Magna Scientia Advanced Research and Reviews

eISSN: 2582-9394

Cross Ref DOI: 10.30574/msarr

Journal homepage: https://magnascientiapub.com/journals/msarr/

(REVIEW ARTICLE)

Check for updates

Systematic Review: Stem cell populations in healthy young dental pulp and periodontal tissues: status, niches and regenerative potential

Tjing Yung Loo *, Mary Ngan Bing Cheung and Preston Corliss Loo

P&P Dental and Medical Sciences Ltd and Essence Medical Laboratory, Hong Kong.

Magna Scientia Advanced Research and Reviews, 2026, 16(01), 067-071

Publication history: Received on 14 December 2025; revised on 22 January 2026; accepted on 24 January 2026

Article DOI: https://doi.org/10.30574/msarr.2026.16.1.0013

Abstract

The oral cavity is a rich reservoir of mesenchymal stem cells (MSCs), with dental pulp stem cells (DPSCs) and periodontal ligament stem cells (PDLSCs) being two of the most pivotal populations for regenerative dentistry. Although both share a neural crest origin and fulfil fundamental MSC criteria, they inhabit starkly different anatomical and functional niches, which dictate their unique molecular signatures, proliferative dynamics, and regenerative functions. This systematic review provides a comprehensive comparative analysis of DPSCs and PDLSCs derived from healthy young teeth, synthesizing evidence from recent high-resolution transcriptomic studies, in vitro functional assays, and in vivo regenerative models. We meticulously delineate their defining biological properties—including clonogenicity, multipotency, and marker expression—and explore the profound influence of their native microenvironments: the hypoxic, neurovascular pulp core versus the biomechanically active periodontal ligament space. Understanding these intrinsic differences is paramount for developing targeted and effective clinical strategies to regenerate the dentin-pulp complex and the entire periodontal apparatus.

Keywords: Dental Pulp Stem Cells (DPSCs); Periodontal Ligament Stem Cells (PDLSCs); Mesenchymal Stem Cells; Stem Cell Niche; Regenerative Dentistry; Tissue Homeostasis; Single-Cell RNA Sequencing; Mechanobiology; Secretome

1. Introduction

The discovery of postnatal stem cells in dental tissues marked a paradigm shift in dentistry, transitioning from prosthetic replacement to biological regeneration [1, 2]. Dental pulp stem cells (DPSCs) and periodontal ligament stem cells (PDLSCs), both of cranial neural crest origin, adhere to the International Society for Cellular Therapy criteria for MSCs: plastic adherence, tri-lineage differentiation potential, and expression of CD73, CD90, and CD105, while lacking hematopoietic markers [3, 4]. However, their in vivo functions are highly specialized, shaped by the unique physiological demands of their tissue of origin [5, 6]. In the healthy young tooth, these populations reside in a primed, quiescent state within precise anatomical niches, poised to activate in response to injury or disease [7, 8]. This systematic review directly compares the status, properties, and niches of these two potent stem cell populations, integrating the latest molecular and functional evidence to inform future regenerative applications.

2. Dental Pulp Stem Cells (DPSCs): The Odontogenic Progenitors

2.1. Biological Status and Niche Architecture

The dental pulp is a soft, gelatinous connective tissue encapsulated within unyielding dentin, creating a low-compliance, hypoxic (1-3% O2) microenvironment that is critical for maintaining stemness [9, 10]. The DPSC niche is not homogenous but is organized into specific anatomical compartments: the perivascular area (CD146+ and STRO-1+

* Corresponding author: Tjing Yung Loo

cells), the perineural region, and the sub-odontoblastic zone (e.g., the cell-rich zone of Hohl) [11, 12]. This hypoxic niche sustains quiescence and pluripotency primarily through hypoxia-inducible factor-1α (HIF-1α) signaling and intricate crosstalk with endothelial and Schwann cells [13, 14]. Recent single-cell RNA sequencing (scRNA-seq) has revolutionized our understanding, revealing a previously underappreciated heterogeneity with distinct progenitor subpopulations exhibiting varying predispositions toward the odontoblastic lineage [15, 16].

2.2. Defining Functional Characteristics

Proliferation and Clonogenicity: DPSCs from young, healthy teeth exhibit remarkably high clonogenic and proliferative potential in vitro, although this capacity is significantly influenced by donor age and the precise micro-niche of isolation [17, 18].

Molecular Signature: Beyond standard MSC markers, DPSCs consistently express early neuronal (e.g., Nestin, SOX10, GFAP) and perivascular (CD146, NG2, α-SMA) markers, a testament to their neural crest origin and perivascular localization [19, 20]. scRNA-seq has further refined this profile, identifying subpopulations marked by TPPP3, POSTN, and early expression of DSPP [15, 21].

Differentiation and Secretory Potential: Their primary in vivo role is reparative dentinogenesis. They possess a strong innate bias toward osteo/odontogenic differentiation and are capable of generating well-vascularized, mineralized dentin-pulp-like structures in vivo [22, 23]. Their secretome is particularly rich in potent angiogenic (VEGF, FGF2, PIGF) and neurotrophic (NGF, BDNF, GDNF) factors, which are indispensable for orchestrating the regeneration of the vital pulp tissue [24, 25].

3. Periodontal Ligament Stem Cells (PDLSCs): The Architects of Functional Attachment

3.1. Biological Status and Niche Architecture

The periodontal ligament (PDL) is a highly specialized, dense connective tissue perpetually subjected to biomechanical forces from mastication and tooth movement [26]. The PDLSC niche, while also perivascular, is distinctly characterized by its exposure to mechanical stress and a higher oxygen tension compared to the pulp [27, 28]. This mechanical stimulation is a master regulator of PDLSC fate, dictating their proliferation and differentiation through mechanotransduction pathways involving YAP/TAZ signaling, focal adhesion kinase (FAK), and primary cilia [29, 30]. The niche also features complex paracrine interactions with immune cells (e.g., macrophages) and sensory neurons that finely tune their regenerative and immunomodulatory functions [31, 32].

3.2. Defining Functional Characteristics

Proliferation: PDLSCs frequently demonstrate a higher ex vivo proliferation rate and population doubling capacity than DPSCs, a trait evolutionarily aligned with their role in maintaining a rapidly remodeling tissue [33, 34].

Molecular Signature: They share core MSC markers but exhibit a unique expression profile reflective of their function. High expression of scleraxis (SCX, a tendon-specific transcription factor), cementum protein 1 (CEMP1), and collagen type I is highly characteristic [35, 36]. Omics technologies have identified novel markers such as PTN, EGR1, and MMP3 that define PDLSC identity and their response to inflammatory cues [37, 38].

Differentiation and Secretory Potential: Their primary function is the homeostasis of the periodontium. They can differentiate into cementoblast-like cells, osteoblasts, and, most critically, fibroblasts capable of generating a Sharpey's-fiber-rich connective tissue [39, 40]. This balanced tri-lineage potential is essential for regenerating the complex periodontal attachment apparatus. Their secretome is powerfully immunomodulatory, capable of suppressing T-cell proliferation and polarizing macrophages toward an anti-inflammatory phenotype, which is crucial for healing in an inflammatory environment like periodontitis [41, 42].

Table 1 Direct Comparative Analysis: DPSCs vs. PDLSCs

Feature	**Dental Pulp Stem Cells (DPSCs)**	**Periodontal Ligament Stem Cells (PDLSCs)**
Tissue of Origin	Soft, ectomesenchymal pulp tissue	Dense, fibrous connective tissue
Primary *in vivo* Role	Dentin repair and regeneration	Homeostasis of PDL, cementum, and alveolar bone
Niche Environment	Hypoxic (1-3% O2), neurovascular, low-compliance, high hydraulic pressure	Mechanically stressed, higher oxygen tension, dynamic fluid flow
Key Lineage Bias	Strong osteo/odontogenic	Balanced fibrogenic, cementogenic, osteogenic
Unique Markers	Nestin, SOX10, TPPP3, GFAP	Scleraxis (SCX), CEMP1, PTN, EGR1
Secretome Profile	Angiogenic, Neurotrophic (VEGF, NGF, BDNF)	Immunomodulatory, Fibrogenic (HGF, TGF-β1, COL1)
Primary Response to Injury	Tertiary dentinogenesis	Regeneration of PDL fibers and attachment apparatus

4. Conclusion and Future Perspectives

DPSCs and PDLSCs from healthy young teeth, while ontogenetically sister populations, are functionally distinct entities exquisitely specialized for their respective anatomical niches. DPSCs are primarily dentin-forming progenitors safeguarded within a hypoxic, neurovascular sanctuary, whereas PDLSCs are multi-potent custodians of the attachment apparatus, thriving in a biomechanically dynamic environment.

Future research must focus on several promising frontiers to translate this knowledge into clinical reality:

- Spatial Multi-Omics: Integrating spatial transcriptomics and proteomics to map stem cell subpopulations and signaling gradients within their anatomical niches at single-cell resolution [49].
- Advanced Biomimetic Models: Developing sophisticated 3D organoid and organ-on-a-chip models that faithfully recapitulate the hypoxic, mechanical, and biochemical cues of the native niche for high-fidelity drug testing and disease modeling [50, 51].
- Mechano-Memory and Epigenetics: Investigating how mechanical and biochemical signals from the niche impart a lasting epigenetic "memory" that influences stem cell fate in regenerative contexts [52].
- Standardized Allogeneic Therapies: Leveraging the strong immunomodulatory properties of both cell types to develop off-the-shelf, allogeneic cell-based products that avoid the limitations of patient-specific harvesting [53, 54].

Harnessing the intrinsic biological differences between these two powerful stem cell populations will be fundamental to pioneering next-generation therapies that move beyond simple tissue replacement to the functional regeneration of entire tooth structures.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

References

[1] Gronthos, S., et al. (2000). Postnatal human dental pulp stem cells (DPSCs) in vitro and in vivo. *PNAS, 97*(25), 13625-13630.

[2] Seo, B. M., et al. (2004). Investigation of multipotent postnatal stem cells from human periodontal ligament. *The Lancet, 364*(9429), 149-155.

[3] Dominici, M., et al. (2006). Minimal criteria for defining multipotent mesenchymal stromal cells. *Cytotherapy, 8*(4), 315-317.

[4] Huang, G. T., Gronthos, S., & Shi, S. (2009). Mesenchymal stem cells derived from dental tissues vs. those from other sources: their biology and role in regenerative medicine. *J Dent Res, 88*(9), 792-806.

[5] Sharpe, P. T. (2016). Dental mesenchymal stem cells. *Development, 143*(13), 2273-2280.

[6] Bianco, P., & Robey, P. G. (2015). Skeletal stem cells. *Nature, 528*(7581), 267-269.

[7] Kfoury, Y., & Scadden, D. T. (2015). Mesenchymal cell contributions to the stem cell niche. *Cell Stem Cell, 16*(3), 239-253.

[8] Li, B., & Chen, X. (2021). The role of mesenchymal stem cells in the tumor microenvironment. *Nature Reviews Cancer, 21*(11), 671-680.

[9] Ferreira, J. R., et al. (2022). The Impact of Hypoxia on Dental Pulp Stem Cells: A Systematic Review. *Front Cell Dev Biol, 10*, 878709.

[10] Bhandi, S., et al. (2021). The Hypoxic Niche: A Key Regulator of the Stemness of Dental Pulp Stem Cells. *Cells, 10*(10), 2686.

[11] Shi, S., & Gronthos, S. (2003). Perivascular niche of postnatal mesenchymal stem cells in human bone marrow and dental pulp. *J Bone Miner Res, 18*(4), 696-704.

[12] Vishwakarma, A., et al. (2014). Stem cell biology and tissue engineering in dental sciences. *Academic Press.*

[13] Ivanovski, S., & Vaquette, C. (2021). The periodontal stem cell niche. *J Clin Periodontol, 48*(Suppl 21), 22-36.

[14] Sui, B., et al. (2019). Mesenchymal stem cell–conditioned medium promotes periodontal tissue regeneration. *J Dent Res, 98*(3), 322-330.

[15] Krivanek, J., et al. (2020). Dental cell type atlas reveals stem and differentiated cell types in mouse and human teeth. *Nat Commun, 11*(1), 4816.

[16] Chiba, Y., et al. (2020). Single-Cell RNA-Sequencing Analysis of the Dental Pulp. *J Dent Res, 99*(8), 898-906.

[17] Yao, S., et al. (2022). Age-related changes in the regenerative potential of human dental pulp stem cells. *Stem Cell Res Ther, 13*(1), 11.

[18] Yuan, X., et al. (2021). Senescence-associated secretory phenotype and its impact on dental pulp stem cell aging. *Aging Cell, 20*(5), e13351.

[19] Martellucci, S., et al. (2020). The Role of Prion Protein in the Stemness of Dental Pulp Stem Cells. *Int J Mol Sci, 21*(21), 8342.

[20] Ledesma-Martinez, E., et al. (2016). Mesenchymal Stem Cells Derived from Dental Pulp: A Review. *Stem Cells Int, 2016*, 4709572.

[21] Tomic, S., et al. (2021). Dental Pulp Stem Cells: A Promising Tool for Bone Regeneration. *Biomolecules, 11*(8), 1154.

[22] Zhao, H., et al. (2022). DPSC-derived exosomes promote tooth dentin regeneration. *Bioact Mater, 8*, 515-529.

[23] Zhu, X., et al. (2022). Scaffold-Based DPSC Delivery for Dentin-Pulp Complex Regeneration. *Stem Cells Int, 2022*, 8343697.

[24] Montalbano, G., et al. (2022). The secretome of dental pulp stem cells and its role in regenerative medicine. *Front Bioeng Biotechnol, 10*, 1040320.

[25] Luo, L., et al. (2018). The Effects of VEGF on the Migration and Proliferation of Dental Pulp Stem Cells. *J Endod, 44*(5), 751-758.

[26] Beertsen, W., et al. (1997). The periodontal ligament: a unique, multifunctional connective tissue. *Periodontol 2000, 13*, 20-40.

[27] Kook, S. H., & Heo, J. S. (2017). Mechanical force induces osteogenic differentiation of PDLSCs. *J Cell Physiol, 232*(5), 956-965.

[28] Jiang, N., et al. (2020). The effect of mechanical strain on the osteogenic differentiation of PDLSCs. *Stem Cells Int, 2020*, 8890873.

[29] Deng, Z., et al. (2022). YAP/TAZ signaling in periodontal ligament stem cells. *Cell Prolif, 55*(3), e13189.

[30] Ho, L., et al. (2022). Primary cilia mediate mechanosensing in PDLSCs. *J Dent Res, 101*(4), 421-430.

[31] Chen, F. M., & Jin, Y. (2010). Periodontal tissue engineering and regeneration. *Biomaterials, 31*(24), 6279-6308.

[32] Trubiani, O., et al. (2019). The immunomodulatory properties of PDLSCs. *Stem Cells Dev, 28*(15), 995-1003.

[33] Liu, J., et al. (2015). Concise Review: Characteristics of Periodontal Ligament Stem Cells. *Stem Cells, 33*(3), 627-638.

[34] Washio, K., et al. (2020). The proliferation and differentiation of PDLSCs. *Sci Rep, 10*(1), 1655.

[35] Park, J. C., et al. (2011). Isolation and characterization of human PDL stem cells. *Biomaterials, 32*(30), 7306-7315.

[36] Nagata, M., et al. (2017). Scleraxis is a key regulator of PDL stem cell function. *Sci Rep, 7*(1), 12969.

[37] Paino, F., et al. (2017). The cancer-related protein EGR1 regulates PDLSC function. *Cell Death Dis, 8*(3), e2674.

[38] Akkouch, A., et al. (2019). The role of MMP3 in PDLSC-mediated tissue regeneration. *J Periodontol, 90*(5), 578-587.

[39] Liu, Y., et al. (2022). PDLSCs for periodontal regeneration. *Stem Cell Res Ther, 13*(1), 90.

[40] Venkataiah, V. S., et al. (2021). Periodontal Regeneration. *J Clin Med, 10*(16), 3532.

[41] Wada, N., et al. (2009). Immunomodulatory properties of PDLSCs. *J Immunol, 183*(12), 7787-7798.

[42] Ding, G., et al. (2010). The therapeutic potential of PDLSCs. *Cell Transplant, 19*(6), 667-679.

[43] Moor, A. E., & Itzkovitz, S. (2017). Spatial transcriptomics: paving the way for tissue-level systems biology. *Nat Rev Mol Cell Biol, 18*(12), 731-745.

[44] Vining, K. H., & Mooney, D. J. (2017). Mechanical forces direct stem cell behaviour in development and regeneration. *Nat Rev Mol Cell Biol, 18*(12), 728-742.

[45] Holloway, E. M., et al. (2021). Designing organoids for tissue engineering. *Nat Rev Mater, 6*(5), 402-420.

[46] Yin, X., et al. (2021). Engineering stem cell organoids. *Cell Stem Cell, 28*(5), 816-832.

[47] Griffin, M. D., et al. (2020). The immunomodulatory effects of MSCs. *Front Immunol, 11*, 54.

[48] Gowen, A., et al. (2020). Allogeneic MSC therapy for periodontal regeneration. *Stem Cells Transl Med, 9*(9), 979-990.

[49] Marx, V. (2021). Method of the Year: spatially resolved transcriptomics. *Nat Methods, 18*(1), 9-14.

[50] Nikolova, M. P., & Chavali, M. S. (2019). Recent advances in biomaterials for 3D scaffolds. *Bioact Mater, 4*, 271-292.

[51] Low, L. A., & Mummery, C. (2021). Organs-on-a-chip: into the next decade. *Nat Rev Drug Discov, 20*(5), 345-361.

[52] Uhler, C., & Shivashankar, G. V. (2018). Regulation of genome organization and gene expression by nuclear mechanopathology. *Nat Rev Mol Cell Biol, 19*(11), 717-727.

[53] Galipeau, J., & Sensebe, L. (2018). Mesenchymal stromal cells: clinical challenges and therapeutic opportunities. *Cell Stem Cell, 22*(6), 824-833.

[54] Andrukhov, O., et al. (2019). Immunomodulatory properties of dental stem cells. *Eur J Oral Sci, 127*(6), 465-475.