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EDITORIAL

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"Regulation of Metabolism and Inflammation: Links with Oral and Systemic Health"

Part I Host-Microbial Interactions

The oral cavity has one of the most complex microbial communities in the human body, harboring over 1000 species of microorganisms (Lamont et al., 2018). This microbial ecosystem interacts dynamically and bidirectionally with the host, influencing various physiological processes. Under normal conditions, the oral microbiome and host are in a state of equilibrium. However, disruptions in this equilibrium can lead to dysbiosis, triggering inflammatory responses. Dysregulated and unresolved inflammatory responses can progress to chronic inflammation, as seen in periodontitis. Emerging research suggests that there is a strong association between periodontitis and systemic diseases (Hajishengallis, 2022; Hajishengallis & Chavakis, 2021). It is believed that in periodontitis, systemic dissemination of inflammatory mediators and oral bacteria into the bloodstream can potentially contribute to the initiation and aggravation of systemic conditions such as cancer, cardiovascular diseases, diabetes, rheumatoid arthritis, and Alzheimer's disease, via trained immunity.

Metabolism is another key player in the intricate web of oral and systemic health. On one hand, the oral microbiota actively participates in the host metabolic processes by metabolizing dietary components and producing metabolites that impact the host's metabolism (Minty et al., 2019). On the other hand, host metabolic dysfunction can alter the composition of oral microbiome, leading to oral dysbiosis (Pirih et al., 2021). Therefore, dysregulation of metabolic pathways in oral microbiome and host may contribute to the development of diseases both locally in the oral cavity and systemically throughout the body.

In the last few decades, significant advances have been made to understand the dynamic complexity of oral microbiome and its interaction with the host immune and metabolic systems and how this delicate relationship can be the major driver of health and disease not only within the oral cavity but also at distant tissues. Here, we present a three-part special issue entitled "Regulation of metabolism and inflammation: links with oral and systemic health." Ten original articles and five reviews are collected for scientists to share recent advances in understanding host–microbial interactions, inflammation, and metabolism in periodontal disease and associated systemic diseases. Understanding this intricate relationship is essential for identifying therapeutic interventions to aid in the control and prevention of periodontal disease and its systemic comorbidities.

In this part of the special issue (Part I), five original articles are present. Two in vitro studies provide proof-of-concept evidence about how periodontal pathogens regulate host immune response. Sahingur and colleagues (Albuquerque-Souza et al., 2023) demonstrated that prolong exposure to *Fusobacterium nucleatum* triggers a pro-senescence response in gingival epithelia cells and impairs their reparative capacity, which may impact periodontal tissue homeostasis, thus increasing host susceptibility to periodontitis during aging. Sharma and colleagues (Settem et al., 2023) showed that *Tannerella forsythia* can scavenge nucleotide oligomerization domain (NOD) ligand peptidoglycan fragments secreted by *F. nucleatum* and dampen NOD-mediated inflammation of oral epithelial cells, which may affect innate immunity and promote microbial colonization and dysbiosis, leading to increased host susceptibility to periodontitis.

Porphyromonas gingivalis infection and disruption of microbial community homeostasis are believed to affect the progression of tumorigenesis (Gao et al., 2021). Previous studies have shown that GroEL, a heat shock protein 60 secreted by *P. gingivalis*, enhances migration of endothelial progenitor cells (EPCs) and promotes angiogenesis and tumor growth in animal models (Lin et al., 2015). In this special issue, Lin et al. (2023) demonstrated that GroEL-induced microRNAs accelerate tumor neovascularization and tumor growth by downregulating membrane-bound thrombomodulin expression in EPCs, and targeting specific microRNAs can reduce the effect of GroEL on tumor growth.

Emerging epidemiological and clinical evidence support the existence of a two-way relationship between periodontitis and diabetes (Stohr et al., 2021). However, the mechanisms underlying the links between these two conditions are not fully understood. Using high-resolution whole metagenomic shotgun analysis, Scapoli and colleagues (Favale et al., 2023) explored the compositional and functional profile of the subgingival microbiome in type 2 diabetics (T2D) and nondiabetics human subjects with or without periodontitis. They found that patients with different clinical conditions have different subgingival microbiome composition and that a set of dysregulated metabolic pathways is significantly enriched in the subgingival microbiome in periodontitis and/or diabetic patients. The results of this study provide evidence that dysregulated metabolic pathways in oral microbiome

underlie systemic inflammation and the bidirectional relationship between T2D and periodontitis.

Along this line, the study by Xin and colleagues (Thomas et al., 2023) demonstrated that dysregulated host metabolite profile can change microbial community structure of T2D. They found that T2D mice harbor a significantly different gut microbiome compared with control mice, due to elevated levels of succinate in host circulation and tissues. Elevated levels of succinate have been found in T2D and periodontitis in both mice and human studies (Guo et al., 2022). The study suggests that targeting succinate G protein-coupled receptor (SUCNR1) signaling pathway is a promising therapeutic approach in metabolic, inflammatory, and immune disorders with elevated succinate levels, such as periodontitis and T2D.

We would like to thank all the authors for their contribution to this special issue. We hope this research topic will foster the understanding of the complex and dynamic interplay between oral microbiome, inflammation, and metabolism in oral and systemic diseases.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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PEER REVIEW

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