e-ISSN 2371-770X

Modern Medical Laboratory Journal

DOI: 10.30699/mmlj17.6.1.42

Application of Dental Pulp Stem Cells in Modern Dentistry: A Narrative Review

Melika Zangeneh Motlagh[1], Nikoo Hossein-Khannazer[4], Nazanin Mahdavi[5], Pouyan Aminishakib[5,6], Massoud Vosough[2,3]

1. Dentist, School of Dentistry, Tehran University of Medical Sciences, Tehran, Iran.

2. Department of Regenerative Medicine, Cell Science Research Center, Royan Institute for Stem Cell Biology and Technology, ACECR, Tehran, Iran.

3. Experimental Cancer Medicine, Institution for Laboratory Medicine, Karolinska Institute, Stockholm, Sweden.

4. Gastroenterology and Liver Diseases Research Center, Research Institute for Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

5. Department of Oral and Maxillofacial Pathology, School of Dentistry, Tehran University of Medical Sciences, Tehran, Iran.

6. Department of Pathology, Cancer Institute Hospital, IKHC, Tehran University of Medical Sciences, Tehran, Iran.

KEYWORDS

Dental pulp stem cells;

Dentistry;

Applications;

Osseointegration;

Tissue engineering;

Regeneration

Article Info

Received 2023/04/20;

Accepted 2023/05/15;

Published Online 2023

ABSTRACT

Dental pulp stem cells (DPSCs) are a class of stem cells which originate from dental pulp tissue and possess multiple stem cell characteristics including high clonogenicity, differentiation capacity and immunomodulatory effects. DPSCs can be used in different stem cell-based therapy to treat a variety of diseases, such as autoimmune, orthopedic, and neurological diseases.

Recent studies showed that DPSCs combined with biomaterials provides an effective approach to craniofacial bone regeneration and reconstruction of bone defects. Scaffolds improve cell attachment, proliferation, differentiation, and migration. In the present study we discuss different combination of biomaterials with DPSCs.

Corresponding Information: *Massoud Vosough, Department of Regenerative Medicine, Cell Science Research Center, Royan Institute for Stem Cell Biology and Technology, ACECR, Tehran, Iran. Email: masvos@royaninstitute.org.*

Abbreviations

ALP, Alkaline Phosphatase; BMP-2, Bone Morphogenetic Protein 2; BMPs, Bone morphogenetic proteins; BSP, Bone sialoprotein; CBFA1, Core-binding factor alpha 1; Col I, Collagen type I ; DFPCs, Dental Follicle Progenitor Cells; DPSCs, Dental Pulp Stem Cells; HA, Hydroxyapatite; IDO, Indoleamine 2, 3-dioxygenase; IL-10, Interleukin 10; MTA, Mineral Trioxide Aggregate; OCN, Osteocalcin; ON, Osteonectin; OPN, Osteopontin; PCL, Poly(caprolactone); PDLSCs, Periodontal Ligament Stem Cells, PET, Positron Emission Tomography; PGE2, Prostaglandin E2; PLGA, Poly(lactic-co-glycolic acid); PU, Polyurethane; RUNX2, Runt-related transcription factor 2; SCAP, Stem Cells from Apical Papillae; SHED, Exfoliated Deciduous Teeth Stem Cells; TCP, Tricalcium Phosphate; TGF-β1, Transforming growth factor-beta 1; TGSCs, Tooth Germ Stem Cells; VEGF, Vascular Endothelial Growth Factor

Introduction

Stem cells are a class of remarkable cells that possess unique abilities that make them highly sought after in the field of regenerative medicine. These cells are considered undifferentiated as they have the potential to differentiate into multiple cell types, tissues, and even organs. This incredible feature has led to their designation as "universal cells" due to their versatility in responding to specific signals to differentiate into the needed cell types. Stem cell therapy refers to the use of these cells to replace or repair damaged cells, tissues, and organs in the body. This is achieved through the cells' capacity for multidirectional differentiation, which enables them to be used in a wide range of regenerative applications. For instance, stem cells have been used to regenerate cardiac muscle tissue, repair spinal cord injuries, and regenerate bone tissue. One of the most accessible sources of stem cells is the oral cavity, and more specifically, dental stem cells. Dental stem cells such as dental pulp stem cells, dental follicle progenitor cells, and stem cells from apical papillae, have been identified as having unique properties and great potential for use in regenerative medicine. These cells possess the ability to differentiate into a range of tissues including neuronal, adipose, osteogenic, chondrogenic, and angiogenic cells (1) (Figure 1). One of the most accessible and promising sources for stem cells in oral cavity are dental stem cells. The stem cells of the oral cavity have different origins such as: Dental Pulp Stem Cells (DPSCs), Dental Follicle Progenitor Cells (DFPCs), Stem Cells from Apical Papillae (SCAP), Tooth Germ Stem Cells (TGSCs), Periodontal Ligament Stem Cells (PDLSCs), Exfoliated Deciduous Teeth Stem Cells (SHED) (2) (Figure 2). Their differentiation capacities vary from neurogenesis, adipogenesis, osteogenesis, chondrogenesis, angiogenesis and dentinogenesis. (3) The stem cells derived from the oral cavity possess not only ectodermal characteristics, but also mesodermal and endodermal, which makes them able to differentiate into different tissues. (4)

In addition to stem cells, fibroblastic cells, capillary blood vessels, peripheral nerves, lymphatic components, extracellular matrices, and odontoblasts in the pulp tissue's periphery make up dental pulp, which is an unmineralized connective tissue.

DPSCs are isolated from adult human pulp tissue that has been characterized as having impacted cells with third molars, high clonogenicity, orthodontic teeth, proliferative and supernumerary activity, and teeth, as well as the capacity to form characterized mineralization as nodules. (2)

According to the mesenchymal features of the dental pulp stem cells, they have been taken into practice in lot of areas and they have shown very promising results in regenerative medicine. (3) These cells are not only readily available, but also expandable with comparatively long-term genetic stability. Notably, they can transdifferentiate into ectodermal and endodermal lineages in addition to mesodermal lineages. DPSCs have the ability to modulate the immune system by anti-secreting inflammatory cytokines and mediators like TGF-Beta, IL-10, IDO, PGE2. DPSCs can be used in stem cell-based therapy. DPSCs have been used in a number of preclinical research and clinical trials to treat a variety of diseases, such as autoimmune, orthopedic, and neurological diseases (4).

The aim of this narrative review is to discuss the potential applications of dental pulp stem cells in modern dentistry and shed light into possible perspectives of them in this field.

Osseointegration

Following the meticulous preparation of the implant bed and the precise insertion of the dental implant, a complex interplay of molecular and cellular processes ensues, culminating in the phenomenon known as osseointegration. Osseointegration represents the direct adherence of newly formed bone to the implant's surface, fostering a harmonious integration (5). This intricate process hinges upon a profound comprehension of the intricate healing and reparative mechanisms within both hard and soft tissues—a crucial facet in achieving successful clinical outcomes in dentistry.

Historically, clinicians turned to allografts and synthetic materials derived from diverse species to augment bone volume. While these materials facilitated increased bone volume, they lacked inherent osteogenic potential, leading to extended healing periods and the development of lower-quality, poorly vascularized bone. Evidently, these limitations translated to suboptimal biomechanical attributes, thus jeopardizing overall success rates.

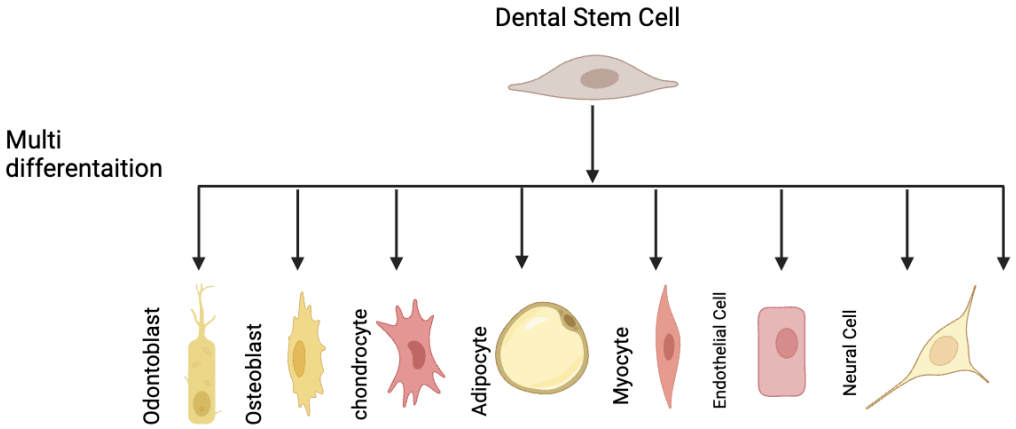

Figure 1. Applications of dental stem cells and their multi differentiation capacity.

Detecting the failure of regeneration could be attributed to the dearth of migratory osteogenic and vascular precursor cells, such as osteoblasts, to the regenerative site (6).

The emergence of mesenchymal stem cells as a pivotal player in tissue differentiation has revolutionized our approach to osseointegration. These versatile cells possess the unique capability to differentiate into a spectrum of tissues, including bone, cementum, and periodontal ligament, while also orchestrating angiogenesis. (7) Among these, dental pulp stem cells (DPSCs) stand out, boasting accessibility and a remarkable proliferation rate (8). DPSCs have demonstrated their potential in elevating the success of dental implants through their facilitation of osteointegration. Of paramount importance in implant longevity is the degree of marginal bone resorption, which, if unchecked, can precipitate implant failure. Notably, DPSCs possess the potential to counteract such resorption, actively promoting osteointegration and thus proving indispensable in this arena (5).

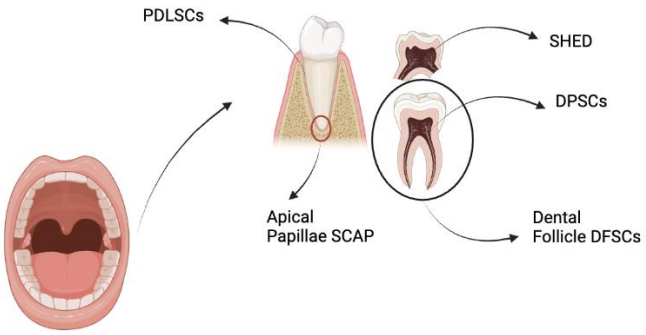

Figure 2. Sources of dental stem cells in oral cavity.

DPSCs exert their influence on osteointegration through both intraosseous and endochondral ossification processes. The orchestration of these mechanisms is governed by key transcription factors, notably Runt-related transcription factor 2 (RUNX2) and osterix. RUNX2, also known as core-binding factor alpha 1 (CBFA1), takes the reins early in osteoblast differentiation, steering mesenchymal stem cells towards an osteoblastic fate. This master regulator guides osteoblast maturation, extracellular matrix synthesis, and mineralization. Its modulation is underpinned by influential signaling pathways such as bone morphogenetic proteins (BMPs) and transforming growth factor-beta 1 (TGF-β1). (Figure 3)

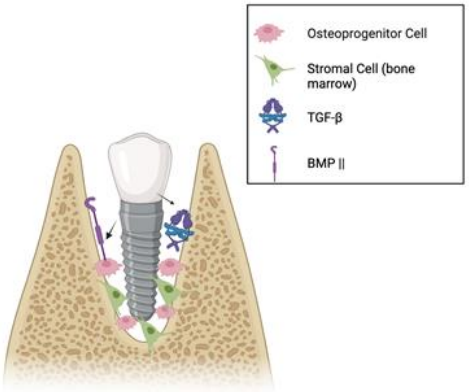

Figure 3. Osseointegration process in dental implant.

Concurrently, osterix, or Sp7, emerges later in differentiation, steering osteoblast maturation. This transcription factor orchestrates the expression of genes encoding bone matrix proteins, encompassing osteocalcin and bone sialoprotein. Wnt signaling and BMP signaling, among other pathways, guide its activity. The harmonious interplay of these factors is central to successful bone formation and, consequently, osseointegration at the implant site.

The orchestration of these factors is further supported by various signaling pathways including BMPs and Transforming growth factor-β1 (TGF-β1), particularly in activating RUNX2. BMPs, ubiquitously present in MSCs, play a pivotal role in this intricate regulatory network. (7)

DPSCs' osteodifferentiation defies singular marker determination, instead involving a panel of expression markers. The assessment of osteoblast proliferation and differentiation can be gauged by monitoring the expression of key osteodifferentiation-specific genes. DPSCs demonstrate their potential to evolve into osteoblast-like cells that not only produce mineralized matrix but also exhibit characteristic osteoblastic markers such as Alkaline Phosphatase (ALP), collagen type I (Col I), osteopontin (OPN), and Osteocalcin (OCN). Further research underscores the escalating expression of ALP and Col I mRNA during initial bone formation stages.

Beyond ALP and Col I, additional markers illuminate the osteogenesis landscape. Osteopontin (OPN), a glycoprotein pivotal in bone formation and mineralization regulation, resides among these markers. Bone sialoprotein (BSP), a phosphoprotein prevalent in mineralized tissues, also plays a crucial role in bone mineralization. Osteonectin (ON), a glycoprotein inherent to osteoblasts, contributes to extracellular matrix organization and bone mineralization regulation. Not to be overlooked, RANKL, a cytokine primarily expressed by osteoblasts, critically steers osteoclast differentiation and ensuing bone resorption. (9)

The ascendancy of dental pulp mesenchymal stem cells (DPSCs) as a bone regeneration conduit stems from a myriad of advantages. Their robust proliferation rate, propitious osteogenic differentiation propensity, and favorable immunomodulatory and paracrine attributes position them as potent candidates. DPSCs, conveniently sourced from discarded teeth, circumvent complications, offering an abundant cell reservoir for regenerative applications. Confirmatory in vivo and in vitro studies attest to the viability of DPSCs in bone regeneration and osteogenesis. Notably, the synergy between DPSCs and biomaterials presents a promising avenue for craniofacial bone regeneration and the amelioration of bone defects (10).

The landscape of dental pulp stem cell (DPSC) research has been invigorated by recent technological strides that are shaping the trajectory of osseointegration in dentistry. Advanced imaging techniques, such as high-resolution micro-CT scanning, enable precise visualization of the dynamic osseointegration process over time. This utilization of micro-CT echoes studies that investigate bone regeneration induced by various scaffolds, including those infused with DPSCs. Moreover, the integration of bioinformatics and computational modeling empowers researchers to predict DPSC behavior and optimize culture conditions for desired outcomes. The mentioned study also harnessed positron emission tomography (PET) analyses to assess tracer incorporation, revealing critical insights into the efficacy of tissue engineering constructs. Furthermore, the advent of single-cell transcriptomics, as demonstrated in the study, unveils the intricate gene expression profiles during DPSC differentiation, unraveling novel regulatory pathways that influence osseointegration. As these cutting-edge tools continue to refine our understanding, they pave the way for innovative strategies to enhance DPSC-mediated bone regeneration and optimize implant outcomes. (2)

Recent Developments in Scaffold and Tissue Engineering with Dental Pulp Mesenchymal Stem Cells

Achieving the optimal integration of dental pulp stem cells (DPSCs) within a scaffold is a pivotal facet that governs their efficacy. To realize the full potential of DPSCs, their combination with scaffolds becomes imperative, offering an environment conducive to multifaceted processes such as cell attachment, proliferation, differentiation, and migration. Various scaffold compositions have been explored, including hydrogels composed of diverse components, as well as scaffolds with intricate physical and chemical attributes such as hyaluronic acid or fibrin. Hydrogels, a notable example, offer distinctive advantages due to their high liquid content and capacity to retain cells without compromising their functionality.

Among them, fibrin-based gels, often referred to as "fibrin glue," have garnered attention in tissue engineering. The gel's formation, initiated by non-cytotoxic agents like thrombin and calcium salts acting on fibrinogen, allows strong cell retention at the injection site. Notably, the substantial water content of fibrin-based gels enables the incorporation of water-soluble biologically active substances. Moreover, the biodegradability of fibrin complements the regenerative journey, offering a scaffold that evolves in harmony with the emerging tissue. Advanced customization is facilitated by the modulation of fibrin-based gel mechanical properties, achievable through parameters like the amount of fibrinogen, the fibrinogen-to-thrombin ratio, and the inclusion of supplementary components such as collagen. This dynamic nature underscores the adaptability of DPSC-associated scaffolds, enhancing their potential to meet varied clinical needs. Notably, the accessibility of fibrinogen from allogeneic or autologous plasma presents an avenue for personalized scaffold fabrication, tailoring the biomaterial to individual patient requirements (11).

The Realm of Scaffold Materials: Balancing Attributes for Regenerative Success

The landscape of scaffold materials is characterized by diverse options, each with its distinctive attributes that impact their suitability for specific applications. Natural scaffolds, exemplified by collagen, fibrin, and chitosan, possess inherent bioactivity, promoting vital cellular processes such as adhesion, proliferation, and differentiation. However, these materials exhibit limited mechanical strength and susceptibility to degradation, necessitating judicious design considerations. In contrast, synthetic scaffolds crafted from polymers like PLGA, PCL, and PU offer enhanced mechanical properties and controlled degradation kinetics. While synthetic scaffolds rival native bone in terms of mechanical strength, achieving optimal biocompatibility may require meticulous refinement. A convergence of natural and synthetic elements within hybrid scaffolds presents an innovative solution to mitigate inherent limitations, harnessing the strengths of each material type. Ceramic scaffolds, such as hydroxyapatite (HA) and tricalcium phosphate (TCP), exhibit commendable biocompatibility, reflecting their alignment with natural bone mineral composition. However, their mechanical characteristics may not parallel those of native bone.

Thus, scaffold selection assumes paramount importance, warranting alignment with the regenerative objectives of a specific clinical scenario.(3)

Scaffolds: Orchestrating a Symphony of Regeneration

Scaffolds occupy a pivotal role in the landscape of bone tissue engineering, transcending their structural function to shape the destiny of regenerative endeavors. Beyond providing a spatial canvas for cellular seeding and proliferation, scaffolds exude transformative capabilities that profoundly influence the outcome of bone regeneration. The essence of scaffold attributes goes beyond physicality, encompassing inherent qualities that synergize with biological processes. A triumvirate of attributes—osteoconductivity, porosity, and biodegradability—embodies the essence of effective scaffold design. Osteoconductivity sets the stage for cellular attachment and proliferation, serving as the foundation for tissue growth and integration. Porosity facilitates the exchange of crucial elements, nurturing tissue maturation through the orchestration of biological cues. Biodegradability, often underestimated, underpins seamless integration. The gradual dissolution of the scaffold in harmony with tissue growth obviates secondary interventions, ensuring an uninterrupted regenerative journey. The scaffold metamorphoses from a supporting entity to an integral part of the evolving tissue architecture. Akin to a conductor, it orchestrates regenerative symphonies, facilitating angiogenesis and bone matrix deposition. Osteoblasts, guided by the scaffold's cues, choreograph the dance of bone formation. In essence, the scaffold embodies the finesse underlying bone tissue engineering. It forges an environment that shapes cellular behavior and directs tissue destiny. From anchoring osteoblasts to orchestrating signaling cascades, the scaffold emerges as an indispensable partner, transforming a void into a tapestry of bone regeneration. Just as a conductor shapes a symphony, the scaffold orchestrates the transformative saga of osseous healing (12).

Aimetti et al reviewed the use of dental stem cells for craniofacial tissue engineering and regeneration. Various types of dental stem cells and their potential for regenerating craniofacial tissues were discussed.

Scaffolds, including natural and synthetic biomaterials, were also examined. Natural scaffolds (collagen, fibrin, and chitosan) promote cell adhesion, proliferation, and differentiation but are weak and prone to degradation. Synthetic scaffolds (PLGA, PCL, and PU) offer better mechanical strength and controlled degradation but may not be as biocompatible as natural scaffolds. Hybrid scaffolds combine both materials to overcome limitations. Ceramic scaffolds (HA and TCP) have excellent biocompatibility but may not match natural bone's mechanical properties. The article also discussed gene therapy's potential to enhance stem cell-mediated regeneration. The review article suggests that future research should focus on optimizing dental stem cell selection, expansion, and delivery and further exploring gene therapy's potential in craniofacial regeneration. (13)

Nakashima and colleagues have proposed various scaffolds to use with DPSCs. These scaffolds include natural materials such as collagen and synthetic materials like PLGA and PCL. DPSCs have been combined with growth factors, such as BMP-2 and VEGF, to improve bone regeneration. These factors help DPSCs differentiate into osteoblasts and form blood vessels necessary for new bone growth. DPSCs hold much potential for bone regeneration and can treat bone defects and diseases such as osteoporosis. However, more research is required to optimize the use of DPSCs with scaffolds and growth factors for bone regeneration in clinical applications. (14)

Clinical Impact of DPSCs in Periodontal Regeneration

The potential of dental pulp stem cells (DPSCs) to enhance periodontal regeneration has been investigated through clinical studies. In a randomized controlled trial by Ferrarotti et al. chronic periodontitis patients with deep intrabony defects were treated using minimally invasive surgical techniques. DPSCs extracted from the patient's dental pulp were utilized in combination with a collagen scaffold. The study demonstrated that the test group, receiving DPSC-seeded micrografts on a collagen sponge, exhibited significantly improved clinical outcomes compared to the control group, which received the scaffold alone.

The test group showed substantial reductions in probing depth, gains in clinical attachment level, and bone defect fill, along with a higher frequency of favorable outcomes such as residual probing depth less than 5 mm and clinical attachment level gain of 4 mm or more. These results emphasize the clinical relevance and positive impact of DPSCs in enhancing periodontal regeneration over a one-year period after treatment. This trial underscores the potential of DPSC-based tissue engineering approaches in advancing periodontal therapy. (4)

Angiogenesis and Endodontics (Pulp Regeneration)

Dental caries and tooth trauma are prevalent conditions that affect the teeth and damage their tough enamel and dentin structure, causing pulp necrosis and periapical disease. Traditional root canal therapy based on pulpectomy is currently the standard clinical treatment for mature permanent teeth. This procedure comprises removing diseased dental pulp tissue, enlarging the root canal, and filling the sterile route with synthetic filling materials. The lack of biological dentin/pulp or dentin-pulp complex and the limitations of available materials may increase the risk of significant reinfection and tooth breakage despite the widespread use of the current standard therapy, contributing to the low survival rate of teeth. (1,4)

In recent years, the field of regenerative endodontics has garnered significant attention among dentists, particularly endodontists. Regenerative endodontics offers a promising avenue to address the limitations of traditional therapies by harnessing the body's innate regenerative potential. This innovative approach aims to not only alleviate clinical signs and symptoms but also promote the maturation of root structures and reestablish neurogenesis processes within the dental pulp. The fundamental principles of regenerative endodontics include thorough root canal cleaning, inducing controlled bleeding to create a scaffold for stem cells, and sealing the coronal portion with biocompatible materials like Mineral Trioxide Aggregate (MTA) (16).

A pivotal aspect of regenerative endodontics lies in the selection of suitable scaffolds to support stem cell activity and guide tissue regeneration. Emerging biomaterials used as scaffolds hold immense promise in advancing dental pulp regeneration. While traditional approaches have relied on synthetic materials, the focus has now shifted to the utilization of natural, bio-based materials.

These biomaterials offer inherent biocompatibility, safety, and minimal release of toxic compounds during biodegradation, making them highly suitable for scaffold fabrication (4).

The quest for the ideal scaffold has led to the convergence of various materials, each contributing unique attributes. Natural scaffolds, including collagen, fibrin, and chitosan, possess innate bioactivity that promotes cellular adhesion, proliferation, and differentiation. However, these materials often exhibit lower mechanical strength and susceptibility to degradation, necessitating careful design considerations (4). On the other hand, synthetic scaffolds, represented by polymers like Poly(lactic-co-glycolic acid) (PLGA), Poly(caprolactone) (PCL), and Polyurethane (PU), offer enhanced mechanical properties and controlled degradation kinetics. While synthetic scaffolds can match the mechanical strength of native bone, optimizing their biocompatibility remains a critical aspect (4).

A promising direction in scaffold development involves hybrid scaffolds that combine the advantages of both natural and synthetic materials. By strategically merging the strengths of these materials, researchers aim to create scaffolds that strike a balance between strength, biocompatibility, and degradation rate. Additionally, ceramic scaffolds, such as Hydroxyapatite (HA) and Tricalcium Phosphate (TCP), showcase excellent biocompatibility due to their resemblance to natural bone mineral composition. However, their mechanical properties might not fully align with native bone, highlighting the importance of selecting scaffolds based on specific clinical requirements (4).

In the realm of regenerative endodontics, the selection of the appropriate scaffold material is pivotal for fostering stem cell proliferation, differentiation, and tissue regeneration. The convergence of natural and synthetic biomaterials in scaffold design paves the way for innovative solutions that hold the potential to revolutionize the field and elevate the success of dental pulp regeneration therapies. (1,4)

Future Prospective

The exploration of dental pulp as a rich source of stem cells for tissue engineering gained momentum in the early 2000s. Researchers embarked on numerous studies employing a diverse array of scaffolds, biomaterials, and in vivo models.

These investigations collectively demonstrated the potential of dental pulp stem cells (DPSCs) to foster bone growth and facilitate lesion repair in vivo. However, the outcomes varied significantly due to the distinct methods and strategies employed across these studies. Factors such as variations in stem cell sources, isolation techniques, scaffold materials, bone defect models, and animal subjects all contributed to the diversity of results. To comprehend the full picture of DPSC research progress, it's crucial to acknowledge the multifaceted nature of these contributing factors. Understanding the historical context sheds light on the motivations that propelled DPSC research. The initial surge of interest was often fueled by the realization of dental pulp's regenerative potential. This realization ignited a pursuit to harness DPSCs for therapeutic applications, aimed at addressing conditions like dental caries, tooth trauma, and pulp necrosis.

Despite the promising strides made in DPSC research, inconsistencies in outcomes underscore the importance of comprehensive analysis. These variations could stem from the multifaceted nature of experimentation, encompassing the choice of stem cell sources, scaffold materials, animal models, and experimental protocols. The culmination of these elements yielded results that were not only diverse but also potentially influenced by a range of variables. A critical aspect that emerged as DPSC research advanced was the need for a well-structured regulatory framework. As awareness of stem cell research grew worldwide, diverse policies and laws emerged across continents and countries. Even the European Union established specific regulations governing stem cell research. The landscape is complex, with varying degrees of permissions and prohibitions. For instance, concerns over the ethical implications of using embryonic stem cells led to their prohibition in most European countries. The regulations that govern the use of human stem cells in research demonstrate both the growing significance of DPSCs and the complex ethical considerations surrounding their application.

Looking forward, the DPSC field holds potential for continued advancements and innovations. The challenges and opportunities are intertwined, with researchers continually refining methods, addressing regulatory hurdles, and considering the ethical implications of their work.

As new techniques and technologies emerge, DPSC research is poised to contribute to the broader landscape of regenerative medicine, bridging gaps in dental therapies and paving the way for novel treatments. (23) (5)

Conclusion

Due to their unique properties, DPSCs have shown significant potential in a wide range of regenerative medicine applications. They have been studied in the context of dental tissue engineering, with promising results in regenerating damaged or lost dental tissues such as pulp, dentin, and periodontal tissue. DPSCs have also shown promise in treating orthopedic conditions such as bone defects, as well as autoimmune and neurological disorders.In a preclinical study, DPSCs were shown to have the ability to repair spinal cord injuries by differentiating into neural cells and promoting nerve regeneration. In another study, DPSCs were used to treat rheumatoid arthritis in rats by modulating the immune system and reducing inflammation. Clinical trials have also been conducted using DPSCs to treat conditions such as ischemic stroke and multiple sclerosis, with promising results. DPSCs are easily accessible, as they can be harvested from dental pulp tissue obtained from teeth that are routinely extracted. Additionally, DPSCs can be expanded in vitro, allowing for the generation of large numbers of cells for use in cell-based therapies. DPSCs also exhibit long-term genetic stability, making them a reliable source for stem cell-based therapies. Overall, dental pulp stem cells represent a promising source of stem cells for regenerative medicine applications. Their unique characteristics, including their ability to differentiate into multiple lineages and modulate the immune system, make them an attractive option for treating a variety of conditions. As research in this field continues, it is likely that DPSCs will play an increasingly important role in the development of effective regenerative therapies.

Declaration

Funding
Not available.

Conflicts of interest/Competing interests
The authors declare no conflict of interest.

Authors' contributions
MZM drafted the manuscript. MZM, MV, NM, PA, and NHK designed the study concept.

Ethics approval
Not applicable.

References

1. Zhai Q, Dong Z, Wang W, Li B, Jin Y. Dental stem cell and dental tissue regeneration. Vol. 13, Frontiers of Medicine. Higher Education Press; 2019. p. 152–9.

2. Yoshida S, Tomokiyo A, Hasegawa D, Hamano S, Sugii H, Maeda H. Insight into the role of dental pulp stem cells in regenerative therapy. Biology (Basel). 2020 Jul 1;9(7):1–24.

3. Tsutsui TW. Dental pulp stem cells: Advances to applications. Vol. 13, Stem Cells and Cloning: Advances and Applications. Dove Medical Press Ltd; 2020. p. 33–42.

4. Gan L, Liu Y, Cui D, Pan Y, Zheng L, Wan M. Dental Tissue-Derived Human Mesenchymal Stem Cells and Their Potential in Therapeutic Application. Vol. 2020, Stem Cells International. Hindawi Limited; 2020.

5. Pellegrini G, Francetti L, Barbaro B, del Fabbro M. Novel surfaces and osseointegration in implant dentistry. Vol. 9, Journal of investigative and clinical dentistry. NLM (Medline); 2018. p. e12349.

6. Egido-Moreno S, Valls-Roca-umbert J, Céspedes-Sánchez JM, López-López J, Velasco-Ortega E. Clinical efficacy of mesenchymal stem cells in bone regeneration in oral implantology. Systematic review and meta-analysis. Vol. 18, International Journal of Environmental Research and Public Health. MDPI AG; 2021. p. 1–12.

7. Millan C, Vivanco JF, Benjumeda-Wijnhoven IM, Bjelica S, Santibanez JF. Mesenchymal stem cells and calcium phosphate bioceramics: Implications in periodontal bone regeneration. In: Advances in Experimental Medicine and Biology. Springer New York LLC; 2018. p. 91–112.

8. Anitua E, Troya M, Zalduendo M. Progress in the use of dental pulp stem cells in regenerative medicine. Vol. 20, Cytotherapy. Elsevier B.V.; 2018. p. 479–98.

9. Mortada I, Mortada R. Dental pulp stem cells and osteogenesis: an update. Vol. 70, Cytotechnology. Springer Netherlands; 2018. p. 1479–86.

10. Lee YC, Chan YH, Hsieh SC, Lew WZ, Feng SW. Comparing the Osteogenic Potentials and Bone Regeneration Capacities of Bone Marrow and Dental Pulp Mesenchymal Stem Cells in a Rabbit Calvarial Bone Defect Model. Int J Mol Sci [Internet]. 2019 Oct 2 [cited 2023 Mar 9];20(20). Available from: /pmc/articles/PMC6834129/

11. Enukashvily NI, Dombrovskaya JA, Kotova A v., Semenova N, Karabak I, Banashkov RE, et al. Fibrin glue implants seeded with dental pulp and periodontal ligament stem cells for the repair of periodontal bone defects: A preclinical study. Bioengineering. 2021 Jun 1;8(6).

12. Motamedian SR, Hosseinpour S, Ahsaie MG, Khojasteh A. Smart scaffolds in bone tissue engineering: A systematic review of literature. World J Stem Cells [Internet]. 2015 Apr 4 [cited 2022 Oct 22];7(3):657. Available from: /pmc/articles/PMC4404400/

13. Ferrarotti F, Romano F, Gamba MN, Quirico A, Giraudi M, Audagna M, et al. Human intrabony defect regeneration with micrografts containing dental pulp stem cells: A randomized controlled clinical trial. J Clin Periodontol [Internet]. 2018 Jul 1 [cited 2023 Mar 9];45(7):841–50. Available from: https://onlinelibrary.wiley.com/doi/full/10.1111/jcpe.12931

14. Nakashima M, Iohara K, Murakami M. Dental pulp stem cells and regeneration. Endod Topics [Internet]. 2013 Mar 1 [cited 2023 Mar 9];28(1):38–50. Available from: https://onlinelibrary.wiley.com/doi/full/10.1111/etp.12027

15. Kim SG, Malek M, Sigurdsson A, Lin LM, Kahler B. Regenerative endodontics: a comprehensive review. Vol. 51, International Endodontic Journal. Blackwell Publishing Ltd; 2018. p. 1367–88.

16. Matichescu A, Ardelean LC, Rusu LC, Craciun D, Bratu EA, Babucea M, et al. Advanced biomaterials and techniques for oral tissue engineering and regeneration—a review. Vol. 13, Materials. MDPI AG; 2020. p. 1–37.

17. Liu Y, Gan L, Cui DX, Yu SH, Pan Y, Zheng LW, et al. Epigenetic regulation of dental pulp stem cells and its potential in regenerative endodontics. World J Stem Cells. 2021;13(11):1647–66.

18. Saghiri MA, Asatourian A, Sorenson CM, Sheibani N. Role of angiogenesis in endodontics: Contributions of stem cells and proangiogenic and antiangiogenic factors to dental pulp regeneration. Vol. 41, Journal of Endodontics. Elsevier Inc.; 2015. p. 797–803.

19. Liu Y, Gan L, Cui DX, Yu SH, Pan Y, Zheng LW, et al. Epigenetic regulation of dental pulp stem cells and its potential in regenerative endodontics. World J Stem Cells [Internet]. 2021 [cited 2022 Oct 21];13(11):1647–66. Available from: https://pubmed.ncbi.nlm.nih.gov/34909116/

20. Nakashima M, Iohara K, Murakami M, Nakamura H, Sato Y, Ariji Y, et al. Pulp regeneration by transplantation of dental pulp stem cells in pulpitis: a pilot clinical study. Stem Cell Res Ther. 2017 Mar 9;8(1).

21. Xuan K, Li B, Guo H, Sun W, Kou X, He X, et al. Deciduous autologous tooth stem cells regenerate dental pulp after implantation into injured teeth [Internet]. Vol. 10, Sci. Transl. Med. 2018. Available from: http://stm.sciencemag.org/

22. Itoh Y, Sasaki JI, Hashimoto M, Katata C, Hayashi M, Imazato S. Pulp Regeneration by 3-dimensional Dental Pulp Stem Cell Constructs. J Dent Res. 2018 Sep 1;97(10):1137–43.

23. Ercal P, Pekozer GG, Kose GT. Dental stem cells in bone tissue engineering: Current overview and challenges. In: Advances in Experimental Medicine and Biology. Springer New York LLC; 2018. p. 113–27.

How to cite this article: Zangeneh Motlagh M, Nikoo Hossein-Khannazer N, Mahdavi N, Pouyan Aminishakib P, Vosough M. Application of Dental Pulp Stem Cells in Modern Dentistry: A Narrative Review. Mod Med Lab J. 2023;6(1): 42-50.