



Stem cell therapy – An Oral Surgeon’s Perspective

**Dr. Ramesh Kunusoth¹, Dr. Aditya Mohan², Dr. A Prensagar³, Dr. Megha Kadani⁴,
Dr. Rathod Prakash⁵, Dr. S Sai Charan⁶, Dr. Shakeel Ahmed⁷**

¹Professor & Head, ²Professor, ^{3,6,7}Postgraduate Student, ⁴Reader in Department of Oral & Maxillofacial Pathology, ⁵Senior Lecturer, Department of Oral & Maxillofacial Surgery, MNR Dental College & Hospital, Sangareddy, Telangana

***Corresponding Author:**

Dr. Megha Kadani

Reader, Department of Oral & Maxillofacial Pathology, MNR Dental College & Hospital, Narsapur Road, Fasalwadi, Sangareddy, Telangana-502294

Type of Publication: Original Research Paper

Conflicts of Interest: Nil

Abstract

In recent few years, we can see rapid advancement in clinical trials about stem cell therapies, researches recently translated stem cell therapies successfully to patients which enriched the hopes of regenerative studies. These stem cells are self-renewal and capable of differentiation. Stem cell therapy is used for the regeneration of craniofacial defects like tumor resection, cyst enucleation, and trauma. With the limitations of reconstructive techniques, tissue engineering and regenerative medicine have been new advancements explored by scientists and clinicians for the restoration of anatomy and function. To regenerate a tissue, a source of stem cells and signaling molecules are needed.

Keywords: Oral and maxillofacial region, stem cell therapy, tooth regeneration, and cell therapy

Introduction

Many clinicians have challenged the reconstruction and regeneration of oral and craniofacial defects. Stem cell therapy has become a very promising and advanced scientific research topic, like all scientific research and medical advances stem cells should be vetted for ethical use and safety. More research should be done on stem cells before it is used and applied.

Stem cells have two capabilities one is self-renewal and the other is differentiation. Self-renewal is the ability of cells to replicate and produce the same originating cell. Differentiation is the ability to produce desired specialized cell type. Conditions like tumor resections, cyst enucleation, trauma-induced bone or cartilage defects, and congenital defects are common in the oral and maxillofacial region. To repair the skeletal damage and defects currently use of bone grafts is the Golden standard. Due to the

shortage of bone graft material and donor-site morbidity, there is a problem in the availability of grafts.

Due to limited self-healing of teeth, dental caries are treated by fillings, Missing teeth are replaced and restored by implants, Removable partial dentures, and fixed partial dentures. For these new strategies of treatment is necessary, so the introduction of stem cell-based tissue engineering techniques and advancements in the oral and maxillofacial region is important.

Maxillofacial defects:

Maxillofacial tissues are important to all individuals. Individuals feel trouble living confidently, aesthetically, and psychologically. There is much influence on the patients with congenital defects, tumor sections, accident injuries, and infections. Effective reconstruction or regeneration of these

tissues would be beneficial to patients both psychologically and physiologically.

Currently, flap transplants with dental implants and obturators are used methods to rehabilitate damaged tissues, however, esthetics and functions are needed to be improved.

Treatment:

Four main types of stem cells are

1. Embryonic stem cells
2. Adult stem cells
3. Perinatal stem cells in amniotic fluid
4. Induced pluripotent stem cells

Embryonic stem cells are best with pluripotency, but legally, esthetically and with medical considerations these cells have hindered the development in clinical applications, where the embryo has to be destructed for the collection of stem cells. Amniotic fluid stem cells should be studied more for their potential. Therefore, there is a need to focus on Adult Stem cells and oral derived induced pluripotent stem cells, which can be used for the treatment of oral and maxillofacial defects.

Oral derived Adult stem cells:

These adult stem cells are also called somatic stem cells or postnatal stem cells, which are harvested from adults. These are multipotent cells, which can be differentiated into the limited type of cells.

Dental tissues including Dental pulp, bone marrow, apical papilla, periodontal ligament, and gingiva are good sources of adult stem cells. These cells can be isolated and they express specific molecular markers.

Harvesting stem cells from the oral cavity is easy for the surgeons without causing any trauma to the patient.

Different stem cells found in the oral and maxillofacial region are

1. Stem cells of apical papilla
2. Inflammatory periapical progenitor cells
3. Dental pulp stem cells
4. Dental follicle stem cells
5. Periodontal ligament stem cells
6. Bone-marrow stem cells
7. Tooth germ progenitor cells

8. Salivary gland stem cells
9. oral epithelial stem cells
10. stem cells from human exfoliated deciduous teeth
11. gingival derived mesenchymal stem cells
12. periosteal derived stem cells

most of these Adult stem cells are Mesenchymal stem cells. Preclinical studies are conducted in animal models.

Oral derived induced pluripotent stem cells

Induced pluripotent stem cell technology is a great discovery that contributes a lot to the treatment of diseases. The introduction of this technology solves ethical problems encountered by the application of Human Embryonic cells and solves the limited source problem of both embryonic and adult stem cells.

Induced pluripotent stem cell technology made good signs of progress in regenerative medicine, replacing damaged organ parts. As this has greater potential, researchers are interested in the application of these cells in dental tissue regeneration.

Human deciduous tooth dental pulp cells are a good source of Induced pluripotent stem cells, gingival fibroblasts are another wise choice, As gingiva can be easily acquired without extraction have high reprogramming efficiency.

Mesenchymal stem cells derived from dental pulps

Postnatal human dental pulp stem cells have the ability and potential to regenerate dentin and pulp-like complexes, and be as progenitor cells in need of repair. Both bone marrow stem cells and dental pulp stem cells express endothelial and smooth muscle cell markers. Dental pulp stem cells have been used in swine to create bio-engineered dental roots (Bio root complex). Investigators created it in swine by using autologous dental pulp stem cells, scaffold constructs composed of tricalcium phosphate hydroxyapatite, and appropriate growth factors.

A biological scaffold is a 3-D construct with different growth factors, a bone morphogenic protein that provides the required 3D morphology. Such scaffolds are introduced into the engineered structure, like hydroxyapatite.

In this study, the created bio root was harvested after six months and implanted in an extraction socket in the swine jaw bone. By using correct scaffolds the

potential of creating a biological root complex with dental pulp stem cells is studied.

References

1. Mao, J. J., and Prockop, D. J. (2012). Stem cells in the face: tooth regeneration and beyond. *Cell Stem Cell* 11, 291–301. doi: 10.1016/j.stem.2012.08.010
2. Wijbenga, J. G., Schepers, R. H., Werker, P. M., Witjes, M. J., and Dijkstra, P. U. (2016). A systematic review of functional outcome and quality of life following reconstruction of maxillofacial defects using vascularized free fibula flaps and dental rehabilitation reveals poor data quality. *J. Plast. Reconstr. Aesthet. Surg.* 69, 1024–1036. doi: 10.1016/j.bjps.2016.05.003
3. Weissman, I. L. (2000). Stem cells: units of development, units of regeneration, and units in evolution. *Cell* 100, 157–168. doi: 10.1016/S0092-8674(00)81692-X
4. Murray, P. E., Garcia-Godoy, F., and Hargreaves, K. M. (2007). Regenerative endodontics: a review of current status and a call for action. *J. Endod.* 33, 377–390. doi: 10.1016/j.joen.2006.09.013
5. Tatullo, M., Marrelli, M., and Paduano, F. (2015). The regenerative medicine in oral and maxillofacial surgery: the most important innovations in the clinical application of mesenchymal stem cells. *Int. J. Med. Sci.* 12, 72–77. doi: 10.7150/ijms.10706
6. Takahashi, K., and Yamanaka, S. (2006). Induction of pluripotent stem cells from mouse embryonic and adult fibroblast cultures by defined factors. *Cell* 126, 663–676. doi: 10.1016/j.cell.2006.07.024
7. Yan, X., Qin, H., Qu, C., Tuan, R. S., Shi, S., and Huang, G. T. (2010). iPS cells reprogrammed from human mesenchymal-like stem/progenitor cells of dental tissue origin. *Stem Cells Dev.* 19, 469–480. doi: 10.1089/scd.2009.0314
8. Tamaoki, N., Takahashi, K., Tanaka, T., Ichisaka, T., Aoki, H., Takeda-Kawaguchi, T., et al. (2010). Dental pulp cells for induced pluripotent stem cell banking. *J. Dent. Res.* 89, 773–778. doi: 10.1177/0022034510366846
9. Egusa, H., Okita, K., Kayashima, H., Yu, G., Fukuyasu, S., Saeki, M., et al. (2010). Gingival fibroblasts as a promising source of induced pluripotent stem cells. *PLoS ONE* 5:e12743. doi: 10.1371/journal.pone.0012743
10. Arakaki, M., Egusa, H., Otsu, K., Saitoh, K., Miura, T., and Harada, H. (2013). Frontier dental research on iPS cells. *J. Oral Biosci.* 55, 191–199. doi: 10.1016/j.job.2013.08.002