using this model identified three distinct inflammatory responder types—high, low, and slow—each with unique microbial and host signatures, with slow responders maintaining high abundance of Streptococcus species (S. sanguinis and S. oralis) [126]. These findings suggest the importance of both microbial and human host immune phenotypes in disease outcomes, potentially enabling personalized treatment and intervention strategies for periodontal disease.

6.3. Oropharyngeal cancers

The oral microbiome dysbiosis contributes to oral cancer through multiple destructive mechanisms [127]. First, certain bacteria and fungi produce carcinogenic metabolites like acetaldehyde (S. gordonii, S. mitis, S. oralis, S. salivarius, S. sanguinis, and Candida [128, 129]) and nitrosamines (Bacteroides and Firmicutes species [130]) that directly damage DNA and promote neoplastic transformation. Second, dysbiotic microbiota trigger chronic inflammation, creating a self-perpetuating cycle where inflammatory mediators (cytokines, ROS, RNS) cause DNA damage and alter the tumor microenvironment [131-134]. Third, specific pathogens like P. gingivalis inhibit natural cell death by suppressing apoptotic pathways, allowing abnormal cells to persist [135]. Fourth, certain oral bacteria (P. gingivalis [136, 137], Treponema denticola [138]) suppress immune responses, enabling cancer cells to evade detection. Finally, oral pathogens (P. gingivalis [135], Treponema denticola [139], Tannerella forsythia [140]) facilitate tumor invasion by activating enzymes that degrade the basement membrane and extracellular matrix, while also increasing nutrient supply to tumor cells.

Distinctive oral microbiota signatures can serve as non-invasive biomarkers for oral cancer detection, including bacterial indicators (Enterobacteriaceae, Oribacterium [84], Capnocytophaga gingivalis, Prevotella melaninogenica, and Streptococcus species [141]), viral markers (HPV [142, 143] and EBV[144], which increase cancer risk 2.82 and 2.5 times respectively), and fungal biomarkers (particularly Candida albicans [145, 146], which increases oropharyngeal cancer risk more than 3-fold).

Remodeling the oral microbiome shows therapeutic potential for oral cancer, as evidenced by the success of microbiota transplantation in other conditions and beneficial effects of commensal bacteria like Lactobacilli and Bifidobacteria [147-149], which can reduce carcinogenic metabolites, modulate immune responses [150], induce apoptosis, and prevent DNA damage through anti-oxidation activities [151].

6.4. Systemic diseases

Research indicates growing links between the oral microbiota and numerous systemic diseases, where particularly periodontal pathogens like P. gingivalis, A. actinomycetemcomitans, and F. nucleatum relate to Alzheimer's disease, diabetes, cardiovascular diseases, colorectal cancers, inflammatory bowel disease, rheumatoid arthritis, nonalcoholic fatty liver disease and obesity (**Fig. 2**) [3]. The periodontal microbiota affects distant organs through two main, often synergistic mechanisms: direct translocation of bacteria to distant sites and indirect effects of dysbiotic microbial communities in the oral cavity. Translocation of oral bacteria to the lungs can lead to aspiration pneumonia [152], while colonization of the gastrointestinal tract is associated with inflammatory bowel disease [153, 154] and colorectal cancer, where F. nucleatum uses specific molecular mechanisms to accelerate tumor development [155, 156]. Periodontal disease breaches epithelial barriers, allowing bacteremia to spread microorganisms to bone marrow, cardiovascular tissues, brain, and liver, where they cause inflammation and organ dysfunction. P. gingivalis, through its enzymes (gingipains), degrades tau proteins in the brain contributing to Alzheimer's disease [157] and weakens the barrier functions of vascular endothelium increasing the risk of cardiovascular diseases [158]. Periodontal pathogens can also act indirectly, for example by promoting citrullination of host proteins associated with rheumatoid arthritis [159, 160], or by stimulating T cells that migrate to the intestines and exacerbate inflammatory conditions [154, 161]. Importantly, the relationships between periodontal diseases and systemic disorders are bidirectional—systemic diseases weaken the immune barrier of the oral cavity, increasing susceptibility to periodontal diseases, creating a positive feedback loop that increases morbidity [162]. Despite numerous pieces of evidence, many connections have only been studied in animal models, and inter-individual variability presents a significant challenge for future human studies [126].

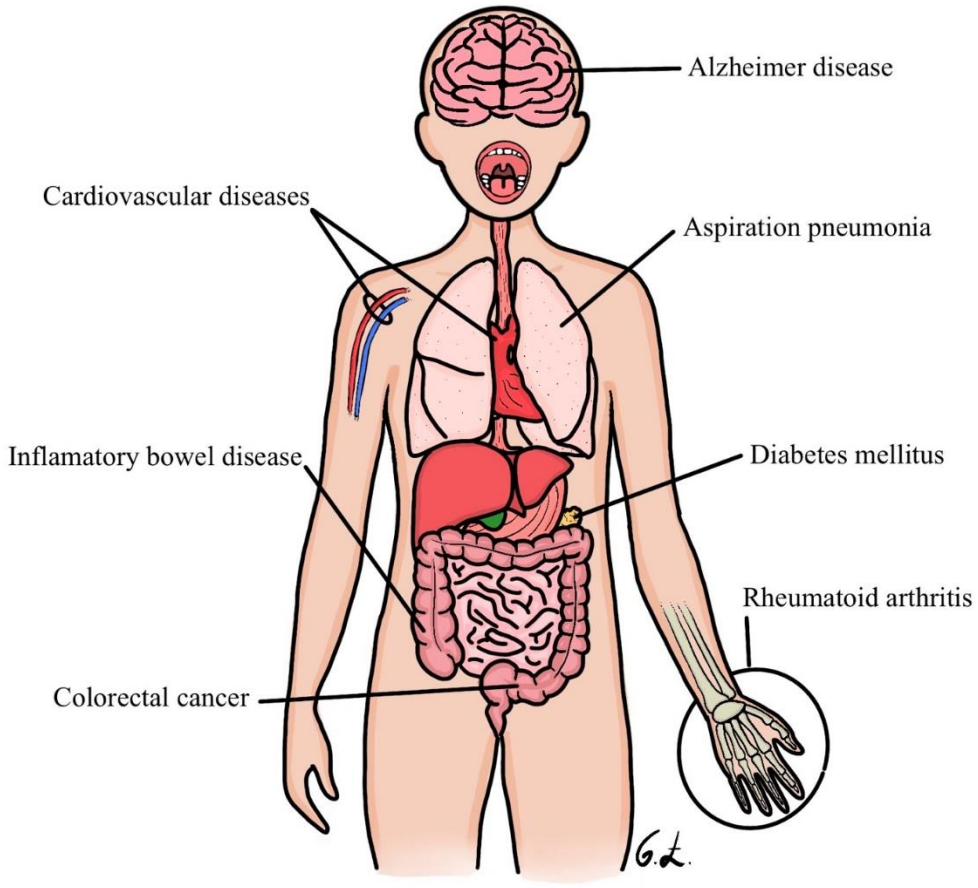

Fig. 2. *This diagram illustrates how oral microbiome dysbiosis impacts multiple body systems. Source: Author's own graphics, G.Łocik.*

Oral pathogens can spread throughout the body, contributing to Alzheimer's disease through P. gingivalis enzymes that degrade tau proteins [157], cardiovascular diseases via bacteria entering the bloodstream [158], and aspiration pneumonia through direct bacterial translocation to lungs [152]. In the digestive system, pathogens like F. nucleatum promote inflammatory bowel disease [153, 154] and colorectal cancer [155, 156]. The relationship with diabetes mellitus is bidirectional—periodontal inflammation worsens glycemic control while hyperglycemia promotes dysbiosis [163]. Periodontal pathogens also contribute to rheumatoid arthritis through protein citrullination triggering autoimmune responses [159, 160]. This visualization emphasizes the critical role of oral microbiome balance in overall health.

7. Conclusions

The oral microbiome represents a critical frontier in modern medicine that demands our urgent attention and increased research investment. As the gateway to our body and a mirror of our overall health, disruptions in this complex ecosystem have now been conclusively linked to not only local conditions like periodontitis and oral cancer, but also to devastating systemic diseases including Alzheimer's, diabetes, cardiovascular disease, and various malignancies. The accessibility of the oral cavity offers unparalleled opportunities for non-invasive sampling and early disease detection through microbial signatures—potentially revolutionizing our approach to preventive healthcare. By deepening our understanding of oral dysbiosis mechanisms, we could develop targeted probiotics, personalized antimicrobial therapies, and microbiome restoration techniques that address disease at its microbial roots rather than merely treating symptoms. The economic burden of treating advanced conditions that begin with oral dysbiosis runs into billions annually, making preventive approaches based on microbiome science not just medically sound but economically imperative. Most compelling is the remarkable possibility that by addressing oral health through microbiome-focused interventions, we might simultaneously prevent or mitigate multiple systemic conditions, creating a cascading positive effect throughout the body. The time has come to recognize oral microbiome research not as a niche specialty but as a cornerstone of comprehensive healthcare that could transform how we diagnose, treat, and ultimately prevent some of our most challenging medical conditions.

Disclossure

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REFERENCES

1. Yamashita, Y. and T. Takeshita, The oral microbiome and human health. J Oral Sci, 2017. 59(2): p. 201-206.https://doi.org/10.2334/josnusd.16-0856
2. Lane, N., The unseen world: reflections on Leeuwenhoek (1677)'Concerning little animals'. Philosophical Transactions of the Royal Society B: Biological Sciences, 2015. 370(1666): p. 20140344.https://doi.org/10.1098/rstb.2014.0344
3. Baker, J.L., et al., The oral microbiome: diversity, biogeography and human health. Nat Rev Microbiol, 2024. 22(2): p. 89-104.https://doi.org/10.1038/s41579-023-00963-6
4. Lim, Y., et al., Oral microbiome: a new biomarker reservoir for oral and oropharyngeal cancers. Theranostics, 2017. 7(17): p. 4313.https://doi.org/10.7150/thno.21804
5. Santacroce, L., et al., Oral microbiota in human health and disease: A perspective. Experimental Biology and Medicine, 2023. 248(15): p. 1288-1301.https://doi.org/10.1177/15353702231187645
6. Mark Welch, J.L., F.E. Dewhirst, and G.G. Borisy, Biogeography of the oral microbiome: the site-specialist hypothesis. Annual review of microbiology, 2019. 73(1): p. 335-358.https://doi.org/10.1146/annurev-micro-090817-062503
7. Mark Welch, J.L., S.T. Ramírez-Puebla, and G.G. Borisy, Oral Microbiome Geography: Micron-Scale Habitat and Niche. Cell Host Microbe, 2020. 28(2): p. 160-168.https://doi.org/10.1016/j.chom.2020.07.009
8. McLean, A.R., et al., Site-tropism of streptococci in the oral microbiome. Molecular oral microbiology, 2022. 37(6): p. 229-243.https://doi.org/10.1111/omi.12387
9. Diaz, P. and A. Dongari-Bagtzoglou, Critically appraising the significance of the oral mycobiome. Journal of Dental Research, 2021. 100(2): p. 133-140.https://doi.org/10.1177/0022034520956975
10. Diaz, P.I., et al., Mining the oral mycobiome: methods, components, and meaning. Virulence, 2017. 8(3): p. 313-323.https://doi.org/10.1080/21505594.2016.1252015
11. Ghannoum, M.A., et al., Characterization of the Oral Fungal Microbiome (Mycobiome) in Healthy Individuals. PLoS Pathogens, 2010. 6(1): p. e1000713.https://doi.org/10.1371/journal.ppat.1000713

12. Hong, B.-Y., et al., The salivary mycobiome contains 2 ecologically distinct mycotypes. Journal of dental research, 2020. 99(6): p. 730-738.https://doi.org/10.1177/0022034520915879
13. Ahmad, K.M., et al., Genome structure and dynamics of the yeast pathogen Candida glabrata. FEMS yeast research, 2014. 14(4): p. 529-535.https://doi.org/10.1111/1567-1364.12145
14. Turner, S.A. and G. Butler, The Candida pathogenic species complex. Cold Spring Harbor perspectives in medicine, 2014. 4(9): p. a019778.https://doi.org/10.1101/cshperspect.a019778
15. Gabaldón, T., et al., Comparative genomics of emerging pathogens in the Candida glabrata clade. BMC genomics, 2013. 14: p. 1-16.https://doi.org/10.1186/1471-2164-14-623
16. Dupuy, A.K., et al., Redefining the human oral mycobiome with improved practices in amplicon-based taxonomy: discovery of Malassezia as a prominent commensal. PLoS One, 2014. 9(3): p. e90899.https://doi.org/10.1371/journal.pone.0090899
17. Bao, X., et al., Entamoeba gingivalis exerts severe pathogenic effects on the oral mucosa. Journal of Dental Research, 2021. 100(7): p. 771-776.https://doi.org/10.1177/00220345211004498
18. Bao, X., et al., Entamoeba gingivalis causes oral inflammation and tissue destruction. Journal of dental research, 2020. 99(5): p. 561-567.https://doi.org/10.1177/0022034520901738
19. Bonner, M., et al., Reassessing the Role of Entamoeba gingivalis in Periodontitis. Frontiers in cellular and infection microbiology, 2018. 8: p. 379.https://doi.org/10.3389/fcimb.2018.00379
20. Belmok, A., et al., The oral archaeome: a scoping review. Journal of Dental Research, 2020. 99(6): p. 630-643.https://doi.org/10.1177/0022034520910435
21. Lepp, P.W., et al., Methanogenic Archaea and human periodontal disease. Proceedings of the national academy of sciences, 2004. 101(16): p. 6176-6181.https://doi.org/10.1073/pnas.0308766101
22. García, G., et al., A new subtype of Entamoeba gingivalis:“E. gingivalis ST2, kamaktli variant”. Parasitology research, 2018. 117: p. 1277-1284.https://doi.org/10.1007/s00436-018-5798-6
23. Deng, Z.-L., et al., Dysbiosis in chronic periodontitis: key microbial players and interactions with the human host. Scientific reports, 2017. 7(1): p. 3703.https://doi.org/10.1038/s41598-017-03804-8
24. Vianna, M., et al., Quantitative analysis of three hydrogenotrophic microbial groups, methanogenic archaea, sulfate-reducing bacteria, and acetogenic bacteria, within plaque biofilms associated with human periodontal disease. Journal of bacteriology, 2008. 190(10): p. 3779-3785.https://doi.org/10.1128/jb.01861-07
25. Camargo, A.P., et al., IMG/VR v4: an expanded database of uncultivated virus genomes within a framework of extensive functional, taxonomic, and ecological metadata. Nucleic acids research, 2023. 51(D1): p. D733-D743.https://doi.org/10.1093/nar/gkac1037
26. Münch, P.C., et al., Identification of natural CRISPR systems and targets in the human microbiome. Cell host & microbe, 2021. 29(1): p. 94-106. e4.https://doi.org/10.1016/j.chom.2020.10.010
27. Yahara, K., et al., Long-read metagenomics using PromethION uncovers oral bacteriophages and their interaction with host bacteria. Nature communications, 2021. 12(1): p. 27.https://doi.org/10.1038/s41467-020-20199-9
28. Matrishin, C.B., et al., Phages are unrecognized players in the ecology of the oral pathogen Porphyromonas gingivalis. Microbiome, 2023. 11(1).https://doi.org/10.1186/s40168-023-01607-w
29. Jahn, M.T., et al., A phage protein aids bacterial symbionts in eukaryote immune evasion. Cell Host & Microbe, 2019. 26(4): p. 542-550. e5.https://doi.org/10.1016/j.chom.2019.08.019
30. Tylenda, C.A., et al., Simultaneous loss of bacteriophage receptor and coaggregation mediator activities in Actinomyces viscosus MG-1. Infection and immunity, 1985. 48(1): p. 228-233.https://doi.org/10.1128/iai.48.1.228-233.1985
31. Chibani, C.M., et al., A catalogue of 1,167 genomes from the human gut archaeome. Nature microbiology, 2022. 7(1): p. 48-61.https://doi.org/10.1038/s41564-021-01020-9
32. Kinsella, C.M., et al., Entamoeba and Giardia parasites implicated as hosts of CRESS viruses. Nature communications, 2020. 11(1): p. 4620.https://doi.org/10.1038/s41467-020-18474-w
33. Rada, P., et al., Double-stranded RNA viruses are released from Trichomonas vaginalis inside small extracellular vesicles and modulate the exosomal cargo. Frontiers in microbiology, 2022. 13: p. 893692.https://doi.org/10.3389/fmicb.2022.893692
34. Graves, K., et al., Trichomonas vaginalis virus: a review of the literature. International journal of STD & AIDS, 2019. 30(5): p. 496-504.https://doi.org/10.1177/0956462418809767
35. Park, M., et al., A novel virus alters gene expression and vacuolar morphology in Malassezia cells and induces a TLR3-mediated inflammatory immune response. Mbio, 2020. 11(5): p. 10.1128/mbio. 01521-20.https://doi.org/10.1128/mbio.01521-20
36. Abbas, A.A., et al., Redondoviridae, a family of small, circular DNA viruses of the human oro-respiratory tract associated with periodontitis and critical illness. Cell host & microbe, 2019. 25(5): p. 719-729. e4.https://doi.org/10.1016/j.chom.2019.04.001
37. Keeler, E.L., et al., Widespread, human-associated redondoviruses infect the commensal protozoan Entamoeba gingivalis. Cell host & microbe, 2023. 31(1): p. 58-68. e5.https://doi.org/10.1016/j.chom.2022.11.002

38. Liang, G. and F.D. Bushman, The human virome: assembly, composition and host interactions. Nature Reviews Microbiology, 2021. 19(8): p. 514-527.https://doi.org/10.1038/s41579-021-00536-5
39. Diaz, P.I., Subgingival fungi, Archaea, and viruses under the omics loupe. Periodontology 2000, 2021. 85(1): p. 82-89.https://doi.org/10.1177/0022034520956975
40. Virgin, H.W., E.J. Wherry, and R. Ahmed, Redefining chronic viral infection. Cell, 2009. 138(1): p. 30-50.https://doi.org/10.1016/j.cell.2009.06.036
41. Kaczorowska, J. and L. Van Der Hoek, Human anelloviruses: diverse, omnipresent and commensal members of the virome. FEMS Microbiology Reviews, 2020. 44(3): p. 305-313.https://doi.org/10.1093/femsre/fuaa007
42. Bearfield, C., et al., Possible association between amniotic fluid micro-organism infection and microflora in the mouth. Bjog, 2002. 109(5): p. 527-33.https://doi.org/10.1016/S1470-0328(02)01349-6
43. Xiao, J., K.A. Fiscella, and S.R. Gill, Oral microbiome: possible harbinger for children's health. Int J Oral Sci, 2020. 12(1): p. 12.https://doi.org/10.1038/s41368-020-0082-x
44. Aagaard, K., et al., The Placenta Harbors a Unique Microbiome. Science Translational Medicine, 2014. 6(237): p. 237ra65-237ra65. https://doi.org/10.1126/scitranslmed.3008599
45. Dzidic, M., et al., Oral microbiome development during childhood: an ecological succession influenced by postnatal factors and associated with tooth decay. The ISME Journal, 2018. 12(9): p. 2292-2306.https://doi.org/10.1038/s41396-018-0204-z
46. Marsh, P.D., Role of the oral microflora in health. Microbial ecology in health and disease, 2000. 12(3): p. 130-137.https://doi.org/10.1080/089106000750051800
47. Crielaard, W., et al., Exploring the oral microbiota of children at various developmental stages of their dentition in the relation to their oral health. BMC Medical Genomics, 2011. 4(1): p. 22.https://doi.org/10.1186/1755-8794-4-22
48. Stecksén-Blicks, C., et al., Prevalence of oral Candida in the first year of life. Mycoses, 2015. 58(9): p. 550-6. https://doi.org/10.1111/myc.12355
49. Ward, T.L., et al., Development of the Human Mycobiome over the First Month of Life and across Body Sites. mSystems, 2018. 3(3).https://doi.org/10.1128/msystems.00140-17
50. Pride, D.T., et al., Evidence of a robust resident bacteriophage population revealed through analysis of the human salivary virome. The ISME Journal, 2012. 6(5): p. 915-926. https://doi.org/10.1038/ismej.2011.169
51. Parras-Moltó, M., et al., Genome Sequence of Two Novel Species of Torque Teno Minivirus from the Human Oral Cavity. Genome Announcements, 2014. 2(5): p. e00868-14-e0086.https://doi.org/10.1128/genomea.00868-14
52. Corstjens, P.L., W.R. Abrams, and D. Malamud, Saliva and viral infections. Periodontol 2000, 2016. 70(1): p. 93-110. https://doi.org/10.1111/prd.12112
53. Mahnert, N., et al., The incidence of neonatal herpes infection. Am J Obstet Gynecol, 2007. 196(5): p. e55-6.https://doi.org/10.1016/j.ajog.2006.10.911
54. Pinninti, S.G. and D.W. Kimberlin, Neonatal herpes simplex virus infections. Semin Perinatol, 2018. 42(3): p. 168-175.https://doi.org/10.1053/j.semperi.2018.02.004
55. Sällberg, M., Oral viral infections of children. Periodontol 2000, 2009. 49: p. 87-95.https://doi.org/10.1111/j.1600-0757.2008.00277.x.
56. Demmitt, B.A., et al., Genetic influences on the human oral microbiome. BMC Genomics, 2017. 18(1).https://doi.org/10.1186/s12864-017-4008-8
57. Gomez, A., et al., Host Genetic Control of the Oral Microbiome in Health and Disease. Cell Host & Microbe, 2017. 22(3): p. 269-278.e3.https://doi.org/10.1016/j.chom.2017.08.013
58. Dominguez-Bello, M.G., et al., Delivery mode shapes the acquisition and structure of the initial microbiota across multiple body habitats in newborns. Proceedings of the National Academy of Sciences, 2010. 107(26): p. 11971-11975.https://doi.org/10.1073/pnas.1002601107
59. Timby, N., et al., Oral Microbiota in Infants Fed a Formula Supplemented with Bovine Milk Fat Globule Membranes - A Randomized Controlled Trial. PLOS ONE, 2017. 12(1): p. e0169831.https://doi.org/10.1371/journal.pone.0169831
60. Ferretti, P., et al., Mother-to-Infant Microbial Transmission from Different Body Sites Shapes the Developing Infant Gut Microbiome. Cell Host & Microbe, 2018. 24(1): p. 133-145.e5.https://doi.org/10.1016/j.chom.2018.06.005
61. Mason, M.R., et al., Characterizing oral microbial communities across dentition states and colonization niches. Microbiome, 2018. 6(1).https://doi.org/10.1186/s40168-018-0443-2
62. Petersen, C. and J.L. Round, Defining dysbiosis and its influence on host immunity and disease. Cellular microbiology, 2014. 16(7): p. 1024-1033.https://doi.org/10.1111/cmi.12308
63. Takeshita, T., et al., Bacterial diversity in saliva and oral health-related conditions: the Hisayama Study. Scientific reports, 2016. 6(1): p. 22164.https://doi.org/10.1038/srep22164
64. Santonocito, S., et al., A Cross-Talk between Diet and the Oral Microbiome: Balance of Nutrition on Inflammation and Immune System's Response during Periodontitis. Nutrients, 2022. 14(12): p. 2426.https://doi.org/10.3390/nu14122426
65. Aas, J.A., et al., Defining the normal bacterial flora of the oral cavity. Journal of clinical microbiology, 2005. 43(11): p. 5721-5732.https://doi.org/10.1128/jcm.43.11.5721-5732.2005

66. Alhassani, A.A., et al., Dietary flavonoid intake and risk of periodontitis. Journal of periodontology, 2020. 91(8): p. 1057-1066.https://doi.org/10.1002/JPER.19-0463
67. Baker, J.L. and A. Edlund, Exploiting the oral microbiome to prevent tooth decay: has evolution already provided the best tools? Frontiers in microbiology, 2019. 9: p. 3323.https://doi.org/10.3389/fmicb.2018.03323
68. Moye, Z.D., L. Zeng, and R.A. Burne, Fueling the caries process: carbohydrate metabolism and gene regulation by Streptococcus mutans. Journal of oral microbiology, 2014. 6(1): p. 24878.https://doi.org/10.3402/jom.v6.24878
69. Klein, M., et al., Structural and molecular basis of the role of starch and sucrose in Streptococcus mutans biofilm development. Applied and Environmental Microbiology, 2009. 75(3): p. 837-841.https://doi.org/10.1128/AEM.01299-08
70. Takahashi, N., Oral microbiome metabolism: from "who are they?" to "what are they doing?". Journal of dental research, 2015. 94(12): p. 1628-1637.https://doi.org/10.1177/0022034515606045
71. Hansen, T.H., et al., Impact of a vegan diet on the human salivary microbiota. Scientific reports, 2018. 8(1): p. 5847.https://doi.org/10.1038/s41598-018-24207-3
72. Takeshita, T., et al., Distinct composition of the oral indigenous microbiota in South Korean and Japanese adults. Scientific reports, 2014. 4(1): p. 6990.https://doi.org/10.1038/srep06990
73. De Filippis, F., et al., The same microbiota and a potentially discriminant metabolome in the saliva of omnivore, ovo-lacto-vegetarian and vegan individuals. PloS one, 2014. 9(11): p. e112373.https://doi.org/10.1371/journal.pone.0112373
74. Huang, C. and G. Shi, Smoking and microbiome in oral, airway, gut and some systemic diseases. J Transl Med, 2019. 17(1): p. 225.https://doi.org/10.1186/s12967-019-1971-7
75. Ertel, A., R. Eng, and S.M. Smith, The differential effect of cigarette smoke on the growth of bacteria found in humans. Chest, 1991. 100(3): p. 628-630.https://doi.org/10.1378/chest.100.3.628
76. Colman, G., et al., Cigarette smoking and the microbial flora of the mouth. Australian dental journal, 1976. 21(2): p. 111-118.https://doi.org/10.1111/j.1834-7819.1976.tb02833.x
77. Mason, M.R., et al., The subgingival microbiome of clinically healthy current and never smokers. The ISME journal, 2015. 9(1): p. 268-272.https://doi.org/10.1038/ismej.2014.114
78. Yuan, W., et al., Plant growth-promoting and antibacterial activities of cultivable bacteria alive in tobacco field against Ralstonia solanacearum. Environmental Microbiology, 2022. 24(3): p. 1411-1429.https://doi.org/10.1111/1462-2920.15868
79. Vishwakarma, A. and D. Verma, Microorganisms: crucial players of smokeless tobacco for several health attributes. Applied Microbiology and Biotechnology, 2021. 105: p. 6123-6132.https://doi.org/10.1007/s00253-021-11460-2
80. Macgregor, I., Effects of smoking on oral ecology. A review of the literature. Clinical preventive dentistry, 1989. 11(1): p. 3-7
81. Hugoson, A. and M. Rolandsson, Periodontal disease in relation to smoking and the use of Swedish snus: epidemiological studies covering 20 years (1983–2003). Journal of clinical periodontology, 2011. 38(9): p. 809-816.https://doi.org/10.1111/j.1600-051X.2011.01749.x
82. Parahitiyawa, N., et al., Microbiology of odontogenic bacteremia: beyond endocarditis. Clinical microbiology reviews, 2009. 22(1): p. 46-64.https://doi.org/10.1128/cmr.00028-08
83. Kato, I., et al., Oral microbiome and history of smoking and colorectal cancer. Journal of epidemiological research, 2016. 2(2): p. 92.https://doi.org/10.5430/jer.v2n2p92
84. Hayes, R.B., et al., Association of oral microbiome with risk for incident head and neck squamous cell cancer. JAMA oncology, 2018. 4(3): p. 358-365.https://doi.org/10.1001/jamaoncol.2017.4777
85. Fan, X., et al., Human oral microbiome and prospective risk for pancreatic cancer: a population-based nested case-control study. Gut, 2018. 67(1): p. 120-127.https://doi.org/10.1136/gutjnl-2016-312580
86. Peters, B.A., et al., Oral microbiome composition reflects prospective risk for esophageal cancers. Cancer research, 2017. 77(23): p. 6777-6787.https://doi.org/10.1158/0008-5472.CAN-17-1296
87. Kumar, P.S., Microbial dysbiosis: The root cause of periodontal disease. Journal of periodontology, 2021. 92(8): p. 1079-1087.https://doi.org/10.1002/JPER.21-0245
88. Abebe, G.M., Oral biofilm and its impact on oral health, psychological and social interaction. Int. J. Oral Dent. Health, 2021. 7: p. 127.https://doi.org/10.23937/2469-5734/1510127
89. Sälzer, S., et al., Contemporary practices for mechanical oral hygiene to prevent periodontal disease. Periodontology 2000, 2020. 84(1): p. 35-44.https://doi.org/10.1111/prd.12332
90. Chapple, I.L., et al., Primary prevention of periodontitis: managing gingivitis. Journal of clinical periodontology, 2015. 42: p. S71-S76.https://doi.org/10.1111/jcpe.12366
91. Pignatelli, P., et al., How periodontal disease and presence of nitric oxide reducing oral bacteria can affect blood pressure. International journal of molecular sciences, 2020. 21(20): p. 7538.https://doi.org/10.3390/ijms21207538
92. Gusberti, F.A., et al., Microbiological and clinical effects of chlorhexidine digluconate and hydrogen peroxide mouthrinses on developing plaque and gingivitis. Journal of clinical periodontology, 1988. 15(1): p. 60-67.https://doi.org/10.1111/j.1600-051X.1988.tb01556.x

93. Menendez, A., et al., Comparative analysis of the antibacterial effects of combined mouthrinses on Streptococcus mutans. Oral microbiology and immunology, 2005. 20(1): p. 31-34.https://doi.org/10.1111/j.1399-302X.2004.00189.x
94. Van Leeuwen, M., et al., Long-term efficacy of a 0.07% cetylpyridinium chloride mouth rinse in relation to plaque and gingivitis: a 6-month randomized, vehicle-controlled clinical trial. International Journal of Dental Hygiene, 2015. 13(2): p. 93-103.https://doi.org/10.1111/idh.12082
95. Teng, F., et al., Cetylpyridinium chloride mouth rinses alleviate experimental gingivitis by inhibiting dental plaque maturation. International journal of oral science, 2016. 8(3): p. 182-190.https://doi.org/10.1038/ijos.2016.18
96. Fan, X., et al., Drinking alcohol is associated with variation in the human oral microbiome in a large study of American adults. Microbiome, 2018. 6: p. 1-15.https://doi.org/10.1186/s40168-018-0448-x
97. Muto, M., et al., Acetaldehyde production by non-pathogenic Neisseria in human oral microflora: implications for carcinogenesis in upper aerodigestive tract. International journal of cancer, 2000. 88(3): p. 342-350.https://doi.org/10.1002/1097-0215(20001101)88:3<342::AID-IJC4>3.0.CO;2-I
98. Nosova, T., et al., Acetaldehyde production and metabolism by human indigenous and probiotic Lactobacillus and Bifidobacterium strains. Alcohol and Alcoholism, 2000. 35(6): p. 561-568. https://doi.org/10.1093/alcalc/35.6.561
99. Liao, Y., et al., The effects of alcohol drinking on oral microbiota in the Chinese population. International Journal of Environmental Research and Public Health, 2022. 19(9): p. 5729.https://doi.org/10.3390/ijerph19095729
100. Valles-Colomer, M., et al., Variation and transmission of the human gut microbiota across multiple familial generations. Nature microbiology, 2022. 7(1): p. 87-96.https://doi.org/10.1038/s41564-021-01021-8
101. Adeva-Andany, M., et al., Comprehensive review on lactate metabolism in human health. Mitochondrion, 2014. 17: p. 76-100.https://doi.org/10.1016/j.mito.2014.05.007
102. Drucker, S.D., Impact of Chewing Betel Nut on the Oral Microbiome. 2016, University of Illinois at Chicago.
103. Harvey, W., et al., Stimulation of human buccal mucosa fibroblasts in vitro by betel-nut alkaloids. Archives of oral biology, 1986. 31(1): p. 45-49.https://doi.org/10.1016/0003-9969(86)90112-3
104. Hoffman, N.W., J.-P. Wuarin, and F.E. Dudek, Whole-cell recordings of spontaneous synaptic currents in medial preoptic neurons from rat hypothalamic slices: mediation by amino acid neurotransmitters. Brain research, 1994. 660(2): p. 349-352.https://doi.org/10.1016/0006-8993(94)91312-9
105. Mangin, I., et al., Amoxicillin treatment modifies the composition of Bifidobacterium species in infant intestinal microbiota. Anaerobe, 2010. 16(4): p. 433-438.https://doi.org/10.1016/j.anaerobe.2010.06.005
106. Schumann, A., et al., Neonatal antibiotic treatment alters gastrointestinal tract developmental gene expression and intestinal barrier transcriptome. Physiological genomics, 2005. 23(2): p. 235-245.https://doi.org/10.1152/physiolgenomics.00057.2005
107. Russell, S.L., et al., Early life antibiotic-driven changes in microbiota enhance susceptibility to allergic asthma. EMBO reports, 2012. 13(5): p. 440-447.https://doi.org/10.1038/embor.2012.32
108. Sekirov, I., et al., Antibiotic-induced perturbations of the intestinal microbiota alter host susceptibility to enteric infection. Infection and immunity, 2008. 76(10): p. 4726-4736.https://doi.org/10.1128/iai.00319-08
109. Iliev, I.D., et al., Interactions between commensal fungi and the C-type lectin receptor Dectin-1 influence colitis. Science, 2012. 336(6086): p. 1314-1317.https://doi.org/10.1126/science.1221789
110. Gomez-Arango, L.F., et al., Antibiotic treatment at delivery shapes the initial oral microbiome in neonates. Scientific reports, 2017. 7(1): p. 43481.https://doi.org/10.1038/srep43481
111. Pitts, N., et al., Dental caries Nat Rev Dis Primers 3: 17030. 2017.
112. Banas, J.A. and D.R. Drake, Are the mutans streptococci still considered relevant to understanding the microbial etiology of dental caries? BMC oral health, 2018. 18: p. 1-8.https://doi.org/10.1186/s12903-018-0595-2
113. Baker, J.L., et al., Deep metagenomics examines the oral microbiome during dental caries, revealing novel taxa and co-occurrences with host molecules. Genome research, 2021. 31(1): p. 64-74.https://doi.org/10.1101/gr.265645.120
114. Simón-Soro, A. and A. Mira, Solving the etiology of dental caries. Trends in microbiology, 2015. 23(2): p. 76-82.https://doi.org/10.1016/j.tim.2014.10.010
115. Teng, F., et al., Prediction of early childhood caries via spatial-temporal variations of oral microbiota. Cell host & microbe, 2015. 18(3): p. 296-306.https://doi.org/10.1016/j.chom.2015.08.005
116. Agnello, M., et al., Microbiome associated with severe caries in Canadian first nations children. Journal of Dental Research, 2017. 96(12): p. 1378-1385.https://doi.org/10.1177/0022034517718819
117. Havsed, K., et al., Bacterial composition and metabolomics of dental plaque from adolescents. Frontiers in cellular and infection microbiology, 2021. 11: p. 716493.https://doi.org/10.3389/fcimb.2021.716493
118. Rosier, B., et al., Nitrate as a potential prebiotic for the oral microbiome. Scientific reports, 2020. 10(1): p. 12895.https://doi.org/10.1038/s41598-020-69931-x
119. Rosier, B.T., et al., The importance of nitrate reduction for oral health. Journal of dental research, 2022. 101(8): p. 887-897.https://doi.org/10.1177/00220345221080982
120. Darveau, R.P., Periodontitis: a polymicrobial disruption of host homeostasis. Nature reviews microbiology, 2010. 8(7): p. 481-490.https://doi.org/10.1038/nrmicro2337

121. Caton, J.G., et al., A new classification scheme for periodontal and peri-implant diseases and conditions–Introduction and key changes from the 1999 classification. 2018, Wiley Online Library. p. S1-S8.
122. Williams, D.W., et al., Human oral mucosa cell atlas reveals a stromal-neutrophil axis regulating tissue immunity. Cell, 2021. 184(15): p. 4090-4104. e15.https://doi.org/10.1016/j.cell.2021.05.013
123. Miralda, I. and S.M. Uriarte, Periodontal Pathogens' strategies disarm neutrophils to promote dysregulated inflammation. Molecular oral microbiology, 2021. 36(2): p. 103-120.https://doi.org/10.1111/omi.12321
124. Cai, Z., et al., Structure and function of oral microbial community in periodontitis based on integrated data. Frontiers in Cellular and Infection Microbiology, 2021. 11: p. 663756.https://doi.org/10.3389/fcimb.2021.663756
125. Martínez, A., R. Kuraji, and Y.L. Kapila, The human oral virome: shedding light on the dark matter. Periodontology 2000, 2021. 87(1): p. 282-298.https://doi.org/10.1111/prd.12396
126. Bamashmous, S., et al., Human variation in gingival inflammation. Proceedings of the National Academy of Sciences, 2021. 118(27): p. e2012578118.https://doi.org/10.1073/pnas.2012578118
127. Wang, S., et al., Oral microbiome and its relationship with oral cancer. J Cancer Res Ther, 2024. 20(4): p. 1141-1149.https://doi.org/10.4103/jcrt.jcrt_44_24
128. Artico, G., et al., Prevalence of C andida spp., xerostomia, and hyposalivation in oral lichen planus–A controlled study. Oral diseases, 2014. 20(3): p. e36-e41.https://doi.org/10.1111/odi.12120
129. Alnuaimi, A.D., et al., Candida virulence and ethanol-derived acetaldehyde production in oral cancer and non-cancer subjects. Oral diseases, 2016. 22(8): p. 805-814.https://doi.org/10.1111/odi.12565
130. Bhatt, A.P., M.R. Redinbo, and S.J. Bultman, The role of the microbiome in cancer development and therapy. CA: a cancer journal for clinicians, 2017. 67(4): p. 326-344.https://doi.org/10.3322/caac.21398
131. Pushalkar, S., et al., Comparison of oral microbiota in tumor and non-tumor tissues of patients with oral squamous cell carcinoma. BMC microbiology, 2012. 12: p. 1-15.https://doi.org/10.1186/1471-2180-12-144
132. Roginskaya, M. and Y. Razskazovskiy, Oxidative DNA damage and repair: mechanisms, mutations, and relation to diseases. 2023, MDPI. p. 1623.
133. Anvarbatcha, R., F. Kunnathodi, and M. Islam, Induction of G0/G1 phase cell cycle arrest and apoptosis by thymol through ROS generation and caspase-9/-3 activation in breast and colorectal cancer cell lines. Journal of Cancer Research and Therapeutics, 2023. 19(7): p. 1915-1924.https://doi.org/10.4103/jcrt.jcrt_308_22
134. Huang, C., et al., TSPYL5 inhibits the tumorigenesis of colorectal cancer cells in vivo by triggering DNA damage. Journal of Cancer Research and Therapeutics, 2023. 19(4): p. 898-903.https://doi.org/10.4103/jcrt.jcrt_1098_21
135. Singh, S., P.K. Yadav, and A.K. Singh, In-silico structural characterization and phylogenetic analysis of Nucleoside diphosphate kinase: A novel antiapoptotic protein of Porphyromonas gingivalis. Journal of Cellular Biochemistry, 2023. 124(4): p. 545-556.https://doi.org/10.1002/jcb.30389
136. Chen, W.A., et al., Local and systemic effects of Porphyromonas gingivalis infection. Microorganisms, 2023. 11(2): p. 470.https://doi.org/10.3390/microorganisms11020470
137. Ren, J., et al., P. gingivalis infection upregulates PD-L1 expression on dendritic cells, suppresses CD8+ T-cell responses, and aggravates oral cancer. Cancer immunology research, 2023. 11(3): p. 290-305.https://doi.org/10.1158/2326-6066.CIR-22-0541
138. Nieminen, M.T., et al., Treponema denticola chymotrypsin-like proteinase may contribute to orodigestive carcinogenesis through immunomodulation. British journal of cancer, 2018. 118(3): p. 428-434.https://doi.org/10.1038/bjc.2017.409
139. Cui, N., M. Hu, and R.A. Khalil, Biochemical and biological attributes of matrix metalloproteinases. Progress in molecular biology and translational science, 2017. 147: p. 1-73.https://doi.org/10.1016/bs.pmbts.2017.02.005
140. Malinowski, B., et al., The role of Tannerella forsythia and Porphyromonas gingivalis in pathogenesis of esophageal cancer. Infectious agents and cancer, 2019. 14: p. 1-8.https://doi.org/10.1186/s13027-019-0220-2
141. Mager, D., et al., The salivary microbiota as a diagnostic indicator of oral cancer: a descriptive, non-randomized study of cancer-free and oral squamous cell carcinoma subjects. Journal of translational medicine, 2005. 3: p. 1-8.https://doi.org/10.1186/1479-5876-3-27
142. Robayo, D.A.G., et al., Oropharyngeal squamous cell carcinoma: human papilloma virus coinfection with Streptococcus anginosus. Brazilian dental journal, 2019. 30(6): p. 626-633.https://doi.org/10.1590/0103-6440201902805
143. Gillison, M.L., Flashback foreword: human papillomavirus and incidence and survival of oropharyngeal cancers. 2023, Wolters Kluwer Health. p. 3079-3080.
144. de Lima, M.A.P., et al., Association between Epstein-Barr virus and oral carcinoma: a systematic review with meta-analysis. Critical Reviews™ in Oncogenesis, 2019. 24(4).https://doi.org/10.1615/CritRevOncog.2019031897
145. Vesty, A., et al., Microbial and inflammatory-based salivary biomarkers of head and neck squamous cell carcinoma. Clinical and experimental dental research, 2018. 4(6): p. 255-262.https://doi.org/10.1002/cre2.139
146. Abidullah, M., et al., Investigation of candidal species among people who suffer from oral potentially malignant disorders and oral squamous cell carcinoma. Journal of Pharmacy and Bioallied Sciences, 2021. 13(Suppl 2): p. S1050-S1054.https://doi.org/10.4103/jpbs.jpbs_357_21

147. Parisa, A., et al., Anti-cancer effects of Bifidobacterium species in colon cancer cells and a mouse model of carcinogenesis. PloS one, 2020. 15(5): p. e0232930.https://doi.org/10.1371/journal.pone.0242387
148. Wang, Q., et al., Expert consensus on the relevance of intestinal microecology and hematopoietic stem cell transplantation. Clinical Transplantation, 2024. 38(1): p. e15186.https://doi.org/10.1111/ctr.15186
149. Wang, J., et al., Chinese expert consensus on intestinal microecology and management of digestive tract complications related to tumor treatment (version 2022). Journal of Cancer Research and Therapeutics, 2022. 18(7): p. 1835-1844.https://doi.org/10.4103/jcrt.jcrt_1444_22
150. Stringer, A.M., et al., Chemotherapy-induced mucositis: the role of gastrointestinal microflora and mucins in the luminal environment. 2008.https://doi.org/10.1258/ebm.2012.012260
151. Amin, M., et al., Tumor-targeted induction of intrinsic apoptosis in colon cancer cells by Lactobacillus plantarum and Lactobacillus rhamnosus strains. Molecular Biology Reports, 2023. 50(6): p. 5345-5354.https://doi.org/10.1007/s11033-023-08445-x
152. Mammen, M.J., F.A. Scannapieco, and S. Sethi, Oral-lung microbiome interactions in lung diseases. Periodontology 2000, 2020. 83(1): p. 234-241.https://doi.org/10.1111/prd.12301
153. Atarashi, K., et al., Ectopic colonization of oral bacteria in the intestine drives TH1 cell induction and inflammation. Science, 2017. 358(6361): p. 359-365.https://doi.org/10.1126/science.aan4526
154. Kitamoto, S., et al., The intermucosal connection between the mouth and gut in commensal pathobiont-driven colitis. Cell, 2020. 182(2): p. 447-462. e14.https://doi.org/10.1016/j.cell.2020.05.048
155. Abed, J., et al., Fap2 mediates Fusobacterium nucleatum colorectal adenocarcinoma enrichment by binding to tumor-expressed Gal-GalNAc. Cell host & microbe, 2016. 20(2): p. 215-225.https://doi.org/10.1016/j.chom.2016.07.006
156. Gur, C., et al., Binding of the Fap2 protein of Fusobacterium nucleatum to human inhibitory receptor TIGIT protects tumors from immune cell attack. Immunity, 2015. 42(2): p. 344-355.https://doi.org/10.1016/j.immuni.2015.01.010
157. Dioguardi, M., et al., The role of periodontitis and periodontal bacteria in the onset and progression of Alzheimer's disease: a systematic review. Journal of clinical medicine, 2020. 9(2): p. 495.https://doi.org/10.3390/jcm9020495
158. Miles, B., et al., Secondary lymphoid organ homing phenotype of human myeloid dendritic cells disrupted by an intracellular oral pathogen. Infection and immunity, 2014. 82(1): p. 101-111.https://doi.org/10.1128/iai.01157-13
159. Konig, M.F., et al., Aggregatibacter actinomycetemcomitans–induced hypercitrullination links periodontal infection to autoimmunity in rheumatoid arthritis. Science translational medicine, 2016. 8(369): p. 369ra176-369ra176.https://doi.org/10.1126/scitranslmed.aaj1921
160. Gully, N., et al., Porphyromonas gingivalis peptidylarginine deiminase, a key contributor in the pathogenesis of experimental periodontal disease and experimental arthritis. PloS one, 2014. 9(6): p. e100838.https://doi.org/10.1371/journal.pone.0100838
161. Calderón-Gómez, E., et al., Commensal-specific CD4+ cells from patients with Crohn's disease have a T-helper 17 inflammatory profile. Gastroenterology, 2016. 151(3): p. 489-500. e3.https://doi.org/10.1053/j.gastro.2016.05.050
162. Hajishengallis, G. and T. Chavakis, Local and systemic mechanisms linking periodontal disease and inflammatory comorbidities. Nature Reviews Immunology, 2021. 21(7): p. 426-440.https://doi.org/10.1038/s41577-020-00488-6
163. Stöhr, J., et al., Bidirectional association between periodontal disease and diabetes mellitus: a systematic review and meta-analysis of cohort studies. Scientific Reports, 2021. 11(1): p. 13686.https://doi.org/10.1038/s41598-021-93062-6