# Stem Cell Therapy in Oral Medicine: Status and Clinical Application Prospects

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Abstract: When it comes to stem cell therapy in oral medicine, exploring its status and clinical application prospects is crucial. This abstract focuses on reviewing the latest advancements in stem cell therapy within the field of oral medicine. It discusses the current status of clinical research and applications of stem cell therapy in oral diseases like periodontitis, dental injuries, and this paper focuses on assessing the potential of stem cell therapy in oral medicine, particularly in addressing oral maxillofacial and defects. Through literature compilation and summarization, it demonstrates the potential benefits and challenges of stem cell therapy in oral medicine. Particularly, in promoting oral tissue regeneration, alleviating patient discomfort, and enhancing oral functional restoration, stem cell therapy exhibits extensive prospects. Stem cell therapy in oral medicine has not only made significant strides in laboratory research but has also shown tremendous potential in clinical applications. However, further research and clinical trials are needed to address challenges related to safety, efficacy, and scalability to propel the practical application of stem cell therapy in oral medicine.

Keywords: Stem Cell Therapy; Oral Tissue Regeneration; Clinical Application Prospects; Cellular Engineering

#### 1. Introduction

When it comes to stem cell therapy in dentistry, it's a field full of promise and potential. Stem cell therapy, as an innovative medical approach, harnesses the self-renewal and multipotent differentiation abilities of stem cells, presenting a novel avenue for oral tissue regeneration and repair. These cells have the capacity for and they also possess the ability to transform into various cell types, including bone, muscle, nerve, and fat cells, making them immensely valuable for tissue repair and regeneration. Chambers et al. reviewed the current concepts regarding endothelial stem cells, emphasizing the significance of vascular regeneration in ischemic vascular diseases and proposed a more stringent definition based on stem cell biology principles. However, conflicting clinical trial results highlighted several challenges faced by stem cell therapies[1]. Glauche et al. summarized an international workshop on stem cell clonality and dynamics. Discussions revolved around methods for determining clone numbers, the nature of stem cell clonality involved in tissue maintenance, and theoretical models of clonal dynamics, underscoring the importance quantifying of clonal dynamics[2]. Liu et al. suggested that the concept of stem cells might be replaced by cellular plasticity. They explored the plasticity exhibited by cells under different conditions and offered viewpoints on rethinking the concept of stem cells, which holds significance for understanding their characteristics and clinical applications[3]. Matchett and Lappin reviewed the concept of cancer stem cells and their role in tumor initiation and therapy. They emphasized the similarities between cancer stem cells and normal stem cells, discussing their potential role in cancer treatment[4]. Méndez-Ferrer et al. underscored the interaction between hematopoietic stem cells and stromal cells in the bone marrow. They highlighted mesenchymal stem cells as crucial constituents of the hematopoietic stem cell niche while noting limitations in describing these cell populations[5]. Narayanan et al. highlighted the importance of engineering

ongoing division, generating new stem cells,

concepts in stem cell research. They discussed engineering approaches in stem cell research and regenerative medicine, emphasizing the focus on long-term effects and systems biology[6].

### 1.1 Sources of Stem Cells

In dentistry, Adipose tissue-derived stem cells have attracted considerable interest owing to their straightforward extraction method and plentiful supply. Moreover, dental pulpderived stem cells. Egusa et al.'s study in 2012 extensively delved into the origin of dental stem cells and their clinical applications in dentistry. They highlighted the presence of mesenchymal stem cells (MSCs) within oral and maxillofacial tissues, offering potential options for regenerative therapies, while also detailing the methods of obtaining these stem cells and their immunological characteristics [7]. Subsequently, Eiro et al. in 2018 focused on the uterus as a potential source of mesenchymal stem cells (MSCs). They emphasized the uniqueness of endometrial stem cells (eMSCs) and human uterine cervical stem cells (hUCESCs), highlighting their ease of retrieval, high proliferation rates, and exploring their potential therapeutic effects and the prospects of their secretions in treatments [8]. Lastly, Monti et al. in 2012 provided an overview of the history, sources, and therapeutic applications of stem cells. They discussed the potential value of embryonic stem cells, adult stem cells, and umbilical cord blood, emphasizing the scientific and societal value of umbilical cord blood donations[9]. The evaluation included the expectations and challenges of cell therapy in treating conditions such as diabetes.

#### **1.2 The Applications of Stem Cell Therapy**

Stem cell therapy in dental medicine has been extensively explored and applied. Its potential efficacy has been demonstrated in various areas such as periodontitis, tooth injuries, maxillofacial defects, and alveolar bone regeneration. Clinical studies indicate that stem cell therapy not only promotes regeneration and repair of oral tissues but also enhances patients' quality of life by alleviating pain and improving oral function. Dziubinska et al. provided an overview of stem cell applications in various dental regenerative areas. Their focus encompassed dental pulp

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cells, periodontal ligament cells, and cells related to tooth development. Their objective was to establish the fundamental principles of dental cell engineering [10]. Mitsiadis et al. explored the potential uses of stem cells for treating dental pulp and periodontal diseases. Their work emphasized stem cell therapy as a burgeoning alternative approach in dentistry, offering enhanced structural and functional improvements in physiological outcomes. However, it also pointed out several challenges including the consistency and quality control populations, of stem cell treatment Rodríguezapproaches[11]. Additionally, Lozano et al. emphasized the potential value of dental stem cells in tissue engineering, particularly due to their ease of access, high proliferation rates, multipotent differentiation capabilities, and immunomodulatory properties [12]. Sede et al. focused on the perception and attitudes of Nigerian dental practitioners towards stem cells in dentistry. The research revealed that while most dental practitioners had some awareness of stem cell applications in dentistry, their grasp of related knowledge remained relatively limited[13]. Stem cell therapy in dental medicine stands as a cuttingedge and highly promising field, offering new hope for the regeneration and repair of oral tissues. However, further clinical research and trials are required to enhance its safety and efficacy for widespread application in dental medicine.

# 2. Literature Review

#### 2.1 Clinical Applications of Stem Cell Therapy in Oral Diseases

Initially, explore the prospects of utilizing three-dimensional culture systems for stem cells in organogenesis and functional studies. Stem cells exhibit extensive potential in applications within various dentistry, showcasing a wide array of possibilities. Baena et al. focused on the role of 3D cell culture in the in vitro tooth regeneration using dental stem cells[14], while Brozek et al. emphasized the significance of stem cells in oral tissues, particularly their potential in bone regeneration[15]. Capparè et al. examined evolving concepts and technical intricacies regarding stem cells in bone and tooth regeneration[16]. Kong et al. suggested the potential use of dental mesenchymal stem cells

and their extracellular vesicles in dental regeneration[17]. Lauritano et al. explored adipose-derived stem cells as an alternative source in regenerative dentistry[18]. Stem cell applications in dentistry display vast diversity, underscoring their promise in dental treatment and tissue engineering.

The dental realm has witnessed considerable interest in stem cell applications. Malhotra (2016) delved into the use of induced pluripotent stem cells (iPS) in dentistry, focusing on their potential for dental regeneration derived from various stem cell sources[19]. Mozaffari et al. highlighted the correlation between stem cells and dental regeneration, envisioning the prospects of 'personalized dentistry'[20].

# 2.2 The Future Trends and Challenges of Stem Cell Therapy

Exploring the future of stem cell therapy in dentistry involves envisioning new avenues for its application in oral repair and regeneration, foreseeing technological breakthroughs, and anticipating advancements in clinical trials. Addressing potential challenges—such as ensuring safety, scaling up applications, and standardized establishing treatment protocols-is crucial. Proposing strategies and directions to tackle these challenges in the future will pave the way for enhanced utilization and efficacy of stem cell therapy in dentistry. Mendi et al. emphasized the rich source of mesenchymal stem cells in orofacial tissues, exploring their potential prospects in repairing damaged tooth tissues, bone regeneration, and treatment of neurological diseases [21]. Miran et al. conducted an indepth discussion about the extensive prospects of stem cells in dental regeneration, highlighting its successful clinical applications and its potential to revolutionize dental treatments [22]. These studies underscore the promising prospects of stem cells in dentistry, offering critical directions for future innovative treatment approaches and advancements in dental medicine.

# 3. Methods

Stem cell therapy in oral medicine involves critical stages, from stem cell acquisition to treatment quality control and clinical trial design. This section aims to extensively cover the methodology behind stem cell therapy in oral medicine.

The initial step of crucial importance lies in selecting the stem cell source. In oral medicine, commonly utilized sources encompass bone marrow, adipose tissue, and dental pulp. Bone marrow-derived stem cells can be acquired via bone marrow aspiration or extraction techniques; adipose stem cells are obtained from adipose tissue, and dental pulp stem cells are sourced from dental pulp tissue. These stem cells from different origins possess distinct characteristics and potential applications, demanding rigorous handling procedures and a series of laboratory technical support during their extraction. Following this is the cultivation and amplification of stem cells. Stem cells under cultivation conditions suitable require culture media and environments to maintain their stability and proliferation. Typically, these cells are cultured specific temperature, humidity, and in atmospheric conditions within culture dishes. The cultivation process demands strict control to ensure cell purity, vitality, proliferation capability, and to prevent cell contamination and mutation. At this stage, choices such as the selection of culture medium, cultivation duration, and passaging methods significantly impact subsequent treatments.

In clinical trials, experimental design and treatment protocol formulation are paramount. Clinical trials require clear recruitment criteria, stem cell treatment protocols, treatment cycles, and follow-up plans. For example, in treating periodontitis, factors such as stem cell quantity, administration route, and frequency are critical considerations. The design of clinical trials must be meticulous to ensure the study's reliability and the credibility of results. Furthermore, quality control and safety assessment are crucial aspects of the stem cell treatment process. In laboratory settings, stem cells need to undergo quality control measures to ensure their purity, activity, and stability. For clinical applications, safety assessment needs to consider patient health conditions and treatment safety, including risk assessment and the establishment of monitoring mechanisms. The methodology of stem cell therapy in oral medicine involves multiple stages, ranging from stem cell acquisition, cultivation, amplification, to the design and quality control of clinical experiments. Ensuring strict control

and meticulous design across these stages is imperative to guarantee the safety and efficacy of stem cell therapy in oral medicine. This approach aims to establish a dependable solution for future oral tissue regeneration and repair.

# 4. Conclusion

Stem cell therapy in oral medicine is a field brimming with promise, ushering in new opportunities for oral tissue regeneration and disease management. An in-depth exploration spanning stem cell sources, clinical applications, methodologies, and future prospects sheds light on the significance and hurdles within this domain. The inherent pluripotency of stem cells stands as a rich resource for therapeutic advancements in oral medicine. Diverse sources such as bone marrow, adipose tissue, and dental pulp possess unique traits and potentials, applicable across various realms like oral tissue regeneration, treatment of periodontal diseases, and alveolar bone regeneration. The wide range of stem cell sources lays a solid foundation for the advancement of oral medicine. Furthermore, stem cell therapy presents vast prospects in clinical applications within oral medicine. In addressing oral diseases such as periodontitis, alveolar bone defects, and tooth injuries, stem cell therapy exhibits significant clinical efficacy and potential advantages. Clinical trial outcomes indicate that stem cell therapy not only promotes oral tissue regeneration and repair but also enhances treatment outcomes and patients' quality of life.

However, stem cell therapy in oral medicine still encounters challenges. These include standardizing the treatment process, assessing safety, observing long-term efficacy, and promoting large-scale applications. Additionally, there remains a need for strengthened clinical practice and scientific research to further validate the safety and effectiveness of stem cell therapy.

In the future, stem cell therapy in oral medicine is poised for greater breakthroughs. With ongoing technological advancements and accumulated clinical experiences, we are confident in overcoming current challenges and elevating the application of stem cell therapy in oral medicine. Future research can delve deeper into exploring the applications of stem cell therapy in tooth regeneration, periodontal disease treatment, and repair of oral and maxillofacial defects. Concurrently, emphasis on studying treatment mechanisms and safety will bring more innovation and progress to the field of oral medicine. In summary, while stem cell therapy in oral medicine holds immense potential, continued efforts are essential in addressing its challenges in practice. Only through persistent dedication can stem cell therapy bring forth more opportunities and achievements for the development of oral medicine.

# References

- Chambers, S. E. J., Pathak, V., Pedrini, E., et al., Current concepts on endothelial stem cells definition, location, and markers. Stem Cells Translational Medicine, 2021. 10: p. S54-S61.
- [2] Glauche, I., Bystrykh, L., Eaves, C., et al., Stem cell clonality - Theoretical concepts, experimental techniques, and clinical challenges. Blood Cells Molecules and Diseases, 2013. 50 (4): p. 232-240.
- [3] Liu, T., Chen, L., Zhao, Z. J., et al., Toward a Reconceptualization of Stem Cells from Cellular Plasticity. International Journal of Stem Cells, 2019. 12 (1): p. 1-7.
- [4] Matchett, K.B. and T.R. Lappin, Concise Reviews: Cancer Stem Cells: From Concept to Cure. Stem Cells, 2014. 32 (10): p. 2563-2570.
- [5] Méndez-Ferrer, S., D.T. Scadden, and A. Sánchez-Aguilera, Bone marrow stem cells: current and emerging concepts, in Marrow, M. Zaidi, Editor. 2015. p. 32-44.
- [6] Narayanan, K., Mishra, S., Singh, S., et al., Engineering Concepts in Stem Cell Research. Biotechnology Journal, 2017. 12 (12).
- [7] Egusa, H., Sonoyama, W., Nishimura, M., et al., Stem cells in dentistry - Part I: Stem cell sources. Journal of Prosthodontic Research, 2012. 56 (3): p. 151-165.
- [8] Eiro, N., Fraile, M., Schneider, J., et al., Non-Pregnant Human Uterus as Source of Mesenchymal Stem Cells. Current Stem Cell Research & Therapy, 2018. 13 (6): p. 423-431.
- [9] Monti, M., Perotti, C., Del Fante, C., et al., Stem cells: sources and therapies.

Biological Research, 2012. 45 (3): p. 207-214.

- [10] Dziubinska, P., Jaskólska, M., Przyborowska, P., et al., Stem cells in dentistry - Review of literature. Polish Journal of Veterinary Sciences, 2013. 16 (1): p. 135-140.
- [11] Mitsiadis, T.A., G. Orsini, and L. Jimenez-Rojo, STEM CELL-BASED APPROACHES IN DENTISTRY. European Cells & Materials, 2015. 30: p. 248-257.
- [12] Rodríguez-Lozano, F. J., Insausti, C. L., Iniesta, F., et al., Mesenchymal dental stem cells in regenerative dentistry. Medicina Oral Patologia Oral Y Cirugia Bucal, 2012. 17 (6): p. E1062-E1067.
- [13] Sede, M.A., O. Audu, and C.C. Azodo, Stem cells in Dentistry: knowledge and attitude of Nigerian Dentists. Bmc Oral Health, 2013. 13.
- [14] Baena, A.R.Y., A. Casasco, and M. Monti, Hypes and Hopes of Stem Cell Therapies in Dentistry: a Review. Stem Cell Reviews and Reports, 2022. 18 (4): p. 1294-1308.
- [15] Brozek, R., M. Kurpisz, and R. Koczorowski, APPLICATION OF STEM CELLS IN DENTISTRY FOR BONE REGENERATION. Journal of Physiology and Pharmacology, 2018. 69 (1): p. 23-33.
- [16] Capparè, P., Tetè, G., Sberna, M. T., et al., The Emerging Role of Stem Cells in Regenerative Dentistry. Current Gene Therapy, 2020. 20 (4): p. 259-268.

- [17] Kong, H. Y., Liu, P. Q., Li, H. W., et al., Mesenchymal Stem Cell-Derived Extracellular Vesicles: The Novel Therapeutic Option for Regenerative Dentistry. Stem Cell Reviews and Reports, 2023. 19 (1): p. 46-58.
- [18] Lauritano, D., Annalisa, P., Valentina, C. and Francesco, C., Regenerative Dentistry and Stem Cells: A Multilineage Differentiation as a Safe and Useful Alternative Way of Harvesting and Selection Adipose Derived Mesenchymal Stem Cells. Current Drug Targets, 2018. 19 (16): p. 1991-1997.
- [19] Malhotra, N., Induced Pluripotent Stem (iPS) Cells in Dentistry: A Review. International Journal of Stem Cells, 2016. 9 (2): p. 176-185.
- [20] Mozaffari, M. S., Emami, G., Khodadadi, H., et al., Stem cells and tooth regeneration: prospects for personalized dentistry. Epma Journal, 2019. 10 (1).
- [21] Mendi, A., Ulutürk, H., Ataç, M. S., Stem Cells for the Oromaxillofacial Area: Could they be a promising source for regeneration in dentistry?, in Cell Biology and Translational Medicine, Vol 5, Stem Cells: Translational Science to Therapy, K. Turksen, Editor. 2019. p. 101-121.
- [22] Miran, S., T.A. Mitsiadis, and P. Pagella, Innovative Dental Stem Cell-Based Research Approaches: The Future of Dentistry. Stem Cells International, 2016. 2016.