# Short-Chain Fatty Acids and Oral Diseases

Subjects: Dentistry, Oral Surgery & Medicine

Contributor: Georgy E. Leonov , Yurgita R. Varaeva , Elena N. Livantsova , Antonina V. Starodubova

The human oral microbiome has emerged as a focal point of research due to its profound implications for human health. The involvement of short-chain fatty acids in oral microbiome composition, oral health, and chronic inflammation is gaining increasing attention. Locally, SCFAs are a part of normal oral microbiota metabolism, but the increased formation of SCFAs usually attribute to dysbiosis; excess SCFAs participate in the development of local oral diseases and in oral biota gut colonization and dysbiosis. On the other hand, a number of studies have established the positive impact of SCFAs on human health as a whole, including the reduction of chronic systemic inflammation, improvement of metabolic processes, and decrease of some types of cancer incidence. Thus, a complex and sophisticated approach with consideration of origin and localization for SCFA function assessment is demanded.

short-chain fatty acids | oral microbiota | gut microbiota | oral–gut microbiome axis | biofilms | oral diseases

## 1. Introduction

Increased levels of SCFAs have been linked to the development of numerous oral diseases, including dental caries, periodontitis, oral cancer, and various viral infections [1]. SCFAs take part in the regulation of bacterial growth by reshaping the microbiome structure, thereby promoting the proliferation of predominantly periodontal pathogens. Furthermore, specific SCFAs contribute to the formation of biofilms on the oral cavity's surface [2]. The mentioned harm inflicted on oral tissues, primarily by butyrate and propionate, also contributes to the progression of oral diseases. A common underlying mechanism associated with oral lesions involves an intensified inflammatory response and heightened oxidative stress [3]. Acetate, propionate, and butyrate have been identified as ligands for transmembrane G-protein receptors known as FFAR2 (GPR43), FFAR3 (GPR41), and GPR109a [4]. These receptor types are expressed in cells throughout the body and serve various functions. Among the diverse SCFAs, FFAR2 shows a preference for acetate and propionate as ligands, while FFAR3 primarily binds to butyrate. For instance, one of the functions of FFAR2 is to signal about excess energy intake, inhibit insulin signaling in adipocytes, and thus reduce fat accumulation in adipose tissue [5]. Also, activation of FFAR3 induces changes in the hematopoietic activity of the bone marrow, characterized by an increased production of macrophages and dendritic cell precursors. As a result, highly phagocytic dendritic cells can infiltrate the lung tissue during allergic inflammation, for instance, where they establish the immune microenvironment and influence the severity of the reaction [6]. Notably, within the context of the oral cavity, the FFAR2 receptor is expressed in various immune cell types, including monocytes, neutrophils, eosinophils, and regulatory T cells (Treg). The finding that FFAR2

activation, particularly through SCFA administration such as acetate, confers resistance against several bacterial and viral infections is of particular significance [7].

Describing the contribution of SCFAs to the pathogenesis of oral cavity diseases, it should be considered that they are generally multifactorial pathologies, and SCFAs participate in the development of the diseases as an element of the sophisticated pathological chain consistent with the list of numerous factors working in joint action.

## 2. SCFAs and Dental Caries

Dental caries, a chronic infectious disease, results in the demineralization of dental hard tissues. This demineralization arises from a complex interplay between the resident flora and fermentable carbohydrates found in plaque [8]. The pathological processes associated with caries involve numerous microorganisms, including *Actinomyces gerencseriae*, *Bifidobacterium*, *S. mutans*, *Veillonella*, *S. salivarius*, *S. constellatus*, *S. parasanguinis*, and *Lactobacillus fermentum* [9].

The extent of contribution by oral bacteria to dental caries hinges on metabolic pathways that encompass the absorption and metabolism of carbohydrates, including the production of SCFAs. Among these microorganisms, *S. mutans* plays a pivotal role as a major initiator of dental caries. This is due to its capacity to synthesize exopolysaccharides, metabolize carbohydrates into organic acids, particularly lactic acid, and maintain a low pH environment within the oral cavity [10]. SCFAs, as organic acids, also contribute to the environment conducive to the proliferation of acidogenic bacteria. On the other hand, the most relevant producers of SCFAs in the oral cavity are generally periodontal pathogens such as *P. gingivalis* and *F. nucleatum*. These bacteria compete with the main saccharolytic bacteria and actually increase the pH of the environment through amino acid metabolism, whereas they also directly inhibit the growth of cariogenic bacteria caused by SCFAs [11].

Studies centered on oral biofilms have revealed that acetate, propionate, and butyrate exhibit effective inhibitory activity against the formation of *S. gordonii* biofilms [12]. Furthermore, research has demonstrated that *Lactobacillus casei* possesses the capability to suppress the growth of *S. mutans*, including the conversion of lactate into acetate [11]. While it has been hypothesized that *Veillonella's* conversion of lactic acid, produced by streptococci, into less potent acids like acetic acid may reduce the host's susceptibility to caries, experimental evidence supporting this notion is lacking. Conversely, a molecular study suggests that *Veillonella* coexists with *Streptococcus* in carious lesions [13]. Understanding the complex relationships between oral bacteria and their metabolic pathways is essential for developing effective strategies for dental caries prevention and management.

## 3. SCFAs and Periodontitis

Periodontitis is a chronic inflammatory disease characterized by the destruction of the alveolar bone and periodontal tissues, leading to clinical manifestations such as deepening gum pockets and tooth loss. Early signs of periodontitis may involve bleeding during tooth-brushing, tooth mobility during eating, and conditions like halitosis (bad mouth odor), with additional signs emerging at later stages [14]. The dysbiosis of the oral microbiome,

particularly within the periodontal pocket, represents a primary factor in the pathogenesis of periodontitis [15]. The most important periodontal pathogens are Gram-negative rod-shaped bacteria such as *P. gingivalis*, *P. intermedia*, *T. forsithia*, *T. denticola,* and *F. nucleatum* [16]. The development of periodontal diseases is significantly influenced by the formation of biofilms. Butyrate has been shown to stimulate fimbrilin-dependent colonization of *Actinomyces oris* and promote biofilm growth in the early stages of biofilm formation [17]. Higher expression of enzymes involved in *F. nucleatum* butyrate production is observed during biofilm formation compared to planktonic growth, suggesting the importance of butyrate as a virulence factor for certain bacteria [18]. SCFA-producing bacteria such as *Porphyromonas gingivalis*, *Tannerella forsythia*, *Prevotella intermedia,* and *Treponema denticola* also contribute to the multi-species expansion of biofilms [19]. Research has demonstrated significant alterations in local concentrations of SCFAs among subjects with periodontitis. Specifically, in the gingival crevicular fluid of individuals with chronic periodontitis, notably higher levels of propionate (11.68 ± 8.84 vs. 5.87 ± 3.35 mM) and butyrate (3.11 ± 1.86 vs. 1.10 ± 0.87 mM) have been observed when compared to their healthy counterparts. Furthermore, individuals with aggressive periodontitis exhibited elevated concentrations of acetic, propionic, and butyric acids (26.0 versus 11.3, 8.8 versus 2.1, and 2.5 versus 0.0 mM, respectively) [20]. The evidence suggests that periodontal treatment leads to a reduction in the concentrations of lactic, propionic, butyric, and isovaleric acids in the sulcular fluid, effectively returning them to levels comparable to those of a healthy control group. Although the post-treatment concentrations of formic acid tend to increase, these effects persist for several months [21]. Patients with periodontitis have significantly higher concentrations of succinic, acetic, propionic, butyric, and isovaleric acids, as well as a predominance of both *P. gingivalis* and *T. denticola*, compared to healthy individuals. The level of SCFAs positively correlates with the number of these bacteria [22]. In addition to the periodontal pocket, SCFAs, including propionate and butyrate, were detected in tissue samples from the root canals during the treatment of apical periodontitis. It should be pointed out that prior to treatment, the predominant bacterial species included *F. nucleatum* and members of the *Actinobacteria phylum*, but after treatment, representatives of the *Streptococcus* genus were prevalent [23]. In a study on a murine periodontitis model, butyrate was shown to modulate periodontal mechanical nociception through FFAR3 signaling, which may explain the often observed absence of pain in periodontitis [24]. Studies in vitro have shown that mainly acetate and butyrate, which are released in large amounts as metabolic end products of *F. nucleatum* and *P. gingivalis*, induce human neutrophil chemotaxis and cytosolic $Ca^{2+}$ signals via the FFAR2 receptor [25][26]. However, SCFAs in the oral cavity may not only act locally; a recent study in rats found that butyrate injected directly into the gum was able to enter the systemic circulation and adversely affect distant organs [27]. To summarize, SCFAs play a critical role in periodontitis pathogenesis.

## 4. SCFAs and Oral Cancer

Oral cancer comprises a substantial portion of head and neck cancers, accounting for 48%, with approximately 90% of oral cancer cases being histologically classified as oral squamous cell carcinoma [28]. Acidogenic and aciduric species play a significant role in facilitating the invasion and metastasis of malignant cells. This is achieved through the promotion of an acidic tumor microenvironment via acid production [29]. Numerous in vitro studies have underscored the significance of acidic conditions in amplifying the metastatic potential of tumor cells [30]. Furthermore, SCFAs have been implicated in inhibiting the development of an effective immune response against

tumor cells. They accomplish this process by attracting myeloid suppressive cells, thus expanding the population of immunosuppressive cells within the tumor microenvironment [31]. Butyrate has been observed to suppress the cytokine-induced expression of intercellular ICAM-1 on oral squamous carcinoma cells [32], which results in the promotion of leukocyte transmigration to pathologically affected areas and the activation of macrophage polarization toward the M2 tumor phenotype [33].

Human studies indicate a potential connection between the oral microbiota and carcinogenesis in several organs, including the gastrointestinal tract, head and neck, oral cavity, and pancreas. Moreover, recent research on the genera *Lactobacillus* and *Streptococcus* has identified the production of volatile sulfur compounds, SCFAs, reactive oxygen species, reactive nitrogen species, hydrogen peroxide, and lactate, which are associated with carcinogenesis, chronic inflammation, genomic instability, and tumor angiogenesis [34]. Also, investigations have shown that *P. gingivalis* promotes the development and progression of oral cancer by promoting oral cell proliferation and inducing the expression of key molecules such as nuclear factor kappa B (NF-κB), IL-6, signal transducer and activator of transcription 3 (STAT3), cyclin D1, and matrix metallopeptidase 9 (MMP-9) [35]. The relationship between *F. nucleatum* and the development of oral cancer has been extensively researched. Epidemiological studies indicate that *F. nucleatum* is the most prevalent species colonizing oral mucosal sites affected by tumors. Although *F. nucleatum* is positively correlated with oral cancer, the bacterium is specifically less common in advanced cancers and is also associated with better survival [36]. *F. nucleatum* is a significant producer of SCFAs, especially propionate and butyrate, and while there has been previous evidence of *F. nucleatum*'s ability to activate neutrophils via the FFAR2 pathway, there is no direct evidence of *F. nucleatum's* effect on cancer development via SCFAs [37]. In a recent study investigating the correlation between oral microbiota, their metabolites, and the development of different cancer types, it was discovered that cancer patients had lower levels of *Leuconostoc*, *Streptococcus*, *Abiotropia*, and *Prevotella*. Conversely, the concentration of *Haemophilus* and *Neisseria* increased in this group. The control group presented higher expression levels of SCFA and FFAR2, while the cancer group had higher levels of TNFAIP8, IL6, and STAT3 [34]. Therefore, early-stage studies suggest that some SCFA-producing bacteria may promote cancer development in the oral cavity. However, SCFAs' effects are associated with possible activation of immune suppression of carcinogenesis.

## 5. SCFAs and Viral Disease

The oral cavity is a site of active viral replication and shedding, including human immunodeficiency viruses (HIV) and herpesviruses, Kaposi's sarcoma-associated herpesvirus (KSHV), and Epstein–Barr virus (EBV) [38]. Although these viruses are the causative agents of their respective infections, the oral microbiome can have a significant impact on them. Disruption of host-microbial homeostasis in the epithelial tissues of the oral cavity contributes to viral replication [39], which is characterized by a change in the composition of the polymicrobial community of the oral cavity towards a dysbiotic and often pathogenic one. Consequently, the described shifting contributes to overactivation of the immune system and inflammatory conditions. *S. mutans*, *Lactobacillus*, *Candida*, *Haemophilus parahaemolyticus*, *Actinomyces*, *Neisseria subflava*, and *Corynebacterium diphtheriae* species are more prevalent in the saliva of HIV patients, while Streptococcus mitis is less frequently found [40]. Furthermore, the

potential increase in opportunistic bacterial load, which can facilitate HIV reactivation and expedite the progression of AIDS, exists in the context of AIDS-associated immunosuppression. Notably, periodontitis-associated bacteria-produced SCFAs have demonstrated the capability to reactivate KSHV. This reactivation process is mediated through the inhibition of histone deacetylase (HDAC) and the downregulation of various epigenetic modulators (EZH2, SUV39H1) responsible for histone trimethylation repression. As a result, exposition of SCFAs to KSHV-infected cells exhibits histone hyperacetylation, thereby facilitating the transactivation of viral chromatin [41]. Consequently, individuals afflicted with periodontal diseases may exhibit increased lytic reactivation of KSHV and a higher risk of the development of oral Kaposi's sarcoma. Comparable effects of butyrate were described for Epstein–Barr virus activation [42].

Overall, in some medical conditions, viruses can replicate in the oral cavity, inducing complicated relationships with the oral microbiome. SCFAs are one of the factors that determine the interaction between the virus and the epithelial cells of the oral cavity due to immune mechanisms and epigenetic modifications.

## References


1. Hojo, K.; Nagaoka, S.; Ohshima, T.; Maeda, N. Bacterial Interactions in Dental Biofilm Development. J. Dent. Res. 2009, 88, 982–990.
2. Parada Venegas, D.; De la Fuente, M.K.; Landskron, G.; González, M.J.; Quera, R.; Dijkstra, G.; Harmsen, H.J.M.; Faber, K.N.; Hermoso, M.A. Short Chain Fatty Acids (SCFAs)-Mediated Gut Epithelial and Immune Regulation and Its Relevance for Inflammatory Bowel Diseases. Front. Immunol. 2019, 10, 227.
3. Martin-Gallausiaux, C.; Marinelli, L.; Blottière, H.M.; Larraufie, P.; Lapaque, N. SCFA: Mechanisms and Functional Importance in the Gut. Proc. Nutr. Soc. 2021, 80, 37–49.
4. May, K.S.; den Hartigh, L.J. Gut Microbial-Derived Short Chain Fatty Acids: Impact on Adipose Tissue Physiology. Nutrients 2023, 15, 272.
5. Corrêa-Oliveira, R.; Fachi, J.L.; Vieira, A.; Sato, F.T.; Vinolo, M.A.R. Regulation of Immune Cell Function by Short-Chain Fatty Acids. Clin. Transl. Immunol. 2016, 5, e73.
6. Ney, L.-M.; Wipplinger, M.; Grossmann, M.; Engert, N.; Wegner, V.D.; Mosig, A.S. Short Chain Fatty Acids: Key Regulators of the Local and Systemic Immune Response in Inflammatory Diseases and Infections. Open Biol. 2023, 13, 230014.
7. Sencio, V.; Barthelemy, A.; Tavares, L.P.; Machado, M.G.; Soulard, D.; Cuinat, C.; Queiroz-Junior, C.M.; Noordine, M.-L.; Salomé-Desnoulez, S.; Deryuter, L.; et al. Gut Dysbiosis during Influenza Contributes to Pulmonary Pneumococcal Superinfection through Altered Short-Chain Fatty Acid Production. Cell Rep. 2020, 30, 2934–2947.e6.

8. Valm, A.M. The Structure of Dental Plaque Microbial Communities in the Transition from Health to Dental Caries and Periodontal Disease. J. Mol. Biol. 2019, 431, 2957–2969.
9. Peters, B.M.; Jabra-Rizk, M.A.; O'May, G.A.; Costerton, J.W.; Shirtliff, M.E. Polymicrobial Interactions: Impact on Pathogenesis and Human Disease. Clin. Microbiol. Rev. 2012, 25, 193–213.
10. Wu, J.; Jiang, X.; Yang, Q.; Zhang, Y.; Wang, C.; Huang, R. Inhibition of Streptococcus mutans Biofilm Formation by the Joint Action of Oxyresveratrol and Lactobacillus casei. Appl. Environ. Microbiol. 2022, 88, e02436-21.
11. Nyvad, B.; Takahashi, N. Integrated Hypothesis of Dental Caries and Periodontal Diseases. J. Oral Microbiol. 2020, 12, 1710953.
12. Park, T.; Im, J.; Kim, A.R.; Lee, D.; Jeong, S.; Yun, C.-H.; Han, S.H. Short-Chain Fatty Acids Inhibit the Biofilm Formation of Streptococcus Gordonii through Negative Regulation of Competence-Stimulating Peptide Signaling Pathway. J. Microbiol. 2021, 59, 1142–1149.
13. Mashima, I.; Nakazawa, F. Interaction between Streptococcus Spp. and Veillonella tobetsuensis in the Early Stages of Oral Biofilm Formation. J. Bacteriol. 2015, 197, 2104–2111.
14. Mann, J.; Bernstein, Y.; Findler, M. Periodontal Disease and Its Prevention, by Traditional and New Avenues. Exp. Ther. Med. 2020, 19, 1504.
15. Siddiqui, R.; Badran, Z.; Boghossian, A.; Alharbi, A.M.; Alfahemi, H.; Khan, N.A. The Increasing Importance of the Oral Microbiome in Periodontal Health and Disease. Future Sci. OA 2023, 9, FSO856.
16. Mohanty, R.; Asopa, S.J.; Joseph, M.D.; Singh, B.; Rajguru, J.P.; Saidath, K.; Sharma, U. Red Complex: Polymicrobial Conglomerate in Oral Flora: A Review. J. Fam. Med. Prim. Care 2019, 8, 3480–3486.
17. Suzuki, I.; Shimizu, T.; Senpuku, H. Short Chain Fatty Acids Induced the Type 1 and Type 2 Fimbrillin-Dependent and Fimbrillin-Independent Initial Attachment and Colonization of Actinomyces oris Monoculture but Not Coculture with Streptococci. BMC Microbiol. 2020, 20, 329.
18. Llama-Palacios, A.; Potupa, O.; Sánchez, M.C.; Figuero, E.; Herrera, D.; Sanz, M. Proteomic Analysis of Fusobacterium nucleatum Growth in Biofilm versus Planktonic State. Mol. Oral Microbiol. 2020, 35, 168–180.
19. Zhu, Y.; Dashper, S.G.; Chen, Y.-Y.; Crawford, S.; Slakeski, N.; Reynolds, E.C. Porphyromonas gingivalis and Treponema denticola Synergistic Polymicrobial Biofilm Development. PLoS ONE 2013, 8, e71727.
20. Lu, R.; Meng, H.; Gao, X.; Xu, L.; Feng, X. Effect of Non-Surgical Periodontal Treatment on Short Chain Fatty Acid Levels in Gingival Crevicular Fluid of Patients with Generalized Aggressive

Periodontitis. J. Periodontal Res. 2014, 49, 574–583.

21. Qiqiang, L.; Huanxin, M.; Xuejun, G. Longitudinal Study of Volatile Fatty Acids in the Gingival Crevicular Fluid of Patients with Periodontitis before and after Nonsurgical Therapy. J. Periodontal Res. 2012, 47, 740–749.
22. Lu, R.; Feng, L.; Gao, X.; Meng, H.; Feng, X. Relationship between volatile fatty acids and Porphyromonas gingivalis and Treponema denticola in gingival crevicular fluids of patients with aggressive periodontitis. Beijing Da Xue Xue Bao 2013, 45, 12–16.
23. Provenzano, J.C.; Rôças, I.N.; Tavares, L.F.D.; Neves, B.C.; Siqueira, J.F. Short-Chain Fatty Acids in Infected Root Canals of Teeth with Apical Periodontitis before and after Treatment. J. Endod. 2015, 41, 831–835.
24. Murakami, N.; Yoshikawa, K.; Tsukada, K.; Kamio, N.; Hayashi, Y.; Hitomi, S.; Kimura, Y.; Shibuta, I.; Osada, A.; Sato, S. Butyric Acid Modulates Periodontal Nociception in Porphyromonas Gingivalis-Induced Periodontitis. J. Oral Sci. 2022, 64, 91–94. Available online: https://www.jstage.jst.go.jp/article/josnusd/64/1/64_21-0483/_article/-char/ja/ (accessed on 31 August 2023).
25. Dahlstrand Rudin, A.; Khamzeh, A.; Venkatakrishnan, V.; Persson, T.; Gabl, M.; Savolainen, O.; Forsman, H.; Dahlgren, C.; Christenson, K.; Bylund, J. Porphyromonas gingivalis Produce Neutrophil Specific Chemoattractants Including Short Chain Fatty Acids. Front. Cell. Infect. Microbiol. 2021, 10, 620681.
26. Dahlstrand Rudin, A.; Khamzeh, A.; Venkatakrishnan, V.; Basic, A.; Christenson, K.; Bylund, J. Short Chain Fatty Acids Released by Fusobacterium nucleatum Are Neutrophil Chemoattractants Acting via Free Fatty Acid Receptor 2 (FFAR2). Cell. Microbiol. 2021, 23, e13348.
27. Cueno, M.E.; Ochiai, K. Gingival Periodontal Disease (PD) Level-Butyric Acid Affects the Systemic Blood and Brain Organ: Insights Into the Systemic Inflammation of Periodontal Disease. Front. Immunol. 2018, 9, 1158.
28. Irani, S. New Insights into Oral Cancer—Risk Factors and Prevention: A Review of Literature. Int. J. Prev. Med. 2020, 11, 202.
29. Karpiński, T.M. Role of Oral Microbiota in Cancer Development. Microorganisms 2019, 7, 20.
30. Liu, C.; Wang, M.; Zhang, H.; Li, C.; Zhang, T.; Liu, H.; Zhu, S.; Chen, J. Tumor Microenvironment and Immunotherapy of Oral Cancer. Eur. J. Med. Res. 2022, 27, 198.
31. Kostic, A.D.; Chun, E.; Robertson, L.; Glickman, J.N.; Gallini, C.A.; Michaud, M.; Clancy, T.E.; Chung, D.C.; Lochhead, P.; Hold, G.L.; et al. Fusobacterium nucleatum Potentiates Intestinal Tumorigenesis and Modulates the Tumor-Immune Microenvironment. Cell Host Microbe 2013, 14, 207–215.

32. Magrin, G.L.; Di Summa, F.; Strauss, F.-J.; Panahipour, L.; Mildner, M.; Magalhães Benfatti, C.A.; Gruber, R. Butyrate Decreases ICAM-1 Expression in Human Oral Squamous Cell Carcinoma Cells. Int. J. Mol. Sci. 2020, 21, 1679.
33. Ji, J.; Shu, D.; Zheng, M.; Wang, J.; Luo, C.; Wang, Y.; Guo, F.; Zou, X.; Lv, X.; Li, Y.; et al. Microbial Metabolite Butyrate Facilitates M2 Macrophage Polarization and Function. Sci. Rep. 2016, 6, 24838.
34. Nouri, Z.; Choi, S.W.; Choi, I.J.; Ryu, K.W.; Woo, S.M.; Park, S.-J.; Lee, W.J.; Choi, W.; Jung, Y.-S.; Myung, S.-K.; et al. Exploring Connections between Oral Microbiota, Short-Chain Fatty Acids, and Specific Cancer Types: A Study of Oral Cancer, Head and Neck Cancer, Pancreatic Cancer, and Gastric Cancer. Cancers 2023, 15, 2898.
35. Wang, S.; Zhang, X.; Wang, G.; Cao, B.; Yang, H.; Jin, L.; Cui, M.; Mao, Y. Syndecan-1 Suppresses Cell Growth and Migration via Blocking JAK1/STAT3 and Ras/Raf/MEK/ERK Pathways in Human Colorectal Carcinoma Cells. BMC Cancer 2019, 19, 1160.
36. Fan, Z.; Tang, P.; Li, C.; Yang, Q.; Xu, Y.; Su, C.; Li, L. Fusobacterium nucleatum and Its Associated Systemic Diseases: Epidemiologic Studies and Possible Mechanisms. J. Oral Microbiol. 2022, 15, 2145729.
37. Brennan, C.A.; Clay, S.L.; Lavoie, S.L.; Bae, S.; Lang, J.K.; Fonseca-Pereira, D.; Rosinski, K.G.; Ou, N.; Glickman, J.N.; Garrett, W.S. Fusobacterium nucleatum Drives a Pro-Inflammatory Intestinal Microenvironment through Metabolite Receptor-Dependent Modulation of IL-17 Expression. Gut Microbes 2021, 13, 1987780.
38. Johnson, N.W.; Anaya-Saavedra, G.; Webster-Cyriaque, J. Viruses and Oral Diseases in HIV-Infected Individuals on Long-Term Antiretroviral Therapy: What Are the Risks and What Are the Mechanisms? Oral Dis. 2020, 26, 80–90.
39. Coker, M.O.; Cairo, C.; Garzino-Demo, A. HIV-Associated Interactions Between Oral Microbiota and Mucosal Immune Cells: Knowledge Gaps and Future Directions. Front. Immunol. 2021, 12, 676669.
40. Coker, M.O.; Mongodin, E.F.; El-Kamary, S.S.; Akhigbe, P.; Obuekwe, O.; Omoigberale, A.; Langenberg, P.; Enwonwu, C.; Hittle, L.; Blattner, W.A.; et al. Immune Status, and Not HIV Infection or Exposure, Drives the Development of the Oral Microbiota. Sci. Rep. 2020, 10, 10830.
41. Yu, X.; Shahir, A.-M.; Sha, J.; Feng, Z.; Eapen, B.; Nithianantham, S.; Das, B.; Karn, J.; Weinberg, A.; Bissada, N.F.; et al. Short-Chain Fatty Acids from Periodontal Pathogens Suppress Histone Deacetylases, EZH2, and SUV39H1 To Promote Kaposi's Sarcoma-Associated Herpesvirus Replication. J. Virol. 2014, 88, 4466–4479.
42. Imai, K.; Inoue, H.; Tamura, M.; Cueno, M.E.; Inoue, H.; Takeichi, O.; Kusama, K.; Saito, I.; Ochiai, K. The Periodontal Pathogen Porphyromonas gingivalis Induces the Epstein–Barr Virus

Lytic Switch Transactivator ZEBRA by Histone Modification. Biochimie 2012, 94, 839–846.

Retrieved from https://encyclopedia.pub/entry/history/show/114147