Senescent Periodontal Ligament Stem Cells as Drivers of Myeloid-Derived Suppressor Cell Recruitment in Periodontitis-Associated Oral Squamous Cell Carcinoma

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ABSTRACT

OSCC remains one of the most common oral malignancies and continues to be associated with high morbidity and mortality. Several studies suggests that chronic periodontitis contributes to oral carcinogenesis by creating an inflammatory and immunosuppressive microenvironment. Continuous microbial stimulation, oxidative stress, and inflammatory mediator release promotes tissue destruction and favour tumour initiation and progression.

PDLSCs play a central role in maintaining periodontal homeostasis and regeneration; however, a prolonged inflammatory environment induces cellular senescence, resulting in the development of SASP. Senescent PDLSCs secrete inflammatory cytokines, chemokines, growth factors, and MMPs that can alter the local immune microenvironment. Among the immune cells involved in chronic inflammation, MDSCs are key mediators of immune suppression and tumour progression. MDSCs inhibit $CD8^+$ T-cell and NK-cell activity, promote Treg expansion, and facilitate angiogenesis, EMT, tumour invasion, thereby establishing a tumour supportive microenvironment.

Based on the overlap between SASP components and known MDSC-regulating factors, we propose that senescent PDLSCs may promote MDSC recruitment and activation within chronically inflamed periodontal tissues. This proposed PDLSC - MDSC axis provides a potential mechanistic link between chronic periodontitis and OSCC progression. Although direct experimental evidence is currently lacking, the available literature provides a biological basis for this hypothesis. Further experimental and clinical studies are needed to validate this proposed interaction and determine its significance in the pathogenesis of periodontitis- associated OSCC.

INTRODUCTION

Oral squamous cell carcinoma (OSCC) is the most common malignancy of the oral cavity nearly 400,000 individuals worldwide annually, with a five-year survival rate of approximately 50% [1]. Patients with OSCC have a poor prognosis and, typically, more than one-third of the patients die within 5 years of diagnosis [2]. Increasing evidence indicates that chronic inflammation and a sustained pro-inflammatory microenvironment play major roles in the initiation, progression, and immune evasion of OSCC [3]. Periodontitis is a chronic multifactorial inflammatory disease characterized by plaque-induced destruction of the tooth-supporting tissues, resulting in clinical attachment loss, alveolar bone resorption, and periodontal pocket formation [4]. Beyond being a localized oral disease, periodontitis has emerged as an independent risk factor for both OPMDs and OSCC. Persistent periodontal dysbiosis and unresolved inflammation promote continuous production of pro-inflammatory cytokines, chemokines, matrix metalloproteinases (MMPs), reactive oxygen species (ROS), and other inflammatory mediators, thereby establishing a microenvironment that supports extracellular matrix remodeling, genomic instability, angiogenesis, and immune dysregulation, all of which facilitate oral carcinogenesis and tumor progression [5].

Chronic exposure to inflammatory mediators, oxidative stress, microbial infections, and persistent activation of cellular signalling pathways can induce cellular senescence, a stable state of irreversible cell-cycle arrest that

occurs independently due to telomere shortening. Although senescent cells permanently exit the cell cycle, they remain metabolically active and undergo characteristic structural, epigenetic, and signalling alterations, culminating in the development of a senescence-associated secretory phenotype (SASP) [6]. SASP consists of inflammatory and matrix-remodelling factors that maintain chronic inflammation, recruit immune cells, disrupt the extracellular matrix and thereby disturb normal tissue homeostasis [7]. While cellular senescence initially acts as a protective mechanism by preventing the proliferation of damaged cells and limiting malignant transformation, but the persistent accumulation of senescent cells within chronically inflamed periodontal tissues ultimately promotes a pro-inflammatory and pro-tumorigenic microenvironment.

Among the resident cells of the periodontal ligament, periodontal ligament stem cells (PDLSCs) are multipotent mesenchymal stem cells that helps maintains the homeostasis, regeneration and immune response in periodontal tissue [8]. Under the persistent periodontal inflammation, oxidative stress and microbial challenge PDLSCs can become senescent, which reduces their regenerative potential and alters their immune functions. Senescent PDLSCs develop a SASP that further enhances local inflammation and disrupts periodontal tissue homeostasis, indicating that PDLSC senescence may drive the shift from chronic periodontal inflammation to a tumor-promoting microenvironment.[9].

Another important component of the inflammatory tumour microenvironment is the myeloid-derived suppressor cell (MDSC). MDSCs are immature immune cells with strong immunosuppressive activity. During chronic inflammation and cancer, they increase in number and accumulate in the tumour microenvironment. MDSCs suppress both innate and adaptive immune responses, allowing tumour cells to evade immune surveillance and promoting tumour growth, angiogenesis, metastasis, and resistance to therapy. In periodontitis, inflammatory mediators such as IL-6, GM-CSF, PGE_2, CXCL8, vascular endothelial growth factor (VEGF), and transforming growth factor-β (TGF-β) can promote the expansion and activation of MDSCs, suggesting a possible link between chronic periodontal inflammation and oral cancer [10].

Collectively, these observations raise the possibility that senescent PDLSCs may influence the recruitment and activation of MDSCs within chronically inflamed periodontal tissues. Therefore, we propose the PDLSC - MDSC interaction provides a novel explanation for how chronic periodontitis creates an immunosuppressive microenvironment that supports the development and progression of oral squamous cell carcinoma. This review aims to bring together current evidence for this concept, describe the possible interactions between PDLSCs and MDSCs, and also highlights the future directions for understanding their role in periodontitis-associated OSCC.

MATERIALS AND METHOD:

Relevant literature was collected from electronic databases, including PubMed, Scopus, and Google Scholar, using keywords such as *periodontitis*, *oral squamous cell carcinoma*, *periodontal ligament stem cells*, *cellular senescence*, *senescence-associated secretory phenotype*, and *myeloid-derived suppressor cells*. Peer-reviewed English-language articles focusing on periodontitis, PDLSC senescence, SASP, MDSCs, and OSCC were included, whereas conference abstracts, editorials, and non-English publications were excluded.

DISCUSSION

OSCC and the Tumor Immune Microenvironment:

OSCC arises in a complex tumor immune microenvironment. It includes malignant epithelial cells, cancer associated fibroblasts, endothelial cells, extracellular matrix and many types of immune cells such as tumor associated macrophages, regulatory T cells, dendritic cells, natural killer cells, neutrophils and MDSCs. [11]. Continuous interactions among these cellular and non-cellular components influence tumor initiation, progression, invasion, metastasis and response to therapy [12]. Chronic inflammation in the tumor microenvironment releases multiple pro inflammatory mediators which together support immune escape, angiogenesis and remodelling of the extracellular matrix. [13]. Beyond its role in angiogenesis, VEGF-A also modulates vascular permeability and maintains the tissue homeostasis. But in tumors, increased vascular permeability raises interstitial pressure, enabling tumor cell extravasation into the bloodstream and facilitating metastasis [14]. Among the immune cell populations, MDSCs have emerged as key mediators of

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immunosuppression by inhibiting T-cell and natural killer cell functions, thereby enabling tumor cells to evade immune surveillance [15]. Chronic inflammation is a hallmark of both the periodontitis and OSCC, it is crucial to understand the mechanisms that regulate MDSC recruitment and activation may provide insights into how periodontal disease contributes to OSCC.

Periodontitis as a Driver of Oral Carcinogenesis:

Periodontitis is a chronic multifactorial inflammatory disease initiated by microbial dysbiosis of the subgingival biofilm, leading to progressive destruction of the periodontal ligament, alveolar bone and other tooth-supporting tissues [16]. Although periodontitis is primarily a localized oral disease, growing evidence indicates that periodontitis can also show systemic effects and contributes to the development of chronic inflammatory disease, including OSCC [17]. Epidemiological studies shows that individuals with periodontitis have a significantly increased risk of developing OPMDs and OSCC, indicating that patients with chronic periodontal inflammation may act as an independent risk factor for OSCC [18].

The association between periodontitis and OSCC is driven by persistent inflammation caused by interactions between periodontal pathogens and host immune response. Pathogens such as *Porphyromonas gingivalis* and *Fusobacterium nucleatum* activate innate immune receptors, particularly Toll-like receptors (TLRs), leading to activation of the NF-κB and MAPK signaling pathways [19]. This induces continuous production of pro-inflammatory cytokines and mediators, including interleukin IL-1β, IL-6, IL-8, tumor necrosis factor-α (TNF-α), prostaglandin E2 (PGE2) and TGF-β. These inflammatory mediators promote epithelial cell proliferation, inhibit apoptosis, induce epithelial mesenchymal transition (EMT) and stimulate angiogenesis, thereby creating an favourable microenvironment for malignant transformation [20].

Chronic periodontitis which also alters the composition and function of the local immune microenvironment [21]. Persistent inflammation promotes the recruitment of immunosuppressive cells, including Tregs, tumor-associated macrophages (TAMs), and MDSCs, while reducing the cytotoxic activity of $CD8^+$ T cells and natural killer cells. As a result, transformed epithelial cells evade immune surveillance and facilitates the tumour initiation and progression [22]. In addition, inflammatory cytokines and chemokines released within periodontal tissues influence neighbouring stromal cells, including PDLSCs to undergo cellular senescence and altering their immune functions [23]. These observations indicates that chronic periodontal inflammation not only promotes immune dysregulation but also modifies the stromal microenvironment, creating conditions favourable for progression for oral carcinogenesis. Understanding how these senescent PDLSCs interact with immune cells, particularly MDSCs, may provide new insights into the pathogenesis of periodontitis-associated OSCC.

PDLSC Senescence in Chronic Periodontitis

Under normal conditions, PDLSCs maintain self-renewal, differentiate into multiple lineages and modulate immune responses, thereby supporting the periodontal repair after injury [7]. However, the chronic inflammatory microenvironment of periodontitis significantly alters the PDLSC function [24]. Prolonged exposure to bacterial components particularly lipopolysaccharide (LPS) from *Porphyromonas gingivalis* together with persistent stimulation by inflammatory cytokines and elevated ROS, induces cellular stress and accelerates PDLSC senescence [25].

Cellular senescence is stable state of irreversible cell-cycle arrest characterized by reduced proliferative capacity, impaired osteogenic and regenerative potential, resistance to apoptosis, and altered cellular metabolism [26]. With aging or chronic stress, PDLSCs undergo senescence exhibiting decreased proliferation, impaired osteogenic differentiation and reduced capacity for periodontal tissue regeneration [27]. Senescent PDLSCs exibit the increased expression of senescence-associated markers, including p16/INK4a, p21, p53, and senescence-associated β-galactosidase (SA-β-gal). In addition to the loss of regenerative function, they acquire a SASP [28].

SASP of senescent PDLSCs includes inflammatory mediators such as IL-6, IL-8, IL-1β, CCL2, CXCL1, CXCL8, TGF-β, VEGF, and MMPs [29]. These molecules reinforce chronic inflammation, amplify immune cell recruitment, degrade the extracellular matrix, and disrupt periodontal tissue homeostasis [30]. Persistent SASP

signalling creates a positive feedback loop that alters the neighbouring stromal and immune cells, leading to functional changes that further sustain tissue damage and chronic inflammation [31].

Beyond impaired periodontal regeneration, senescent PDLSCs influence the immune microenvironment of chronically inflamed periodontal tissues. Several SASP factors produced by senescent PDLSCs, particularly IL-6, CCL2, CXCL8, GM-CSF, and VEGF are recognized mediators of myeloid cell recruitment and activation and have been implicated in the expansion of MDSCs in chronic inflammatory diseases and cancer [32]. Although direct evidence linking senescent PDLSCs to MDSC recruitment in OSCC is currently lacking, the overlap between the PDLSC secretome and MDSC-promoting factors suggests a possible interaction.

Myeloid-Derived Suppressor Cells in Periodontitis and OSCC

MDSCs are a heterogeneous population of immature myeloid cells that arise from common myeloid progenitors and represent the precursors of granulocytes, macrophages, and dendritic cells. Under physiological conditions, these immature cells differentiate into mature immune cells [33]. However, continuous exposure to inflammatory mediators disrupts normal myeloid differentiation, resulting in the expansion and accumulation of MDSCs. Based on their morphology and phenotype, MDSCs are broadly classified into two major subsets: polymorphonuclear MDSCs (PMN-MDSCs), which resemble neutrophils, and monocytic MDSCs (M-MDSCs), which share characteristics with circulating monocytes. [34].

The hallmark function of MDSCs is the suppression of innate and adaptive immune responses through various mechanisms. They inhibit T-cell proliferation by depleting L-arginine through arginase-1 (ARG1) activity and suppress T-cell receptor signalling via inducible nitric oxide synthase (iNOS) and ROS. MDSCs also promotes the Treg expansion, inhibit natural killer cell cytotoxicity, impair dendritic cell maturation and secrete immunosuppressive cytokines such as IL-10 and TGF-β [35].

Chronic periodontitis creates an inflammatory microenvironment which favours MDSC expansion [36]. Periodontal pathogens, particularly *Porphyromonas gingivalis*, stimulate the production of inflammatory mediators including IL-1β, IL-6, TNF-α, GM-CSF, G-CSF, CXCL8, PGE_2, VEGF, and TGF-β [37]. These mediators activates the JAK/STAT3 and NF-κB signalling pathways, promoting MDSC recruitment, expansion, activation and survival within the periodontal tissues. As a result, chronic periodontitis establishes an immunosuppressive microenvironment [38].

OSCC cells promote MDSC expansion and activation through upregulation of Arg-1 and ROS as well as activation of TNF-α/NF-κB/CXCR4 signalling pathway. Among the two major MDSC subsets, M-MDSCs exhibit stronger immunosuppressive activity than PMN-MDSCs, with increased expression of phosphorylated STAT3 (pSTAT3), IL-10 and programmed death-ligand 1 (PD-L1). M-MDSCs suppress T-cell proliferation, promote regulatory T-cell (Treg) differentiation through TGF-β signalling, and enhance Th17 responses via cyclooxygenase-2 (COX-2) and nitric oxide synthase (NOS) [39].

Increased infiltration of MDSCs has been reported in OSCC tissues, metastatic lymph nodes, and OPMDs. Higher levels of circulating and tumour-infiltrating MDSCs are associated with advanced tumour stage, lymph node metastasis, disease progression, resistance to immunotherapy and poor prognosis, highlighting their potential as prognostic biomarkers and therapeutic targets in OSCC [40].

Potential Crosstalk Between Senescent PDLSCs and MDSCs

Although direct evidence of an interaction between senescent PDLSCs and MDSCs in periodontitis-associated OSCC is still lacking, findings from studies on cellular senescence, periodontitis, and tumour immunology suggest that such an interaction may exist. Chronic periodontal inflammation and oxidative stress drive PDLSC senescence and promote a SASP, characterized by increased release of IL-6, IL-8, CCL2, GM-CSF, G-CSF, VEGF, TGF-β, CXCL1, CXCL2, and MMPs [22,27]. Several factors may influence this proposed PDLSC-MDSC interaction, including periodontal microbial dysbiosis, particularly *Porphyromonas gingivalis* and *Fusobacterium nucleatum*, as well as systemic inflammatory conditions, ageing, smoking, diabetes, and other

host-related factors. These variables may independently affect immune regulation and should therefore be carefully controlled in future experimental and clinical studies.

Many of these mediators are known to regulate myeloid cell development and migration and play important roles in MDSC expansion, recruitment, and activation [41]. MDSC expansion and survival, while GM-CSF and G-CSF stimulate the production of immature myeloid cells. CXCL8 and CCL2 recruit MDSCs to sites of inflammation through CXCR1/CXCR2 and CCR2 [42]. VEGF supports angiogenesis and facilitates MDSC infiltration into the tumour microenvironment. In addition, TGF-β enhances the immunosuppressive activity of MDSCs and promotes regulatory T-cell differentiation [43].

Following recruitment, MDSCs create an immunosuppressive tumour microenvironment that weakens antitumour immune responses through arginase-1-mediated depletion of L-arginine, production of iNOS -derived nitric oxide and ROS, secretion of IL-10 and TGF-β, and induction or expansion of regulatory T cells, this mechanism helps tumor cells to escape immune surveillance. In addition, MDSCs promotes the OSCC progression [44].

Collectively, these observations support a working hypothesis in which senescent PDLSCs, via their SASP, create a chronic inflammatory niche. This inflammatory environment favours MDSC accumulation and immunosuppressive activity, thereby contributing to the establishment of a tumour supportive microenvironment in periodontitis associated OSCC. However, this PDLSC - MDSC axis remains speculative and requires an direct experimental validation in appropriate in vitro and in vivo models.

CONCLUSION

Chronic periodontitis creates a microenvironment that promotes immune dysregulation and tissue remodelling, both of which are implicated in oral carcinogenesis. Emerging evidence suggests that senescent PDLSCs, through the SASP, may influence the recruitment and activation of MDSCs, thereby contributing to immune suppression and the establishment of a tumour-supportive microenvironment. Overall, this hypothesis highlights the potential role of senescent PDLSCs and MDSCs in shaping the inflammatory and immunosuppressive microenvironment associated with periodontitis-associated OSCC. A better understanding of this interaction may improve our knowledge of the molecular events underlying periodontitis-associated OSCC and guide future research in this field.

Future Directions

Further research should focus on identifying the key SASP factors released by PDLSCs that regulate MDSC recruitment and function. Advanced technologies such as single-cell RNA sequencing, spatial transcriptomics and proteomic analyses may provide deeper insights into the cellular interactions within the periodontal and tumor microenvironments. Understanding these molecular mechanisms could facilitate patient risk stratification, enable earlier diagnosis and would support the development of targeted drug therapies aimed at disrupting the inflammatory and immunosuppressive pathways linking periodontitis with OSCC. If the proposed PDLSC-MDSC interaction is experimentally validated, it could serve as a potential therapeutic target. Strategies aimed at reducing senescent PDLSCs, suppressing the senescence-associated secretory phenotype, or targeting key mediators such as IL-6, CCR2, and VEGF may help limit MDSC recruitment and restore anti-tumour immune responses. However, these approaches require further preclinical and clinical validation before clinical application.

REFERENCES

1. Reyes M, Urra H, Peña-Oyarzún D. Evaluating the link between periodontitis and oral squamous cell carcinoma through Wnt/β-catenin pathway: a critical review. Front Oral Health. 2025;6:1575721.
2. Chandra A, Singh A, Sebastian B, Agnihotri A, Bali R, Verma P. Oral squamous cell carcinomas in age distinct population: A comparison of p53 immunoexpression. J Cancer Res Ther. 2013;9(4):587.

3. Chang K-P, Kao H-K, Wu C-C, Fang K-H, Chang Y-L, Huang Y-C, et al. Pretreatment interleukin-6 serum levels are associated with patient survival for oral cavity squamous cell carcinoma. Otolaryngol Head Neck Surg. 2013;148(5):786–91.
4. Könönen E, Gursoy M, Gursoy U. Periodontitis: A multifaceted disease of tooth-supporting tissues. J Clin Med . 2019;8(8):1135
5. Colonia-Garcha A, Vilez G, Duque-Duque M, De Andrade A. Possible association of periodontal disease with oral cancer and oral potentially malignant disorders: a sys tematic review. Acta Odontol Scand. 2020;78(7):553–9.
6. Niklander SE, Aránguiz P, Faunes F, Martínez-Flores R. Aging and oral squamous cell carcinoma development: the role of cellular senescence. Front Oral Health. 2023;4:1285276.
7. Coppé J-P, Desprez P-Y, Krtolica A, Campisi J. The senescence-associated secretory phenotype: the dark side of tumor suppression. Annu Rev Pathol . 2010;5(1):99–118.
8. Zhu W, Liang M. Periodontal ligament stem cells: Current status, concerns, and future prospects. Stem Cells In. 2015;2015:1–11.
9. Zhao X, Lin H, Ding T, Wang Y, Liu N, Shen Y. Overview of the main biological mechanisms linked to changes in periodontal ligament stem cells and the inflammatory microenvironment. J Zhejiang Univ Sci B. 2023;24(5):373–86.
10. Gabrilovich DI. Myeloid-derived suppressor cells. Cancer Immunol Res. 2017;5(1):3–8.
11. Babu S, Manavalan MJ, Jasmine SH, Krishnan M. Tumor microenvironment in oral squamous cell carcinoma: Implications for novel therapies. Oral Oncol Rep. 2024;12(100666):100666
12. Biray Avci C, Goker Bagca B, Nikanfar M, Takanlou LS, Takanlou MS, Nourazarian A. Tumor microenvironment and cancer metastasis: molecular mechanisms and therapeutic implications. Front Pharmacol [Internet]. 2024;15(1442888).
13. Obeagu EI. Inflammation, immunity, and invasion: the pivotal role of cytokine storms in cervical carcinogenesis. Ann Med Surg (Lond) . 2026;88(1):492–9
14. Azzi S, Hebda JK, Gavard J. Vascular permeability and drug delivery in cancers. Front Oncol. 2013;3
15. Nie F, Wang S, Tian H, Zhang J, Yin Q, Ju J, et al. Periodontitis promotes OSCC and prostate cancer progression and immunosuppression by skewing myeloid differentiation of HSPCs. J Dent Res . 2026;105(1):138–48.
16. Könönen E, Gursoy M, Gursoy U. Periodontitis: A multifaceted disease of tooth-supporting tissues. J Clin Med . 2019;8(8):113
17. Reyes M, Urra H, Peña-Oyarzún D. Evaluating the link between periodontitis and oral squamous cell carcinoma through Wnt/β-catenin pathway: a critical review. Front Oral Health [Internet]. 2025;6:1575721
18. Li R, Wang H. Re: re: Association between periodontal disease and oral squamous cell carcinoma: A systematic review and meta-analysis. Br J Oral Maxillofac Surg. 2024;62(4):384.
19. Groeger S, Jarzina F, Domann E, Meyle J. Porphyromonas gingivalis activates NFκB and MAPK pathways in human oral epithelial cells. BMC Immunol.2017;18(1)
20. Irani S, Barati I, Badiei M. Periodontitis and oral cancer - current concepts of the etiopathogenesis. Oncol Rev . 2020;14(1):465
21. Han N, Liu Y, Du J, Xu J, Guo L, Liu Y. Regulation of the host immune microenvironment in periodontitis and periodontal bone remodeling. Int J Mol Sci . 2023;24(4):3158
22. Bogdan-Andreescu CF, Albu Ștefan-D, Slăvescu DA, Bubulac L, Tudor V, Botoacă O, et al. Periodontitis-induced immune reprogramming: Implications for cancer immunotherapy response. Biomedicines. 2026;14(2):480
23. Lin X-J, Yuan Q, Zhou J, Dong Y-L, Sunchuri D, Guo Z-L. Cellular senescence: A new perspective on the suppression of periodontitis (Review). Mol Med Rep.l..2024;30(6):238.
24. Zhang Z, Deng M, Hao M, Tang J. Periodontal ligament stem cells in the periodontitis niche: inseparable interactions and mechanisms. J Leukoc Biol [Internet]. 2021;110(3):565–76
25. Xu Y, Zheng J, Liu M, Fu Z, Wang P. Exendin-4 reduces senescence of inflammation-induced periodontal ligament stem cells through SIRT1/Notch1 signaling. Stem Cells Int . 2025;2025(1)
26. Hu M, Liu R, Chen X, Yan S, Gao J, Zhang Y, et al. Metabolomics dysfunction in replicative senescence of periodontal ligament stem cells regulated by AMPK signaling pathway. Stem Cells Dev . 2024;33(21–22):607–15

27. Yamashita A, Tenshin H, Matsuki S, Nishino G, Ser-Od S, Saito FM, et al. Inflammatory cytokines secreted from senescent periodontal ligament cells influence the osteocyte network in alveolar bone. JBMR Plus.2026;10(3).
28. Roato I, Baima G, Orrico C, Mosca Balma A, Alotto D, Romano F, et al. Senescent markers expressed by periodontal ligament-derived stem cells (PDLSCs) harvested from patients with periodontitis can be rejuvenated by RG108. Biomedicines. 2023;11(9):2535
29. Coppé J-P, Desprez P-Y, Krtolica A, Campisi J. The senescence-associated secretory phenotype: The dark side of tumor suppression. Annu Rev Pathol. 2010;5(1):99–118
30. Chen S, Zhou D, Liu O, Chen H, Wang Y, Zhou Y. Cellular senescence and periodontitis: Mechanisms and therapeutics. Biology (Basel). 2022;11(10):1419.
31. Rattanaprukskul K, Xia X-J, Jiang M, Albuquerque-Souza E, Bandyopadhyay D, Sahingur SE. Molecular signatures of senescence in periodontitis: Clinical insights. J Dent Res. 2024;103(8):800–8.
32. Salminen A, Kauppinen A, Kaarniranta K. Myeloid-derived suppressor cells (MDSC): an important partner in cellular/tissue senescence. Biogerontology.2018;19(5):325–39.
33. Talarico G, Orecchioni S, Falvo P, Bertolini F. Myeloid-derived suppressor cells (MDSCs) at the crossroad of senescence and cancer. Cancers (Basel). 2025;17(13):2251.
34. Karin N. The development and homing of myeloid-derived suppressor cells: From a two-stage model to a multistep narrative. Front Immunol. 2020;11(557586).
35. Kouketsu A, Haruka S, Kuroda K, Hitoshi M, Kensuke Y, Tsuyoshi S, et al. Myeloid-derived suppressor cells and plasmacytoid dendritic cells are associated with oncogenesis of oral squamous cell carcinoma. J Oral Pathol Med. 2023;52(1):9–19.
36. Valero-Monroy O, Garcia-Cervantes G, Marquez-Corrales LF, Leija-Montoya AG, Sandoval-Basilio J, Martinez-Coronilla G, et al. Myeloid derived suppressor cell: A new player in periodontal disease? Med Hypotheses . 2016;95:35–8.
37. Imatani T, Kato T, Okuda K. Production of inflammatory cytokines by human gingival fibroblasts stimulated by cell-surface preparations of *Porphyromonas gingivalis*. Oral Microbiol Immunol. 2001;16(2):65–72.
38. Ambili R, Janam P, Babu PS, Prasad M, Vinod D, Kumar PA, et al. Differential expression of transcription factors NF-κB and STAT3 in periodontal ligament fibroblasts and gingiva of healthy and diseased individuals. Archives of oral biology. 2017;82:19–26.
39. Ali A, Molska GR, Yeo H, Esfandiari N, Jeong W, Huang M, et al. Immune microenvironment in Oral Potentially Malignant Disorders and oral cancer: A narrative review. Int J Mol Sci . 2025;26(14):6650
40. Pang X, Fan H-Y, Tang Y-L, Wang S-S, Cao M-X, Wang H-F, et al. Myeloid derived suppressor cells contribute to the malignant progression of oral squamous cell carcinoma. PLoS One. 2020;15(2):e0229089.
41. Weber R, Groth C, Lasser S, Arkhypov I, Petrova V, Altevogt P, et al. IL-6 as a major regulator of MDSC activity and possible target for cancer immunotherapy. Cell Immunol.2021;359(104254):104254
42. Liu Q, Yu S, Li A, Xu H, Han X, Wu K. Targeting interlukin-6 to relieve immunosuppression in tumor microenvironment. Tumour Biol. 2017;39(6):1010428317712445
43. Bronte V, Brandau S, Chen S-H, Colombo MP, Frey AB, Greten TF, et al. Recommendations for myeloid-derived suppressor cell nomenclature and characterization standards. Nat Commun. 2016;7(1):12150.
44. Yang Y, Li C, Liu T, Dai X, Bazhin AV. Myeloid-derived suppressor cells in tumors: From mechanisms to antigen specificity and microenvironmental regulation. Front Immunol. 2020;11:1371