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REVIEW

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The impact of the oral microbiome on oral and systemic health and disease: a systematic review.

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Abstract

Background: The microbiome is a varied and substantial community of microorganisms in the human body. A deeper understanding of oral diseases requires understanding the microbial ecological mechanisms that drive disease progression. This review structures different techniques that have significantly advanced our understanding of oral biofilm maturation and species interactions. Oral microbes interact with the body's immune system and are essential for sustaining oral and systemic health. **Methods**: A systematic search was conducted using PubMed and the Cochrane Library in accordance with PRISMA guidelines. A total of 67 studies were initially identified, of which 32 were excluded based on predefined criteria. Finally, 35 cross-sectional studies published between January 1, 2020, and July 28, 2024, were included in the analysis. **Results**: Most studies on the oral microbiome used 16S rRNA gene sequencing and primarily examined bacterial populations. Oral microbial dysbiosis was found to be significant in the development of oral diseases like caries and periodontal disease. Moreover, it is associated with systemic conditions like asthma and allergies, autoimmune disorders, colon cancer, hypertension, depression, inflammatory bowel diseases, obesity, metabolic syndrome, and peripheral vascular diseases. **Conclusions**: The oral microbiome offers significant potential for diagnostic applications. Therapeutic strategies directed at promoting beneficial bacteria while inhibiting pathogenic oral bacteria could innovate ways of preventing various health conditions.

Keywords: dysbiosis; oral health; microbiome; general health; 16S rRNA.

Introduction

Microbiology traces its origins to the 1670s, when Antony van Leeuwenhoek used lenses he crafted himself to view tiny organisms like bacteria and protozoa. His observations marked the beginning of what would become modern microbiology [1]. In the 19th century, Louis Pasteur expanded on this early work by revealing how microorganisms contribute to fermentation and disease, and by introducing major innovations, including pasteurization and the development of vaccines. [2]. Robert Koch further shaped the discipline by showing that specific pathogens are responsible for particular diseases, using a systematic investigative approach that helped establish microbiology as a defined scientific field [3].

The term oral microbiome was first introduced in 2008, initiating a rapidly growing area of research into the diverse microbial communities residing in the oral cavity [4]. Since then, studies on the oral microbiome have increased steadily, although early interest remained modest [5]. Research has revealed that the oral cavity harbours over 700 bacterial species across seven phyla [6], along with fungi, viruses, archaea, amoebas, and flagellates [7]. Although the general composition of the oral microbiome is relatively consistent across individuals, differences in species, strains, and rare organisms add to its complexity. Interactions between these microbes are important for oral health and disease – Streptococcus species can promote the growth of Candida albicans, while Pseudomonas species act to inhibit it [8]. These interactions also involve metabolic cooperation, such as cross-feeding between Streptococcus and Candida species, which promotes biofilm formation and acid production – critical factors in dental caries, especially when acting alongside Streptococcus mutans [9]. Additionally, archaea, amoebas, and flagellates have been associated with periodontal disease, with archaea potentially facilitating the growth of fermentative bacteria [10].

Recent progress in bioinformatics and sequencing technologies, such as metagenomic and metatranscriptomic approaches, allows researchers to identify microorganisms that lack 16S rRNA genes, greatly expanding the range of detectable microbes [11]. Moreover, injectable platelet-rich fibrin (i-PRF) has important applications in dentistry for its regenerative effects, supporting tissue healing and reducing inflammation in treatments of periodontitis management, to bone regeneration, and orthodontic procedures [12]. This review aims to synthesize current knowledge on the oral microbiome, with a particular focus on its microbial diversity, functional interactions, and implications for both oral and systemic health.

No specific null hypothesis was formulated, as the objective of this review is to summarize and critically analyze existing evidence on the oral microbiome.

Materials and Methods

Eligibility Criteria Review

The study methodology was submitted for PROSPERO database inclusion, registration number 1076917. The PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) 2020 statement was the guideline we used to create an updated set of guidelines for reporting systematic reviews. For analysis, the authors included the PRISMA checklist in Supplementary Figures 1 and 2, a key tool that enhances clarity and allows easy assessment of our reporting in its entirety. The PRISMA framework ensures that all relevant aspects of the methodology and findings are represented. By following these guidelines and using the PRISMA checklist, we can produce reliable and reproducible results essential for future research and clinical practice [13].

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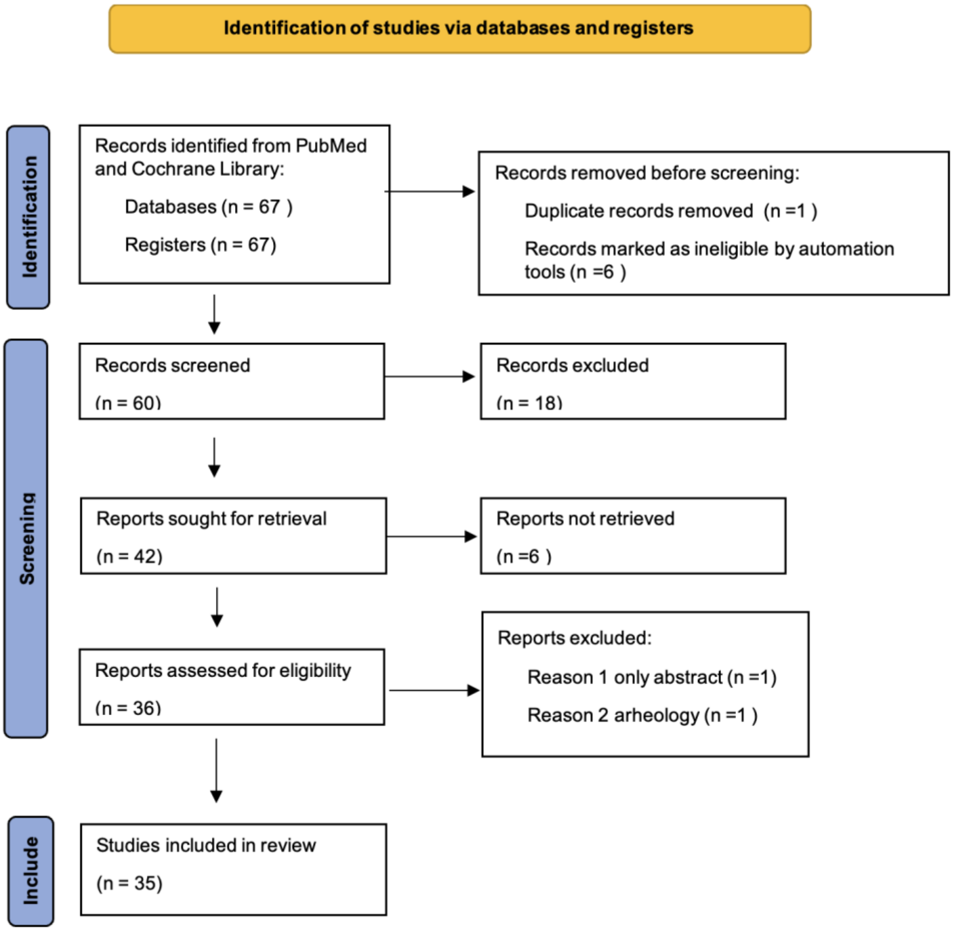

Figure 1. The PRISMA flow diagram was used during the methodology regarding the study selection process. Schemes follow the same formatting.

Search Strategy

The search was conducted in PubMed and Cochrane Library using the following search string: [(oral health) AND (systemic health) AND (oral dysbiosis) OR (oral microbiome) OR (oral dysbiosis OR 16S rRNA)]. (Figure 1) This search included results up to July 28, 2024, and no language or study design restrictions were applied during the search process (Supplementary Table 1-Detailed search strategy).

Eligibility and Selection Criteria

Based on the PICO framework, the following question was created: How does the oral microbiome influence both oral health (e.g., caries, periodontal disease) and systemic health (e.g., asthma, autoimmune disorders, metabolic syndrome) in humans? Including the following elements: Research Question (PICO Format): Population (P): Humans, both children and adults, with or without specific conditions such as oral health issues (e.g., caries, periodontal disease) or systemic diseases (e.g., autoimmune disorders, obesity, metabolic syndrome). Intervention (I): Oral microbiome. Comparison (C): No specific comparison group, but studies comparing oral health with systemic health and the role of the microbiome in each. Outcome (O): The impact of the oral microbiome on oral health (e.g., caries, periodontal disease) and its association with systemic health conditions (e.g., asthma, hypertension, depression, obesity, etc.).

Data Extraction

The authors collected data using an Excel table, systematically organizing information such as the first author's name, study title, publication year, number of participants, research methodology, and main findings.

Risk-of-Bias

A quality and risk of bias evaluation was conducted for all studies. (Supplementary Table 2-Risk of Bias)

Systematic Search and Selection

The authors conducted a systematic review using the PubMed and Cochrane Library databases, conducting keyword searches such as "microbiome" and "oral microbiome" between July 15 and July 28, 2024. The review focused on studies published from 2020 to 2024. Articles unrelated to the topic were excluded following a preliminary screening, and older relevant studies cited in the initial search results were also included. After removing duplicates, 35 pertinent articles were identified from the databases.

Results

Description of Excluded Studies

The studies that did not meet the expectations of the inclusion criteria were definitively excluded. The articles that were not considered for evaluation comprise summaries that provide condensed overviews, reviews that critically analyze existing literature, studies that lack human participant involvement, and submissions focused on archaeological calls for papers that aim to invite research contributions in that specific field. (Table 1).

The main findings are summarized in Table 2 for clarity and easy reference.

Table 1. Reasons for the exclusion of records during full-text assessment.

Studies	Reason of exclusion
Sedghi L et al. 2021 [14]	Review
Baker J et al. 2024 [15]	Review
Moraitou M et al. 2022 [16]	Animal study
Kozak M et al. 2023 [17]	Summary
Kreth J et al. 2022 [18]	Review
D'Agostino S et al. 2022 [19]	Review
Merritt J et al. 2023 [20]	Review
Baker JL et al. 2023 [21]	Review
Moon JH et al. 2023 [22]	Review
Jafari N et al. 2022 [23]	Review
Ebersole J et al. 2021 [24]	Animal study
Moussa D et al. 2022 [25]	Review

Santonocito S et al. 2022 [26]	Review
Nguyen T et al. 2020 [27]	Review
Peluso G et al. 2020 [28]	Animal study
Dahlquist-Axe G et al. 2024 [29]	Review
Bhaumik H et al. 2021 [30]	Review
Dahlen G et al. 2020 [31]	Review
Diakoumopoulou D et al. 2021 [32]	Review
Hashim A et al. 2021 [33]	Summary
Gao L et al. 2022 [34]	Summary
Scannapieco F et al. 2021 [35]	Assessment
Granehall L et al. 2021 [36]	The study excluded items categorized as archaeological.
Tang B et al. 2022 [37]	Summary
Sharma R et al. 2023 [38]	Animal study
Lutz HL et al. 2022 [39]	Animal study
Krutyholowa A et al. 2022 [40]	Review
Tan L et al. 2023 [41]	Meta-analysis
Neculae E et al. 2023 [42]	Review
Pignatelli P et al. 2022 [43]	Review
Huang X et al. 2023 [44]	Review
Sun Y et al. 2023 [45]	Review

Table 2. Included studies.

Authors/References	Year	Country	Type of study	Individuals	Sample size	Localization/ Origin	Microbiome components studied	Conclusion
Liu X. et al [46]	2021	China	cohort	2984	3932	Dorsum tongue, saliva	Bacteria	Human genetic variations account for the stability or recurrence of oral microbiome in individuals.
Tierney BT et al. [47]	2024	USA	Longitudinal study	4 (astronauts)	750	Oral, nasal, skin	Microbiome	An increase in plaque-associated bacteria is associated with the gene expression of immune cells.
Liu X. et al. [48]	2022	China	cohort	4478	7198	Dorsum tongue, saliva	Bacteria	Sex-specific microbe-hormone interactions explain most observed differences between sex hormones, such as significant causal enrichment for aldosterone in women and androstenedione in men.
Valles-Colomer M et al. [49]	2023	Argentina, Colombia, USA, Guine	Multi-cohort	2764	9715	Stool, saliva	Bacteria	Approximately 50% of microbial strains are transmitted from mother to child, significantly influencing the

		a-Bissau, China, Italy, Ghana,Tanzania						development of the infant's microbiome and remaining detectable throughout the child's growth.
Freire M et al. [50]	2020	Australia	Longitudinal study	143 (twins)	429	Dental plaque	Microbiome	The development of the microbiome is essential for particular bacteria, with some specific bacteria being more prevalent in monozygotic twins and others in dizygotic twins. Additionally, certain bacteria are more commonly found in younger individuals, while others become more associated with age or correlate with a higher frequency of tooth brushing.
Saito S et al. [51]	2021	Japan	Prospective cohort study	1349	2694	Saliva, supragingival plaque	Microbiome	The association between the saliva and the *Actinobacteria* and *Bacilli* classes suggests differences in microbial variability and community organization between saliva and plaque and a relationship among microbial species and the gravity of periodontal disease.
Blostein F et al. [52]	2023	USA	Cohort study	783	138	Saliva	Bacteria	The composition of saliva microbiota at 2 years was associated with early childhood caries, even after adjusting for polygenic scores.
Baker J et al. [53]	2021	USA	Cross-sectional study	47	47	Saliva	Microbiome	*Rothia, Neisseria,* and *Haemophilus species* are correlated with satisfying oral health. In contrast, *Prevotella species, Streptococcus mutans,* and *Human herpesvirus* (*Epstein-*

								Barr virus) were more common in children with caries.
Vanzele P et al. [54]	2023	Brazil	Longitudinal-observational study	23	89	Saliva	Microbiome	Time notably alters oral microbes; oral feeding improves them and can persist as lifelong colonizers in the host.
Cheung M et al. [55]	2022	China	Cohort study	968	968	Oral rinse	Bacteria, Fungus	The interrelation between bacteria and fungi is restricted in healthy oral microbiota, but there is a correlation between *Pseudomonas sp.* and *Rhodotorula dairenensis.*
Sukumar S et al. [56]	2023	Australia	Longitudinal study	221	542	Oral biofilm	Antimicrobial resistance	The mobile genetic element associated with antimicrobial resistance in older children is found against various species and resistance genes.
Bor B et al. [57]	2020	USA	Case study	44	88	Saliva, supragingival plaque	*Saccharibacteria*	The ultrasmall cells of *Saccharibacteria* from the mouth may attach to *Actinobacteria* hosts, leading to their death and lysis.
Charalambous E et al. [58]	2021	Luxembourg	Cohort study	115	212	Saliva, bucal swab	Salivary microbiome, buccal microbiome	The early life microbiome leads to increased activation and senescence of the immune system. Oral composition differences correlate with early life adversity and the immunosenescence of CD4 T cells, the circulating numbers and activation status of NK cells, and anti-CMV titers.
Hendrickson EL et al. [59]	2022	USA	In vitro experimental study	XH001 monoculture, XH001/TM7x	-	-	*Saccharibacteria*	TM7x and the host bacteria hold onto a delicate balance to support an episymbiotic lifestyle.
Jiang Y et al. [60]	2021	China	In vitro experimental study	6 saliva donors	6	Saliva	Microcosm biofilm	The introduction of *Porphyromonas gingivalis* into a biofilm derived from

								saliva resulted in the formation of bacterial films that resemble the dysbiotic subgingival microbiota associated with periodontitis.
Nibali L et al. [61]	2023	Spain	Clinical trial	103	206	Blood, subgingival plaque	Microbiome	Host genotypes can cause abnormal immunity reactions in periodontitis, influencing oral health, the microbiome, and overall systemic health.
Cen L et al. [62]	2022	USA	In vitro experimental study	6	-	Saliva	Bacteriophages	The enzymatic activity of the LT protein from the ltg-1 gene may enhance the availability of the phage receptor.
Zhong Q et al. [63]	2024	China	In vitro experimental study	-	-	-	*Saccharibacteria*	The mechanism is symbiont modulation of gene expression in host bacteria, which impacts their susceptibility to phage predation and the human microbiome.
Esberg A et al. [64]	2020	Sweden	Cohort study	176	175	saliva	Microbiome	There is an association between sugar consumption and oral microbiome bionomics, but the response to sugar varies depending both on host and microbial factors.
Münch PC et al. [65]	2021	Germany	Cohort study	256	-	Supragingival plaque, subgingival plaque, tongue dorsum, saliva, palatine tonsils, throat, hard palate, buccal mucosa, keratinized gingiva, anterior nares, retroauricular crease,	Microbiome	The oral microbiome contains more CRISPR elements than the gut and urogenital regions.

						antecubital fossa, posterior fornix, mid vagina, vaginal introitus, stool		
Treerat P et al. [66]	2020	USA	In vitro experimental study	-	-	Saliva	*Corynebacterium* *Streptococcus sanguinis*	*Corynebacterium durum* influences the *Streptococcus sanguinis* process, likely supporting oral symbiotic colonization and survival.
Izawa K et al. [67]	2021	Japan	Cohort study	33	64	Subgingival plaque	Microbiome	The comparative abundance of functional gene categories, glycolysis, glycosylation, and amino acid processes showed important differences between healthy sites and sites with gingival sulcus.
Dong PT et al. [68]	2024	USA	In vitro experimental study	6	-	Saliva	*Saccharibacteria*	There is an interaction between *Saccharibacteria* and their microbial host, the benefit of TM7x to its host, and the context-dependent nature of symbiotic relationships.
Oku S et al. [69]	2020	Japan	Cross-sectional study	209	209	Tongue dorsum	Bacteria	The oral cavity of transplantation patients with dysbiosis on surgery day indicates that detecting specific nonindigenous taxa could indicate transplant outcomes.
Irfan M et al. [70]	2024	USA	Experimental study	-	-		Virulence factor PGN-_1547	Elimination of PGN_1547 adhesin decreases the virulence of *Porphyromonas gingivalis*, its capacity to form dental plaque, and its ability to fix on host cells.
Shoer S et al. [71]	2023	Israel	Cohort study	200	1632	Subgingival plaque, stool	Oral and gut microbiomes	Nutritional therapy can influence the microbiome, cardiometabolic profile, and host immune reaction.

								They are interconnected and can used for innovative healing procedures.
Overmyer K et al. [72]	2021	USA	In vitro experimental study	97	291	Supragingival plaque	Microbiome (proteins, metabolites, lipids)	There is a crucial interconnection between innovative microbial metabolic pathways and host-derived proteins with periodontal disease.
Lyu X et al. [73]	2021	China	Clinical trial	26	26	Saliva	Bacteriae, *Candida albicans*	There is an interaction among *Candida albicans* and *Streptococcus species*, with alternations in the microbial marker gene during chronic erythematous candidiasis.
Tong Y et al. [74]	2020	China	Cross-sectional study	79	79	Saliva	Microbiome	A characteristic compositional change of salivary microbes in individuals at high risk for rheumatoid arthritis suggests that dysbiosis occurs in the preclinical stage of this disease and is correlated with systemic autoimmune features.
Rosier BT et al. [75]	2020	Spain	Experimental study	12	24	Saliva	Microbiome	Adding nitrate to oral cultures can influence the composition and function of the microbiome, which is beneficial to the host.
Lewis JP et al. [76]	2023	USA	In vitro experimental study	-	-	-	Bacteroidetes	Iron is a key regulator for bacterial persistence on host- an exploration of the molecular mechanisms of iron homeostasis in Bacteroidetes.
Sekaran K et al. [77]	2023	India	Cross-sectional study	111	105	Nasopharyngeal, saliva	Airway, oral microbiomes	In the *SARS-CoV-2* study, both the asthma and non-asthma groups

								exhibited the presence of *Actinobacteria* and *Pseudomonadota* in their salivary microbiome.
Wingfield B et al. [78]	2021	United Kingdom	Cohort study	83	83	Saliva	Microbiome	Significant variability exists in the salivary microbiota alpha and beta heterogeneity, distinguishing between depressed and healthy controls.
Chen JW et al. [79]	2021	Taiwan	Cohort study	75	75	Saliva	Microbiome	The partitioned beta-diversity analysis showed a very high turnover of species but a low turnover of functions.
Annavajhala MK et al. [80]	2020	USA	Clinical trial	20	100	Saliva, oral biofilm, distal esophagus	Esophageal and oral microbiome	Chlorhexidine treatment alters esophageal bacteria and gene activity, and *Haemophilus* is also linked to changes in gene expression.

Discussion

The findings focus on the complex relationship between the oral microbiota and human health, especially when considering the impact of harmful oral pathogens in systemic conditions. Bacteria like *Porphyromonas gingivalis, Aggregatibacter actinomycetemcomitans, Fusobacterium nucleatum,* and others associated with periodontal disease are known to exacerbate a range of health conditions [81,82]. Periodontal disease is correlated with respiratory infections caused by *Chlamydia pneumoniae* and chronic illnesses like chronic obstructive pulmonary disease and cystic fibrosis [83]. Moreover, the systemic effects of oral pathogens extend to neurodegenerative diseases such as Alzheimer's, where oral bacteria are thought to contribute to cognitive decline [84]. Also, the correlation between periodontal disease and cardiovascular diseases highlights the inflammatory response triggered by oral pathogens, which can contribute to the development of these diseases [85]. Oral bacteria also influence metabolic disorders, such as diabetes and insulin resistance, where periodontal disease can complicate insulin management [86]. Furthermore, autoimmune diseases like rheumatoid arthritis and an elevated risk of pancreatic and colorectal carcinoma have been linked to the presence of harmful oral bacteria [87,88]. Operational Taxonomic Units (OTUs) offer a more objective approach to categorizing these populations without the biases of traditional taxonomic methods, with greater precision of microbial community identification [89]. Studies of microbiome in children aged 12 to 24 months reveal that the presence of *Proteobacteria, Fusobacterium, Actinobacteria, Bacteroidetes,* and *Firmicutes* plays key roles in early microbial development [90]. The younger children predominantly have *Firmicutes, Proteobacteria,* and *Actinobacillus*, accentuating the dynamic and evolving nature of the microbiome in early childhood [91]. This dynamic nature of the microbiota, with comparisons between infant and adult microbiota showing significant variability, particularly in the prevalence of *Proteobacteria, Fusobacterium,* and *Rothia,* which are more prevalent in infants [92]. This variation accentuates the importance of considering age-specific microbial communities in studies of microbiota and disease evolution [93].

Exosomes – small extracellular vesicles – are important in facilitating intercellular communication and the transmission of pathogenic factors, such as bacterial toxins, viral proteins, and other pathogenic molecules [94]. In bacterial infections, for example, Staphylococcus aureus exosomes can transfer α-toxin to other cells, amplifying the infection [95]. Similarly, exosomes from *Bacillus anthracis* carry lethal toxins to distant areas, while *Helicobacter pylori* exosomes containing the CagA gene spread toxic factors throughout the body [96] [97]. Viruses like HTLV-1 and HIV-1 exploit these vesicles to transfer viral proteins, such as Tax, and viral RNA to other cells, enhancing infection and helping the virus evade the immune system [98]. Other viruses, like *Human herpesvirus 6 (HHV-6)* and *Hepatitis viruses,* use exosomes to protect themselves from immune responses, further complicating disease progression [99]. Additionally, exosomes are involved in fungal and parasitic infections. Organisms such as *Saccharomyces cerevisiae*, *Trypanosoma brucei*, *Toxoplasma gondii*, and *Trypanosoma cruzi* use exosomes to manipulate host immune responses or to spread prions and other virulence factors [100]. The role of exosomes in spreading pathogens will be essential for developing more efficient methods for preventing and addressing infections and diseases associated with microbial dysbiosis [101].

The oral cavity hosts a polymicrobial community influenced by host-specific factors, such as immune response, diet, and dental care, and environmental elements, like tooth anatomy and exposure to pathogens [102]. Changes in dietary habits, immune function, saliva composition, or environmental stressors induce a dysbiosis and diseases like tooth decay and periodontal disease [103,104]. Elevated levels of host signaling molecules and cytokines have been shown to correlate with the presence of dental caries, specifically dentin caries, indicating the strong relation between host immunity and microbial communities in oral health [6].

Recent research has increasingly focused on integrating omics-based data to better understand host-microbe interactions and microbial diversity in dental caries. However, despite promising advances, much of this research remains fragmented, particularly in integrating multi-omics technologies with clinical data [105]. New models have offered important perspectives on the early stages of disease development, such as novel three-dimensional models that simulate peri-implant disease and offer early detection of molecular changes associated with disease onset [106].

This study demonstrates the important role of the oral microbiome in immune responses; it also shows the differences in microbial communities that vary according to factors such as sex, maternal transmission, and other influences. ECC-associated bacterial profiles, which are influenced by oral feeding practices and dietary habits such as sugar consumption, demonstrate a connection between diet and microbiome composition.

Strengths of the Study

This study clarifies that the genetic markers are associated with oral disease vulnerability. Understanding genetic susceptibility is important to implementing prevention strategies.

Limitations of the Study

One of the research limitations is its diverse sampling and analytical methods, which result in a series of possibilities and outcomes; some of the studies have a small sample, which limits their statistical reliability and reduces the applicability of their results to broader populations.

A detailed evaluation is essential to guarantee that the studies selected are of high quality and relevant to the research objectives. The differences in sequencing technologies and platforms in various studies cause inconsistency in data quality.

Conclusions

The oral microbiome presents significant potential for healthcare diagnostics. Emerging treatment strategies aim to boost populations of commensal bacteria while simultaneously reducing the presence of pathogenic oral microbes. This dual approach has the potential to transform the prevention and management of numerous health conditions, ultimately improving both oral and overall health outcomes.

Author Contributions (CRediT Taxonomy)

Contributor roles: Conceptualization: E.É.K., Data curation: Cs.D., Formal analysis: E.É.K., Funding acquisition: I.É.M., Investigation: E.É.K., Methodology: I.É.M., Project administration: K.M, Resources: Cs.D., Software: I.É.M., Supervision: K.M, Validation: Cs.D., K.M, Visualization I.É.M., Writing – original draft Preparation: E.É.K., Writing – review & editing: E.É.K..

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Conflict of interest

None to declare.

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References

1.Gest, H. The Discovery of Microorganisms by Robert Hooke and Antoni van Leeuwenhoek, Fellows of The Royal Society. Notes Rec. R. Soc. Lond. 2004, 58, 187–201, doi:10.1098/rsnr.2004.0055.

2.Pasteur, L. Mémoire Sur La Fermentation Appelée Lactique (Extrait Par l'auteur). Mol Med 1995, 1, 599–601.

3.[The etiology of tuberculosis by Dr. Robert Koch. From the Berliner Klinische Wochenschrift, Volume 19 (1882)]. Zentralbl Bakteriol Mikrobiol Hyg A Med Mikrobiol Infekt Parasitol 1982, 251, 287–296.

4.Deo, P.N.; Deshmukh, R. Oral Microbiome: Unveiling the Fundamentals. J Oral Maxillofac Pathol 2019, 23, 122–128, doi:10.4103/jomfp.JOMFP_304_18.

5.Krishnan, K.; Chen, T.; Paster, B.J. A Practical Guide to the Oral Microbiome and Its Relation to Health and Disease. Oral Dis 2017, 23, 276–286, doi:10.1111/odi.12509.

6.Spatafora, G.; Li, Y.; He, X.; Cowan, A.; Tanner, A.C.R. The Evolving Microbiome of Dental Caries. Microorganisms 2024, 12, 121, doi:10.3390/microorganisms12010121.

7.Dinis, M.; Agnello, M.; Cen, L.; Shokeen, B.; He, X.; Shi, W.; Wong, D.T.W.; Lux, R.; Tran, N.C. Oral Microbiome: Streptococcus Mutans/Caries Concordant-Discordant Children. Front Microbiol 2022, 13, 782825, doi:10.3389/fmicb.2022.782825.

8.Nearing, J.T.; DeClercq, V.; Van Limbergen, J.; Langille, M.G.I. Assessing the Variation within the Oral Microbiome of Healthy Adults. mSphere 2020, 5, e00451-20, doi:10.1128/mSphere.00451-20.

9.Könönen, E.; Fteita, D.; Gursoy, U.K.; Gursoy, M. Prevotella Species as Oral Residents and Infectious Agents with Potential Impact on Systemic Conditions. J Oral Microbiol 2022, 14, 2079814, doi:10.1080/20002297.2022.2079814.

10.Belmok, A.; de Cena, J.A.; Kyaw, C.M.; Damé-Teixeira, N. The Oral Archaeome: A Scoping Review. J Dent Res 2020, 99, 630–643, doi:10.1177/0022034520910435.

11.Bhandary, R.; Venugopalan, G.; Ramesh, A.; Tartaglia, G.M.; Singhal, I.; Khijmatgar, S. Microbial Symphony: Navigating the Intricacies of the Human Oral Microbiome and Its Impact on Health. Microorganisms 2024, 12, 571, doi:10.3390/microorganisms12030571.

12.Niemczyk, W.; Niemczyk, S.; Odrzywolska, O.; Doroz, P.; Hochuł, D.; Zawadzka, K. Application of I-PRF in Dentistry. Wiad Lek 2024, 77, 2348–2352, doi:10.36740/WLek/195552.

13.Page, M.J.; McKenzie, J.E.; Bossuyt, P.M.; Boutron, I.; Hoffmann, T.C.; Mulrow, C.D.; Shamseer, L.; Tetzlaff, J.M.; Akl, E.A.; Brennan, S.E.; et al. The PRISMA 2020 Statement: An Updated Guideline for Reporting Systematic Reviews. BMJ 2021, n71, doi:10.1136/bmj.n71.

14.Sedghi, L.; DiMassa, V.; Harrington, A.; Lynch, S.V.; Kapila, Y.L. The Oral Microbiome: Role of Key Organisms and Complex Networks in Oral Health and Disease. Periodontol 2000 2021, 87, 107–131, doi:10.1111/prd.12393.

15.Baker, J.L.; Mark Welch, J.L.; Kauffman, K.M.; McLean, J.S.; He, X. The Oral Microbiome: Diversity, Biogeography and Human Health. Nat Rev Microbiol 2024, 22, 89–104, doi:10.1038/s41579-023-00963-6.

16.Moraitou, M.; Forsythe, A.; Fellows Yates, J.A.; Brealey, J.C.; Warinner, C.; Guschanski, K. Ecology, Not Host Phylogeny, Shapes the Oral Microbiome in Closely Related Species. Mol Biol Evol 2022, 39, msac263, doi:10.1093/molbev/msac263.

17.Kozak, M.; Pawlik, A. The Role of the Oral Microbiome in the Development of Diseases. Int J Mol Sci 2023, 24, 5231, doi:10.3390/ijms24065231.

18.Kreth, J.; Merritt, J. Illuminating the Oral Microbiome and Its Host Interactions: Tools and Approaches for Molecular Ecological Studies. FEMS

Microbiol Rev 2022, 47, fuac052, doi:10.1093/femsre/fuac052.

19.D'Agostino, S.; Ferrara, E.; Valentini, G.; Stoica, S.A.; Dolci, M. Exploring Oral Microbiome in Healthy Infants and Children: A Systematic Review. Int J Environ Res Public Health 2022, 19, 11403, doi:10.3390/ijerph191811403.

20.Merritt, J.; Kreth, J. Illuminating the Oral Microbiome and Its Host Interactions: Tools and Approaches for Molecular Microbiology Studies. FEMS Microbiol Rev 2023, 47, fuac050, doi:10.1093/femsre/fuac050.

21.Baker, J.L. Illuminating the Oral Microbiome and Its Host Interactions: Recent Advancements in Omics and Bioinformatics Technologies in the Context of Oral Microbiome Research. FEMS Microbiol Rev 2023, 47, fuad051, doi:10.1093/femsre/fuad051.

22.Moon, J.-H.; Roh, D.-H.; Kwack, K.H.; Lee, J.-H. Bacterial Single-Cell Transcriptomics: Recent Technical Advances and Future Applications in Dentistry. Jpn Dent Sci Rev 2023, 59, 253–262, doi:10.1016/j.jdsr.2023.08.001.

23.Jafari, N.; Khoradmehr, A.; Moghiminasr, R.; Seyed Habashi, M. Mesenchymal Stromal/Stem Cells-Derived Exosomes as an Antimicrobial Weapon for Orodental Infections. Front Microbiol 2021, 12, 795682, doi:10.3389/fmicb.2021.795682.

24.Ebersole, J.L.; Kirakodu, S.S.; Gonzalez, O.A. Oral Microbiome Interactions with Gingival Gene Expression Patterns for Apoptosis, Autophagy and Hypoxia Pathways in Progressing Periodontitis. Immunology 2021, 162, 405–417, doi:10.1111/imm.13292.

25.Moussa, D.G.; Ahmad, P.; Mansour, T.A.; Siqueira, W.L. Current State and Challenges of the Global Outcomes of Dental Caries Research in the Meta-Omics Era. Front Cell Infect Microbiol 2022, 12, 887907, doi:10.3389/fcimb.2022.887907.

26.Santonocito, S.; Ferlito, S.; Polizzi, A.; Ronsivalle, V.; Sclafani, R.; Valletta, A.; Lo Giudice, A.; Cavalcanti, R.; Spagnuolo, G.; Isola, G. Therapeutic and Metagenomic Potential of the Biomolecular Therapies against Periodontitis and the Oral Microbiome: Current Evidence and Future Perspectives. Int J Mol Sci 2022, 23, 13708, doi:10.3390/ijms232213708.

27.Nguyen, T.; Sedghi, L.; Ganther, S.; Malone, E.; Kamarajan, P.; Kapila, Y.L. Host-Microbe Interactions: Profiles in the Transcriptome, the Proteome, and the Metabolome. Periodontol 2000 2020, 82, 115–128, doi:10.1111/prd.12316.

28.Peluso, G.; Tian, E.; Abusleme, L.; Munemasa, T.; Mukaibo, T.; Ten Hagen, K.G. Loss of the Disease-Associated Glycosyltransferase Galnt3 Alters Muc10 Glycosylation and the Composition of the Oral Microbiome. J Biol Chem 2020, 295, 1411–1425, doi:10.1074/jbc.RA119.009807.

29.Dahlquist-Axe, G.; Standeven, F.J.; Speller, C.F.; Tedder, A.; Meehan, C.J. Inferring Diet, Disease and Antibiotic Resistance from Ancient Human Oral Microbiomes. Microb Genom 2024, 10, 001251, doi:10.1099/mgen.0.001251.

30.Bhaumik, D.; Manikandan, D.; Foxman, B. Cariogenic and Oral Health Taxa in the Oral Cavity among Children and Adults: A Scoping Review. Arch Oral Biol 2021, 129, 105204, doi:10.1016/j.archoralbio.2021.105204.

31.Dahlen, G.; Fejerskov, O.; Manji, F. Current Concepts and an Alternative Perspective on Periodontal Disease. BMC Oral Health 2020, 20, 235, doi:10.1186/s12903-020-01221-4.

32.Diakoumopoulou, D.; Magana, M.; Karoussis, I.K.; Nikolaou, C.; Chatzipanagiotou, S.; Ioannidis, A. The Ever-Changing Landscape in Modern Dentistry Therapeutics – Enhancing the Emptying Quiver of the Periodontist. Heliyon 2021, 7, e08342, doi:10.1016/j.heliyon.2021.e08342.

33.Hashim, A.; Alsam, A.; Payne, M.A.; Aduse-Opoku, J.; Curtis, M.A.; Joseph, S. Loss of Neutrophil Homing to the Periodontal Tissues Modulates the Composition and Disease Potential of the Oral Microbiota. Infect Immun 2021, 89, e0030921, doi:10.1128/IAI.00309-21.

34.Gao, L.; Kuraji, R.; Zhang, M.J.; Martinez, A.; Radaic, A.; Kamarajan, P.; Le, C.; Zhan, L.; Ye, C.; Rangé, H.; et al. Nisin Probiotic Prevents Inflammatory Bone Loss While Promoting Reparative Proliferation and a Healthy Microbiome. NPJ Biofilms Microbiomes 2022, 8, 45, doi:10.1038/s41522-022-00307-x.

35.Scannapieco, F.A.; Dongari-Bagtzoglou, A. Dysbiosis Revisited: Understanding the Role of the Oral Microbiome in the Pathogenesis of Gingivitis and Periodontitis: A Critical Assessment. J Periodontol 2021, 92, 1071–1078, doi:10.1002/JPER.21-0120.

36.Granehäll, L.; Huang, K.D.; Tett, A.; Manghi, P.; Paladin, A.; O'Sullivan, N.; Rota-Stabelli, O.; Segata, N.; Zink, A.; Maixner, F. Metagenomic Analysis of Ancient Dental Calculus Reveals Unexplored Diversity of Oral Archaeal Methanobrevibacter. Microbiome 2021, 9, 197, doi:10.1186/s40168-021-01132-8.

37.Tang, B.; Yan, C.; Shen, X.; Li, Y. The Bidirectional Biological Interplay between Microbiome and Viruses in Periodontitis and Type-2 Diabetes Mellitus. Front Immunol 2022, 13, 885029, doi:10.3389/fimmu.2022.885029.

38.Sharma, R.; Gibb, A.A.; Barnts, K.; Elrod, J.W.; Puri, S. Alternative Oxidase Promotes High Iron Tolerance in Candida Albicans. Microbiol Spectr 2023, 11, e0215723, doi:10.1128/spectrum.02157-23.

39.Lutz, H.L.; Gilbert, J.A.; Dick, C.W. Associations between Afrotropical Bats, Eukaryotic Parasites, and Microbial Symbionts. Mol Ecol 2022, 31, 1939–1950, doi:10.1111/mec.16044.

40.Krutyhołowa, A.; Strzelec, K.; Dziedzic, A.; Bereta, G.P.; Łazarz-Bartyzel, K.; Potempa, J.; Gawron, K. Host and Bacterial Factors Linking Periodontitis and Rheumatoid Arthritis. Front Immunol 2022, 13, 980805, doi:10.3389/fimmu.2022.980805.

41.Tan, L.; Zhong, M.-M.; Liu, Q.; Chen, Y.; Zhao, Y.-Q.; Zhao, J.; Dusenge, M.A.; Feng, Y.; Ye, Q.; Hu, J.; et al. Potential Interaction between the Oral Microbiota and COVID-19: A Meta-Analysis and Bioinformatics Prediction. Front Cell Infect Microbiol 2023, 13, 1193340, doi:10.3389/fcimb.2023.1193340.

42.Neculae, E.; Gosav, E.M.; Valasciuc, E.; Dima, N.; Floria, M.; Tanase, D.M. The Oral Microbiota in Valvular Heart Disease: Current Knowledge and Future Directions. Life (Basel) 2023, 13, 182, doi:10.3390/life13010182.

43.Pignatelli, P.; Romei, F.M.; Bondi, D.; Giuliani, M.; Piattelli, A.; Curia, M.C. Microbiota and Oral Cancer as A Complex and Dynamic Microenvironment: A Narrative Review from Etiology to Prognosis. Int J Mol Sci 2022, 23, 8323, doi:10.3390/ijms23158323.

44.Huang, X.; Huang, X.; Huang, Y.; Zheng, J.; Lu, Y.; Mai, Z.; Zhao, X.; Cui, L.; Huang, S. The Oral Microbiome in Autoimmune Diseases: Friend or Foe? J Transl Med 2023, 21, 211, doi:10.1186/s12967-023-03995-x.

45.Sun, Y.; Lu, J.; Yang, J.; Liu, Y.; Liu, L.; Zeng, F.; Niu, Y.; Dong, L.; Yang, F. Construction of a Caries Diagnosis Model Based on Microbiome Novelty Score. Hua Xi Kou Qiang Yi Xue Za Zhi 2023, 41, 208–217, doi:10.7518/hxkq.2023.2022301.

46.Liu, X.; Tong, X.; Zhu, J.; Tian, L.; Jie, Z.; Zou, Y.; Lin, X.; Liang, H.; Li, W.; Ju, Y.; et al. Metagenome-Genome-Wide Association Studies Reveal Human Genetic Impact on the Oral Microbiome. Cell Discov 2021, 7, 117, doi:10.1038/s41421-021-00356-0.

47.Tierney, B.T.; Kim, J.; Overbey, E.G.; Ryon, K.A.; Foox, J.; Sierra, M.A.; Bhattacharya, C.; Damle, N.; Najjar, D.; Park, J.; et al. Longitudinal Multi-Omics Analysis of Host Microbiome Architecture and Immune Responses during Short-Term Spaceflight. Nat Microbiol 2024, 9, 1661–1675, doi:10.1038/s41564-024-01635-8.

48.Liu, X.; Tong, X.; Jie, Z.; Zhu, J.; Tian, L.; Sun, Q.; Ju, Y.; Zou, L.; Lu, H.; Qiu, X.; et al. Sex Differences in the Oral Microbiome, Host Traits, and Their Causal Relationships. iScience 2023, 26, 105839, doi:10.1016/j.isci.2022.105839.

49.Valles-Colomer, M.; Blanco-Míguez, A.; Manghi, P.; Asnicar, F.; Dubois, L.; Golzato, D.; Armanini, F.; Cumbo, F.; Huang, K.D.; Manara, S.; et al. The Person-to-Person Transmission Landscape of the Gut and Oral Microbiomes. Nature 2023, 614, 125–135, doi:10.1038/s41586-022-05620-1.

50.Freire, M.; Moustafa, A.; Harkins, D.M.; Torralba, M.G.; Zhang, Y.; Leong, P.; Saffery, R.; Bockmann, M.; Kuelbs, C.; Hughes, T.; et al. Longitudinal Study of Oral Microbiome Variation in Twins. Sci Rep 2020, 10, 7954, doi:10.1038/s41598-020-64747-1.

51.Saito, S.; Aoki, Y.; Tamahara, T.; Goto, M.; Matsui, H.; Kawashima, J.; Danjoh, I.; Hozawa, A.; Kuriyama, S.; Suzuki, Y.; et al. Oral Microbiome Analysis in Prospective Genome Cohort Studies of the Tohoku Medical Megabank Project. Front. Cell. Infect. Microbiol. 2021, 10, 604596, doi:10.3389/fcimb.2020.604596.

52.Blostein, F.; Zou, T.; Bhaumik, D.; Salzman, E.; Bakulski, K.M.; Shaffer, J.R.; Marazita, M.L.; Foxman, B. Bacterial Community Modifies Host Genetics Effect on Early Childhood Caries. J Dent Res 2023, 102, 1098–1105, doi:10.1177/00220345231175356.

53.Baker, J.L.; Morton, J.T.; Dinis, M.; Alvarez, R.; Tran, N.C.; Knight, R.; Edlund, A. Deep Metagenomics Examines the Oral Microbiome during Dental Caries, Revealing Novel Taxa and Co-Occurrences with Host Molecules. Genome Res. 2021, 31, 64–74, doi:10.1101/gr.265645.120.

54.Vanzele, P.A.R.; Sparvoli, L.G.; De Camargo, P.P.; Tragante, C.R.; Beozzo, G.P.N.S.; Krebs, V.L.J.; Cortez, R.V.; Taddei, C.R. Establishment of Oral Microbiome in Very Low Birth Weight Infants during the First Weeks of Life and the Impact of Oral Diet Implementation. PLoS ONE 2023, 18, e0295962, doi:10.1371/journal.pone.0295962.

55.Cheung, M.K.; Chan, J.Y.K.; Wong, M.C.S.; Wong, P.Y.; Lei, P.; Cai, L.; Lan, L.; Ho, W.C.S.; Yeung, A.C.M.; Chan, P.K.S.; et al. Determinants and Interactions of Oral Bacterial and Fungal Microbiota in Healthy Chinese Adults. Microbiol Spectr 2022, 10, e02410-21, doi:10.1128/spectrum.02410-21.

56.Sukumar, S.; Wang, F.; Simpson, C.A.; Willet, C.E.; Chew, T.; Hughes, T.E.; Bockmann, M.R.; Sadsad, R.; Martin, F.E.; Lydecker, H.W.; et al. Development of the Oral Resistome during the First Decade of Life. Nat Commun 2023, 14, 1291, doi:10.1038/s41467-023-36781-w.

57.Bor, B.; Collins, A.J.; Murugkar, P.P.; Balasubramanian, S.; To, T.T.; Hendrickson, E.L.; Bedree, J.K.; Bidlack, F.B.; Johnston, C.D.; Shi, W.; et al. Insights Obtained by Culturing Saccharibacteria With Their Bacterial Hosts. J Dent Res 2020, 99, 685–694, doi:10.1177/0022034520905792.

58.Charalambous, E.G.; Mériaux, S.B.; Guebels, P.; Muller, C.P.; Leenen, F.A.D.; Elwenspoek, M.M.C.; Thiele, I.; Hertel, J.; Turner, J.D. Early-Life Adversity Leaves Its Imprint on the Oral Microbiome for More Than 20 Years and Is Associated with Long-Term Immune Changes. IJMS 2021, 22, 12682, doi:10.3390/ijms222312682.

59.Hendrickson, E.L.; Bor, B.; Kerns, K.A.; Lamont, E.I.; Chang, Y.; Liu, J.; Cen, L.; Schulte, F.; Hardt, M.; Shi, W.; et al. Transcriptome of Epibiont Saccharibacteria Nanosynbacter Lyticus Strain TM7x During the Establishment of Symbiosis. J Bacteriol 2022, 204, e00112-22, doi:10.1128/jb.00112-22.

60.Jiang, Y.; Brandt, B.W.; Buijs, M.J.; Cheng, L.; Exterkate, R.A.M.; Crielaard, W.; Deng, D.M. Manipulation of Saliva-Derived Microcosm Biofilms To

Resemble Dysbiotic Subgingival Microbiota. Appl Environ Microbiol 2021, 87, e02371-20, doi:10.1128/AEM.02371-20.

61.Nibali, L.; Stephen, A.S.; Allaker, R.P.; Di Pino, A.; Terranova, V.; Pisano, M.; Di Marca, S.; Ferrara, V.; Scicali, R.; Purrello, F.; et al. Associations between Host Genetic Variants and Subgingival Microbiota in Patients with the Metabolic Syndrome. IJMS 2023, 24, 16649, doi:10.3390/ijms242316649.

62.Cen, L.; Chang, Y.; Bedree, J.K.; Ma, Y.; Zhong, Q.; Utter, D.R.; Dong, P.-T.; Lux, R.; Bor, B.; Liu, J.; et al. Exploitation of a Bacterium-Encoded Lytic Transglycosylase by a Human Oral Lytic Phage To Facilitate Infection. J Virol 2022, 96, e01063-22, doi:10.1128/jvi.01063-22.

63.Zhong, Q.; Liao, B.; Liu, J.; Shen, W.; Wang, J.; Wei, L.; Ma, Y.; Dong, P.-T.; Bor, B.; McLean, J.S.; et al. Episymbiotic Saccharibacteria TM7x Modulates the Susceptibility of Its Host Bacteria to Phage Infection and Promotes Their Coexistence. Proc. Natl. Acad. Sci. U.S.A. 2024, 121, e2319790121, doi:10.1073/pnas.2319790121.

64.Esberg, A.; Haworth, S.; Hasslöf, P.; Lif Holgerson, P.; Johansson, I. Oral Microbiota Profile Associates with Sugar Intake and Taste Preference Genes. Nutrients 2020, 12, 681, doi:10.3390/nu12030681.

65.Münch, P.C.; Franzosa, E.A.; Stecher, B.; McHardy, A.C.; Huttenhower, C. Identification of Natural CRISPR Systems and Targets in the Human Microbiome. Cell Host & Microbe 2021, 29, 94-106.e4, doi:10.1016/j.chom.2020.10.010.

66.Treerat, P.; Redanz, U.; Redanz, S.; Giacaman, R.A.; Merritt, J.; Kreth, J. Synergism between Corynebacterium and Streptococcus Sanguinis Reveals New Interactions between Oral Commensals. The ISME Journal 2020, 14, 1154–1169, doi:10.1038/s41396-020-0598-2.

67.Izawa, K.; Okamoto-Shibayama, K.; Kita, D.; Tomita, S.; Saito, A.; Ishida, T.; Ohue, M.; Akiyama, Y.; Ishihara, K. Taxonomic and Gene Category Analyses of Subgingival Plaques from a Group of Japanese Individuals with and without Periodontitis. IJMS 2021, 22, 5298, doi:10.3390/ijms22105298.

68.Dong, P.-T.; Tian, J.; Kobayashi-Kirschvink, K.J.; Cen, L.; McLean, J.S.; Bor, B.; Shi, W.; He, X. Episymbiotic Saccharibacteria Induce Intracellular Lipid Droplet Production in Their Host Bacteria. The ISME Journal 2024, 18, wrad034, doi:10.1093/ismejo/wrad034.

69.Oku, S.; Takeshita, T.; Futatsuki, T.; Kageyama, S.; Asakawa, M.; Mori, Y.; Miyamoto, T.; Hata, J.; Ninomiya, T.; Kashiwazaki, H.; et al. Disrupted Tongue Microbiota and Detection of Nonindigenous Bacteria on the Day of Allogeneic Hematopoietic Stem Cell Transplantation. PLoS Pathog 2020, 16, e1008348, doi:10.1371/journal.ppat.1008348.

70.Irfan, M.; Solbiati, J.; Duran-Pinedo, A.; Rocha, F.G.; Gibson, F.C.; Frias-Lopez, J. A Porphyromonas Gingivalis Hypothetical Protein Controlled by the Type I-C CRISPR-Cas System Is a Novel Adhesin Important in Virulence. mSystems 2024, 9, e01231-23, doi:10.1128/msystems.01231-23.

71.Shoer, S.; Shilo, S.; Godneva, A.; Ben-Yacov, O.; Rein, M.; Wolf, B.C.; Lotan-Pompan, M.; Bar, N.; Weiss, E.I.; Houri-Haddad, Y.; et al. Impact of Dietary Interventions on Pre-Diabetic Oral and Gut Microbiome, Metabolites and Cytokines. Nat Commun 2023, 14, 5384, doi:10.1038/s41467-023-41042-x.

72.Overmyer, K.A.; Rhoads, T.W.; Merrill, A.E.; Ye, Z.; Westphall, M.S.; Acharya, A.; Shukla, S.K.; Coon, J.J. Proteomics, Lipidomics, Metabolomics, and 16S DNA Sequencing of Dental Plaque From Patients With Diabetes and Periodontal Disease. Molecular & Cellular Proteomics 2021, 20, 100126, doi:10.1016/j.mcpro.2021.100126.

73.Lyu, X.; Zheng, H.; Wang, X.; Zhang, H.; Gao, L.; Xun, Z.; Zhang, Q.; He, X.; Hua, H.; Yan, Z.; et al. Oral Microbiota Composition and Function Changes During Chronic Erythematous Candidiasis. Front. Cell. Infect. Microbiol. 2021, 11, 691092, doi:10.3389/fcimb.2021.691092.

74.Tong, Y.; Zheng, L.; Qing, P.; Zhao, H.; Li, Y.; Su, L.; Zhang, Q.; Zhao, Y.; Luo, Y.; Liu, Y. Oral Microbiota Perturbations Are Linked to High Risk for Rheumatoid Arthritis. Front. Cell. Infect. Microbiol. 2020, 9, 475, doi:10.3389/fcimb.2019.00475.

75.Rosier, B.T.; Buetas, E.; Moya-Gonzalvez, E.M.; Artacho, A.; Mira, A. Nitrate as a Potential Prebiotic for the Oral Microbiome. Sci Rep 2020, 10, 12895, doi:10.1038/s41598-020-69931-x.

76.Lewis, J.P.; Gui, Q. Iron Deficiency Modulates Metabolic Landscape of Bacteroidetes Promoting Its Resilience during Inflammation. Microbiol Spectr 2023, 11, e04733-22, doi:10.1128/spectrum.04733-22.

77.Sekaran, K.; Varghese, R.P.; Doss C., G.P.; Alsamman, A.M.; Zayed, H.; El Allali, A. Airway and Oral Microbiome Profiling of SARS-CoV-2 Infected Asthma and Non-Asthma Cases Revealing Alterations–A Pulmonary Microbial Investigation. PLoS ONE 2023, 18, e0289891, doi:10.1371/journal.pone.0289891.

78.Wingfield, B.; Lapsley, C.; McDowell, A.; Miliotis, G.; McLafferty, M.; O'Neill, S.M.; Coleman, S.; McGinnity, T.M.; Bjourson, A.J.; Murray, E.K. Variations in the Oral Microbiome Are Associated with Depression in Young Adults. Sci Rep 2021, 11, 15009, doi:10.1038/s41598-021-94498-6.

79.Chen, J.-W.; Wu, J.-H.; Chiang, W.-F.; Chen, Y.-L.; Wu, W.-S.; Wu, L.-W. Taxonomic and Functional Dysregulation in Salivary Microbiomes During Oral Carcinogenesis. Front. Cell. Infect. Microbiol. 2021, 11, 663068, doi:10.3389/fcimb.2021.663068.

80.Annavajhala, M.K.; May, M.; Compres, G.; Freedberg, D.E.; Graham, R.; Stump, S.; Que, J.; Korem, T.; Uhlemann, A.-C.; Abrams, J.A. Relationship of the

Esophageal Microbiome and Tissue Gene Expression and Links to the Oral Microbiome: A Randomized Clinical Trial. Clin Transl Gastroenterol 2020, 11, e00235, doi:10.14309/ctg.0000000000000235.

81.Peng, X.; Cheng, L.; You, Y.; Tang, C.; Ren, B.; Li, Y.; Xu, X.; Zhou, X. Oral Microbiota in Human Systematic Diseases. Int J Oral Sci 2022, 14, 14, doi:10.1038/s41368-022-00163-7.

82.Willis, J.R.; Gabaldón, T. The Human Oral Microbiome in Health and Disease: From Sequences to Ecosystems. Microorganisms 2020, 8, 308, doi:10.3390/microorganisms8020308.

83.Makkar, H.; Reynolds, M.A.; Wadhawan, A.; Dagdag, A.; Merchant, A.T.; Postolache, T.T. Periodontal, Metabolic, and Cardiovascular Disease: Exploring the Role of Inflammation and Mental Health. Pteridines 2018, 29, 124–163, doi:10.1515/pteridines-2018-0013.

84.Nicholson, J.S.; Landry, K.S. Oral Dysbiosis and Neurodegenerative Diseases: Correlations and Potential Causations. Microorganisms 2022, 10, 1326, doi:10.3390/microorganisms10071326.

85.Arbildo-Vega, H.I.; Cruzado-Oliva, F.H.; Coronel-Zubiate, F.T.; Meza-Málaga, J.M.; Luján-Valencia, S.A.; Luján-Urviola, E.; Echevarria-Goche, A.; Farje-Gallardo, C.A.; Castillo-Cornock, T.B.; Serquen-Olano, K.; et al. Periodontal Disease and Cardiovascular Disease: Umbrella Review. BMC Oral Health 2024, 24, 1308, doi:10.1186/s12903-024-04907-1.

86.Hegde, R.; Awan, K.H. Effects of Periodontal Disease on Systemic Health. Disease-a-Month 2019, 65, 185–192, doi:10.1016/j.disamonth.2018.09.011.

87.Nikitakis, N.; Papaioannou, W.; Sakkas, L.; Kousvelari, E. The Autoimmunity–Oral Microbiome Connection. Oral Diseases 2017, 23, 828–839, doi:10.1111/odi.12589.

88.Su, L.; Yang, R.; Sheng, Y.; Ullah, S.; Zhao, Y.; Shunjiayi, H.; Zhao, Z.; Wang, Q. Insights into the Oral Microbiota in Human Systemic Cancers. Front. Microbiol. 2024, 15, 1369834, doi:10.3389/fmicb.2024.1369834.

89.Lladó Fernández, S.; Větrovský, T.; Baldrian, P. The Concept of Operational Taxonomic Units Revisited: Genomes of Bacteria That Are Regarded as Closely Related Are Often Highly Dissimilar. Folia Microbiol 2019, 64, 19–23, doi:10.1007/s12223-018-0627-y.

90.Yao, Y.; Cai, X.; Ye, Y.; Wang, F.; Chen, F.; Zheng, C. The Role of Microbiota in Infant Health: From Early Life to Adulthood. Front. Immunol. 2021, 12, 708472, doi:10.3389/fimmu.2021.708472.

91.Romano-Keeler, J.; Moore, D.J.; Wang, C.; Brucker, R.M.; Fonnesbeck, C.; Slaughter, J.C.; Li, H.; Curran, D.P.; Meng, S.; Correa, H.; et al. Early Life Establishment of Site-Specific Microbial Communities in the Gut. Gut Microbes 2014, 5, 192–201, doi:10.4161/gmic.28442.

92.Jo, R.; Yama, K.; Aita, Y.; Tsutsumi, K.; Ishihara, C.; Maruyama, M.; Takeda, K.; Nishinaga, E.; Shibasaki, K.; Morishima, S. Comparison of Oral Microbiome Profiles in 18-Month-Old Infants and Their Parents. Sci Rep 2021, 11, 861, doi:10.1038/s41598-020-78295-1.

93.Kim, M.; Benayoun, B.A. The Microbiome: An Emerging Key Player in Aging and Longevity. Translational Medicine of Aging 2020, 4, 103–116, doi:10.1016/j.tma.2020.07.004.

94.Vučemilović, A. Exosomes: Intriguing Mediators of Intercellular Communication in the Organism's Response to Noxious Agents. Archives of Industrial Hygiene and Toxicology 2024, 75, 228–239, doi:10.2478/aiht-2024-75-3923.

95.Wang, J.; Yao, Y.; Chen, X.; Wu, J.; Gu, T.; Tang, X. Host Derived Exosomes-Pathogens Interactions: Potential Functions of Exosomes in Pathogen Infection. Biomedicine & Pharmacotherapy 2018, 108, 1451–1459, doi:10.1016/j.biopha.2018.09.174.

96.Mosquera-Heredia, M.I.; Morales, L.C.; Vidal, O.M.; Barceló, E.; Silvera-Redondo, C.; Vélez, J.I.; Garavito-Galofre, P. Exosomes: Potential Disease Biomarkers and New Therapeutic Targets. Biomedicines 2021, 9, 1061, doi:10.3390/biomedicines9081061.

97.Zhang, W.; Jiang, X.; Bao, J.; Wang, Y.; Liu, H.; Tang, L. Exosomes in Pathogen Infections: A Bridge to Deliver Molecules and Link Functions. Front. Immunol. 2018, 9, 90, doi:10.3389/fimmu.2018.00090.

98.Peng, Y.; Yang, Y.; Li, Y.; Shi, T.; Luan, Y.; Yin, C. Exosome and Virus Infection. Front. Immunol. 2023, 14, 1154217, doi:10.3389/fimmu.2023.1154217.

99.Saad, M.H.; Badierah, R.; Redwan, E.M.; El-Fakharany, E.M. A Comprehensive Insight into the Role of Exosomes in Viral Infection: Dual Faces Bearing Different Functions. Pharmaceutics 2021, 13, 1405, doi:10.3390/pharmaceutics13091405.

100.Lai, Y.; Jiang, B.; Hou, F.; Huang, X.; Ling, B.; Lu, H.; Zhong, T.; Huang, J. The Emerging Role of Extracellular Vesicles in Fungi: A Double-Edged Sword. Front. Microbiol. 2023, 14, 1216895, doi:10.3389/fmicb.2023.1216895.

101.Kaiko, G.E.; Stappenbeck, T.S. Host–Microbe Interactions Shaping the Gastrointestinal Environment. Trends in Immunology 2014, 35, 538–548, doi:10.1016/j.it.2014.08.002.

102.Hajishengallis, G.; Lamont, R.J.; Koo, H. Oral Polymicrobial Communities: Assembly, Function, and Impact on Diseases. Cell Host & Microbe 2023, 31, 528–538, doi:10.1016/j.chom.2023.02.009.

103.Hajishengallis, G. Periodontitis: From Microbial Immune Subversion to Systemic Inflammation. Nat Rev Immunol 2015, 15, 30–44, doi:10.1038/nri3785.

104.Rajasekaran, J.J.; Krishnamurthy, H.K.; Bosco, J.; Jayaraman, V.; Krishna, K.; Wang, T.; Bei, K. Oral Microbiome: A Review of Its Impact on Oral and Systemic Health. Microorganisms 2024, 12, 1797, doi:10.3390/microorganisms12091797.

105.Zhang, J.S.; Huang, S.; Chen, Z.; Chu, C.-H.; Takahashi, N.; Yu, O.Y. Application of Omics Technologies in Cariology Research: A Critical Review with Bibliometric Analysis. Journal of Dentistry 2024, 141, 104801, doi:10.1016/j.jdent.2023.104801.

106.Yin, D.; Zhan, S.; Liu, Y.; Yan, L.; Shi, B.; Wang, X.; Zhang, S. Experimental Models for Peri-Implant Diseases: A Narrative Review. Clin Oral Invest 2024, 28, 378, doi:10.1007/s00784-024-05755-7.

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