International Journal of Science Academic Research
Vol. 07, Issue 05, pp.894-897, May 2026
Available online at http://www.scienceijsar.com

ISSN: 2582-6425

Research Article

RESEARCH PROGRESS OF INDUCED PLURIPOTENT STEM CELLS IN DENTISTRY

[1,*]Jingye, Zhou, [2]Jingbing, Zhou, [1]Xuqin, Tang, [1]Kexin, Cai and [1]Yuyu, Zeng

[1]Department of Stomatology, School of Stomatology Jinan University, China
[2]Guigang first junior Middle School, China

Received 12th March 2026; **Accepted** 18th April 2026; **Published online** 29th May 2026

Abstract

In recent years, induced pluripotent stem cells (iPSCs) have gradually become a research hotspot in tissue engineering. iPSCs are a class of cells with self-renewal capacity and multi-directional differentiation potential, capable of differentiating into various cell types. Oral tissue is a tissue with excellent regenerative capacity; therefore, the research on pluripotent stem cells in the oral cavity holds broad application prospects. iPSCs possess characteristics similar to embryonic stem cells and can be reprogrammed from somatic cells through genetic engineering techniques. Their enormous potential has been extensively studied and applied in oral tissue regeneration, disease treatment, and dental restoration. In the field of oral tissue engineering and regenerative medicine, certain progress has been achieved in the research of pluripotent stem cells in the oral cavity. This article reviews the origin and characteristics of induced pluripotent stem cells, their applications in the oral cavity, and their progress in the fields of tissue engineering and regeneration.

Keywords: Induced pluripotent stem cells, Reprogramming; oral tissue regeneration.

INTRODUCTION

Induced pluripotent stem cells (iPSCs) were obtained by Takahashi K et al. [1] through reprogramming of mouse embryonic or adult fibroblasts by introducing four factors Oct3/4, Sox2, c-Myc, and Klf4 under embryonic stem (ES) cell culture conditions; iPSCs share similar characteristics with embryonic stem cells. Human embryonic stem cells serve as the standard source of pluripotent cells [2]. ES cells can self-renew indefinitely in culture without losing their differentiation capacity, whereas somatic cells require prolonged in vitro culture and their differentiation capacity declines over time along with the occurrence of replicative senescence. The limitations of ES cells in tissue regeneration include the inability to obtain ES cells from patients, immune rejection following transplantation, and ethical concerns. iPSC technology resolves both of these problems: patient-derived somatic cells can be used to generate therapeutic iPSCs (thereby eliminating the possibility of immune rejection), and they can replace the use of human embryos for stem cell transplantation and cell production. An additional benefit is that patient-specific iPSCs can be used in drug and regenerative medicine research. Consequently, extensive research has been devoted to generating pluripotent stem cells from adult (somatic) tissues to achieve broader sources of pluripotent stem cells. In the field of oral medicine, gingival fibroblasts, dental pulp cells, periodontal ligament fibroblasts, and oral mucosal fibroblasts have been successfully induced into iPSCs, and studies have demonstrated that iPSCs derived from these somatic cells can promote the regeneration of dental and periodontal tissues [3].

Origin and Characteristics of Induced Pluripotent Stem Cells

Generation of Induced Pluripotent Stem Cells: To date, iPSCs have been successfully generated using lentiviruses, retroviruses, adenoviruses, plasmids, transposons, and recombinant proteins. Through retroviral transduction of four transcription factors Oct3/4, Sox2, Klf4, and c-Myc iPS cells can be generated from adult dermal fibroblasts and other somatic cells. During iPS cell generation, genes transcribed from retroviruses are silenced when the transduced fibroblasts acquire an ES cell-like state [4]. The established human iPS cells resemble human ES cells in many respects, including morphology, proliferation, feeder cell dependence, surface markers, gene expression, promoter activity, telomerase activity, in vitro differentiation, and teratoma formation. Boyer et al. [5] and Muñoz Descalzo S et al. [6] identified Oct3/4 and Sox2 as core transcription factors with pluripotency functions in their studies. Sumi T et al. [7] found that forced expression of c-Myc induces differentiation and apoptosis in human ES cells, which is contrary to its role in mouse ES cells. With further research on iPSCs, studies [8] found that retroviruses used for iPSC induction may cause mutations, rendering them unsuitable for clinical use. Kaji K et al. [9] used virus-derived 2A peptide sequences to generate stable iPS cells in human and mouse fibroblasts, avoiding the abnormalities in iPSCs that may result from the use of retroviruses. Okita K et al. [10] repeatedly transfected two expression plasmids one containing complementary DNA (cDNA) of Oct3/4, Sox2, and Klf4, and another containing c-Myc cDNA into mouse embryonic fibroblasts to generate iPSCs without plasmid integration, demonstrating that retroviral integration is dispensable in iPSC generation; however, it was also found that without retroviruses, the efficiency of iPSC generation is greatly reduced, which may indicate that retroviral integration promotes iPSC production. Yu J et al. [11] generated human iPSCs by plasmid transfection that were completely free of vector and transgene sequences and were similar to human ES cells in terms of proliferative and developmental potential; however, this method triggers the oncogenes c-MYC and KLF4. The use of c-MYC for iPSC induction should be avoided. Some researchers [12] used mRNA to generate iPSCs, reprogramming human skin cancer cells into a pluripotent ES cell-like state using mir-302, a method that can prevent the generation of oncogenes such as c-MYC and

Corresponding Author:** ***Jingye, Zhou,
Department of Stomatology, School of Stomatology Jinan University, China

KLF4. However, they used human skin cancer cell lines rather than human somatic cells. In a recent study by Salloum-Asfar S et al. [13], the miRNA, piRNA, and snoRNA expression profiles in iPSCs and primary fibroblasts were evaluated, identifying the potential roles of ncRNAs in enhancing iPSC generation, pluripotency, and differentiation. The study also found that A53T-PD2 fibroblasts were associated with increased cell homing and decreased cell proliferation, and that slowing proliferation, increasing cell survival, and increasing cell homing are conducive to iPSC induction. In addition, the study found that vectors for iPSC induction also include transposons and recombinant proteins; the use of transposons to generate iPSCs carries the risk of transcribed genes remaining in the genome, and the efficiency of generating iPSCs through recombinant proteins is low [14].

In addition to vectors, seed cells are also required for iPSC induction. In the oral cavity, the seed cells used as iPSCs are primarily gingival fibroblasts, dental pulp cells, periodontal ligament fibroblasts, and oral mucosal fibroblasts. Gingival fibroblasts proliferate rapidly, undergo rapid turnover, and are easily accessible, making them an ideal source of iPSCs in periodontal regenerative medicine. In 2010, Egusa H [15] successfully generated iPSCs from human and mouse gingival fibroblasts through genomic insertion of reprogramming factors carried by viral vectors. In a study on gingival fibroblasts as autologous feeders for induced pluripotent stem cells [16], high expression of laminin-332 and laminin-511 in hGFs was found to potentially contribute to their superior feeder capacity; therefore, using hGFs as both iPSC sources and autologous feeder cell layers may provide an easier and more efficient approach to obtaining clinical-grade pluripotent stem cells. Li JW et al. [17], in a study comparing the proliferative and periodontal-specific differentiation capacities of iPSCs generated from hGFs of different passage numbers, found that long-term culture does not affect the proliferative capacity or periodontal-specific differentiation tendency of iPSCs, which can still efficiently proliferate and differentiate into periodontal cells under growth factor induction after continuous passaging. Dental pulp cells (DPCs), as an optimal source of iPSCs, can be obtained from extracted teeth and iPSCs can be generated with high efficiency [18].

Characteristics of Induced Pluripotent Stem Cells: The characteristics of iPSCs are primarily: pluripotency, self-renewal capacity, genetic reprogramming, stability, and reproducibility. The most prominent characteristic of iPSCs is their pluripotency [19], referring to the capacity of iPSCs to give rise to all other cell types, capable of differentiating into various cell types derived from the three germ layers, including endoderm, ectoderm, and mesoderm cells. Similar to ES cells, iPSCs possess the capacity for self-renewal, capable of undergoing cell division indefinitely while maintaining their stem cell state, thereby generating large numbers of cells. The genetic reprogramming characteristic [20] refers to the fact that iPSC generation is achieved through genetic reprogramming technology, by introducing a specific set of transcription factors (such as Oct4, Sox2, Klf4, and c-Myc), which can reactivate the stem cell properties of cells and convert them into iPSCs. iPSCs possess stability and reproducibility during their preparation process. This means that researchers can repeatedly prepare identical iPSCs in the laboratory, thereby ensuring the reliability of experimental results. These characteristics of iPSCs endow them with enormous potential in biomedical research and clinical applications.

Applications of Induced Pluripotent Stem Cells in Oral Regeneration

Applications of iPSCs in Periodontal Regeneration: Periodontal disease can lead to extensive destruction of alveolar bone, periodontal ligament (PDL), and cementum, and may even result in progressive oral functional impairment. Periodontal tissue regeneration is the ultimate goal of periodontal disease treatment, aiming to reconstruct structure and function. A study reported [21] that functional mesenchymal stem cells (MSCs) derived from human iPSCs can express characteristic MSC markers, differentiate into osteoblasts, adipocytes, and chondrocytes, and promote vascular and muscle regeneration. Human periodontal ligament stem cells (PDLSCs) are an important cell source for periodontal regeneration. In one study [22], by simulating the in vivo developmental pattern of PDLSCs, large quantities of PDLSCs could be stably generated from iPSCs, and the characteristics of iPSC-derived PDLSCs as well as their bipotential for osteogenic and adipogenic differentiation were validated in vitro. The study by Chien KH et al. [23] found that in vitro and in vivo in an animal model of maxillary molar defects, animals treated with iPSC-BMP-6-hydrogel exhibited new bone formation, new periodontal ligament regeneration, and a decrease in inflammatory factors, indicating that hydrogel-encapsulated iPSCs combined with BMP-6 are highly likely to achieve periodontal regeneration. In summary, the principles underlying the application of iPSCs in periodontal regeneration include the following aspects: (1) iPSCs can be induced from dental-derived cells, such as gingival fibroblasts and periodontal ligament fibroblasts; (2) iPSCs can differentiate into osteoblasts under certain stimulating factors; (3) iPSCs, whether combined with scaffolds or not, can promote the healing of artificial periodontal bone defects and form new periodontal tissues such as alveolar bone, cementum, and periodontal ligament.

Applications of iPSCs in Mucosal Regeneration: The three essential elements of tissue engineering are: seed cells, scaffold materials, and growth factors. In the process of constructing biologically active oral mucosa, the adhesion, proliferative capacity, degree of differentiation, and immunological properties of seed cells must be considered. The seed cells currently used in oral mucosal tissue engineering mainly include: keratinocytes and fibroblasts derived from oral mucosa, bone marrow mesenchymal stem cells, and adipose-derived stromal cells [24]. iPSCs can be directionally induced to differentiate into oral mucosal epithelial cells, which can then be used to construct mucosal epithelial tissue through tissue engineering to accomplish regenerative repair of oral mucosal defects. Oral mucosal lesions are a common oral disease, and induced pluripotent stem cells hold potential application value in their treatment. By transplanting pluripotent stem cells into damaged mucosal areas, the regeneration and repair of normal tissue can be promoted, thereby improving the symptoms of oral lesions.

Applications of iPSCs in Dental Restoration: Teeth are frequently damaged or lost due to dental caries, periodontal disease, and trauma. Currently, external interventional measures are commonly employed clinically for dental restoration, such as dentures, dental implants, inlays, and artificial crowns. To date, cell-based tissue engineering has developed rapidly, and research on dental restoration has gradually shifted from replacement to regeneration. Dental

regeneration encompasses dentin-pulp regeneration, whole tooth regeneration, and root regeneration. iPSCs can not only differentiate into dental epithelial cells, dental mesenchymal cells, and neural crest cells, but can also differentiate into mesenchymal cells and osteoprogenitor cells [25]. Cai J et al. [26] detected in their study that epithelial sheets derived from human urine-induced pluripotent epithelial cells differentiated into ameloblasts secreting enamel within tooth-like structures and generated tooth-like structures. There are two approaches to stem cell-based pulp regeneration: one is the cell transplantation method, in which induced dental pulp stem cells combined with scaffolds are directly transplanted into the body; the other is the cell homing method, in which a series of growth factors are used to induce stem cell/progenitor cell homing to achieve pulp regeneration [27]. Stem cell-based whole tooth regeneration depends on the multipotent differentiation of stem cells. Otsu K et al. [28] demonstrated that neural crest-like cells (NCLCs) derived from mouse iPSCs possess the potential to differentiate into odontogenic mesenchymal cells and can further differentiate toward odontoblasts, indicating that iPSCs can serve as a potential cell source for tooth regeneration.

Challenges and Prospects of Induced Pluripotent Stem Cells

The emergence of induced pluripotent stem cells represents a breakthrough in the field of stem cell research, bringing more possibilities to oral tissue engineering. iPSCs belong to an autologous cell source, derived from the patient's own tissues, with no risk of immune reaction and without the ethical issues associated with human embryonic stem cells. The characteristics of iPSCs have led to significant advances in periodontal regeneration, mucosal regeneration, and dental regeneration in the oral cavity. Although some progress has been made in oral iPSC research, certain challenges remain, including low reprogramming efficiency of iPSCs, as well as concerns regarding safety, tumorigenicity, and genetic instability.

Summary

The clinical application of iPSCs still requires further research, with a focus on achieving safe and effective reprogramming and significant expansion while avoiding the risk of tumor formation after implantation. In conclusion, oral pluripotent stem cells hold important application potential in oral tissue engineering and regenerative medicine. With continuous technological advancement and in-depth research, it is believed that the application of oral pluripotent stem cells will provide new possibilities for the treatment of oral diseases.

REFERENCES

1. Takahashi K, Yamanaka S. Induction of pluripotent stem cells from mouse embryonic and adult fibroblast cultures by defined factors. Cell. 2006;126(4):663-676. doi:10.1016/j.cell.2006.07.024
2. Lengner CJ, Camargo FD, Hochedlinger K, et al. Oct4 expression is not required for mouse somatic stem cell self-renewal. Cell Stem Cell. 2007;1(4):403-415. doi:10.1016/j.stem.2007.07.020
3. Gao P, Liu S, Wang X, Ikeya M. Dental applications of induced pluripotent stem cells and their derivatives. Jpn Dent Sci Rev. 2022; 58:162-171. doi:10.1016/j.jdsr.2022.03.002
4. Takahashi K, Tanabe K, Ohnuki M, et al. Induction of pluripotent stem cells from adult human fibroblasts by defined factors. Cell. 2007;131(5):861-872. doi:10.1016/j.cell.2007.11.019
5. Boyer LA, Lee TI, Cole MF, et al. Core transcriptional regulatory circuitry in human embryonic stem cells. Cell. 2005;122(6):947-956. doi:10.1016/j.cell.2005.08.020
6. Muñoz Descalzo S, Rué P, Faunes F, et al. A competitive protein interaction network buffers Oct4-mediated differentiation to promote pluripotency in embryonic stem cells. Mol Syst Biol. 2013;9:694. Published 2013 Oct 8. doi:10.1038/msb.2013.49
7. Sumi T, Tsuneyoshi N, Nakatsuji N, Suemori H. Apoptosis and differentiation of human embryonic stem cells induced by sustained activation of c-Myc. Oncogene. 2007;26(38):5564-5576. doi:10.1038/sj.onc.1210353
8. Tavernier G, Mlody B, Demeester J, Adjaye J, De Smedt SC. Current methods for inducing pluripotency in somatic cells. Adv Mater. 2013;25(20):2765-2771. doi:10.1002/adma.201204874
9. Kaji K, Norrby K, Paca A, Mileikovsky M, Mohseni P, Woltjen K. Virus-free induction of pluripotency and subsequent excision of reprogramming factors. Nature. 2009;458(7239):771-775. doi:10.1038/nature07864
10. Okita K, Nakagawa M, Hyenjong H, Ichisaka T, Yamanaka S. Generation of mouse induced pluripotent stem cells without viral vectors. Science. 2008; 322(5903):949-953. doi:10.1126/science.1164270
11. Yu J, Hu K, Smuga-Otto K, et al. Human induced pluripotent stem cells free of vector and transgene sequences. Science. 2009;324(5928):797-801. doi:10.1126/science.1172482
12. Lin SL, Chang DC, Chang-Lin S, et al. Mir-302 reprograms human skin cancer cells into a pluripotent ES-cell-like state. RNA. 2008;14(10):2115-2124. doi:10.1261/rna.1162708
13. Salloum-Asfar S, Abdulla SA, Taha RZ, Thompson IR, Emara MM. Combined Noncoding RNA-mRNA Regulomics Signature in Reprogramming and Pluripotency in iPSCs. Cells. 2022;11(23):3833. Published 2022 Nov 29. doi:10.3390/cells11233833
14. Liu SP, Fu RH, Huang YC, et al. Induced pluripotent stem (iPS) cell research overview. Cell Transplant. 2011;20(1):15-19. doi:10.3727/096368910X532828
15. Egusa H, Okita K, Kayashima H, et al. Gingival fibroblasts as a promising source of induced pluripotent stem cells. PLoS One. 2010;5(9):e12743. Published 2010 Sep 14. doi:10.1371/journal.pone.0012743
16. Yu G, Okawa H, Okita K, et al. Gingival Fibroblasts as Autologous Feeders for Induced Pluripotent Stem Cells. J Dent Res. 2016;95(1):110-118. doi:10.1177/0022034515611602
17. Li JW, Yin XH, Luan QX. Beijing Da Xue Xue Bao Yi Xue Ban. 2017;49(1):16-24.
18. Tamaoki N, Takahashi K, Tanaka T, et al. Dental pulp cells for induced pluripotent stem cell banking. J Dent Res. 2010;89(8):773-778. doi:10.1177/0022034510366846
19. Maherali N, Hochedlinger K. Guidelines and techniques for the generation of induced pluripotent stem cells. Cell Stem Cell. 2008;3(6):595-605. doi:10.1016/j.stem.2008.11.008
20. Deng W, Xu Y. Genome integrity: linking pluripotency and tumorgenicity. Trends Genet. 2009;25(10):425-427. doi:10.1016/j.tig.2009.09.004
21. Lian Q, Zhang Y, Zhang J, et al. Functional mesenchymal

stem cells derived from human induced pluripotent stem cells attenuate limb ischemia in mice. Circulation. 2010; 121(9):1113-1123. doi:10.1161/circulationaha.109. 898312
22. Wang Y, Hua Y. Generation of periodontal ligament stem cells from human iPSCs with a chemically defined condition. Biol Futur. 2020;71(3):241-248. doi:10.1007/ s42977-020-00022-8
23. Chien KH, Chang YL, Wang ML, et al. Promoting Induced Pluripotent Stem Cell-driven Biomineralization and Periodontal Regeneration in Rats with Maxillary-Molar Defects using Injectable BMP-6 Hydrogel. Sci Rep. 2018;8(1):114. Published 2018 Jan 8. doi:10.1038/s41598-017-18415-6
24. Liu Ying, Wang Daqing, Mo Jinlong, et al. Research Progress of Cell Sheet Technology in Oral Tissue Engineering. Chinese Journal of Reparative and Reconstructive Surgery, 2014, 28(9): 1168-1172.
25. Hynes K, Menichanin D, Bright R, et al. Induced Pluripotent Stem Cells: A New Frontier for Stem Cells in Dentistry. J Dent Res. 2015;94(11):1508-1515. doi:10.1177/0022034515599769
26. Cai J, Zhang Y, Liu P, et al. Generation of tooth-like structures from integration-free human urine induced pluripotent stem cells. Cell Regen. 2013;2(1):6. Published 2013 Jul 30. doi:10.1186/2045-9769-2-6
27. Kim JY, Xin X, Moioli EK, et al. Regeneration of dental-pulp-like tissue by chemotaxis-induced cell homing. Tissue Eng Part A. 2010;16(10):3023-3031. doi:10.1089/ ten.TEA.2010.0181
28. Otsu K, Kishigami R, Oikawa-Sasaki A, et al. Differentiation of induced pluripotent stem cells into dental mesenchymal cells. Stem Cells Dev. 2012;21(7):1156-1164. doi:10.1089/scd.2011.0210

****