Review Article

Stem Cells in the Oral Cavity – An Overview

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Abstract

Stem cells play a vital role in regenerative medicine and it has the capacity to form any type of tissue under favored circumstances. The stem cells from the oral cavity can be easily removed and used for the regeneration of both hard and soft tissues. This article aimed to review the sources of stem cells from the oral cavity and the application of the same in the orofacial region and the principles of stem cell bank for the betterment of the quality and quantity of stem cells.

Keywords: *Confidentiality, multipotent, papilla, periodontium, pulp, regenerate*

Introduction

Stem cells are special cells called "Universal cells" or "Seed cells" that are able to develop into most cell types of all three germ layers (Sun *et al*., Clevers *et al*.)[1,2]. The types of stem cells include embryonic stem cells and adult stem cells. Embryonic stem cells originate from the inner cell mass of blastocyst in preimplantation stage after *in vitro* fertilization which have transcription factors which help them to maintain a pluripotent state. Adult stem cells, otherwise called somatic stem cells/postnatal stem cells, which are multipotent progenitor cells, reside in a specialized microenvironment called stem cell niche (Ebrahimi M *et al*.)[3]. This article gives information about stem cells in the oral cavity and their uses with the detailed information about stem cell banks.

Stem Cells in the Oral Cavity

Stem cells in the oral cavity include dental pulp stem cells (DPSC), Stem cells from Human Exfoliated Deciduous teeth (SHED), stem cells of apical papilla (SCAP), dental follicle progenitor cells (DFPCs), periodontal ligament stem cells (PLSCs), and bone marrow-derived mesenchymal stem cells (BMMSCs).

a. DPSC: DPSCs are the first type of stem cells that reside in the perivascular niche or cell-rich zone. They are most commonly obtained from the impacted third molar. They are isolated by enzymatic digestion of pulp tissue. They resemble fibroblast and have a higher proliferation rate even after extensive subculturing. They can be transformed into dentinogenic, osteogenic, adipogenic, neurogenic, chondrogenic, and myogenic with different differentiation media (Gronthos S *et al*.)[4]
b. SHED: The deciduous teeth are a good source of stem cells obtained from exfoliating deciduous teeth. It has high proliferative rate and high number of colonies forming units. They do not grow as individual cells but cluster into several colonies and it will grow as individual cells only after separation. The tendency of these cells to heal calvarial defects due to their osteogenic potential has been proved in animal studies (Seo BM *et al*.)[5]
c. SCAP: They are isolated at certain specific stages of tooth development. It has greater potential to form dentin when compared to stem cells from other parts of the oral cavity. The nerve tissue has been formed *in vitro* from the stem cells derived from apical papilla (Kim BC *et al*.)[6]
d. DFPC: Stem cells from the dental follicle have the capacity to change to cementoblast, osteoblast, and fibroblast. It expresses higher osteocalcin and hence has faster bone regeneration. These cells have been proved to form mammary gland regeneration when acquired from the cervical loop of rodent incisors (Jimenez-Rojo L *et al*.)[7]
e. PLSC: It has the potential to regenerate typical cementum and PDL-like structures. It can be

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obtained from two sources – root surface and alveolar bone surface, among which the one scrapped off from alveolar bone surface has higher bone regeneration, higher osteogenic potential, and higher proliferation and the one scraped from root surface has less alkaline phosphatase activity and has lesser bone-forming capacity (Wang L *et al*.)[8]

f. BMMSC: It is derived from maxilla or mandible during surgical procedures. The quantity and quality of the bone marrow-derived stem cells are superlative and it is less chondrogenic and lipogenic; however, the proliferation rate and differentiation potential are limited (Ebrahimi M *et al*.)[3]
g. STEM CELLS FROM LINING MUCOSA: It is either derived from oral epithelium and gingiva. The cells from neural crest origin are scattered in the oral mucosa which has osteogenic potential and hence helps in bone regeneration. The gingival-derived stem cells have anti-inflammatory and immunomodulatory properties. Animal studies revealed that it has the potential to regenerate periodontium (Zhang Q *et al*.)[9]
h. STEM CELLS FROM ADIPOSE TISSUE: Buccal fat pad is the richest source of adipose tissue from where stem cells have been collected. It has been proved from animal studies that they are capable of regenerating pulp and periodontal complex in an extracted socket (Mizuno H and *et al*., Tobita M *et al*.)[10,11]
i. STEM CELLS FROM SALIVARY GLAND: The stem cells from the stromal and parenchymal components of the salivary gland are still under research; however, the stromal component has stem cells that are chondrogenic, osteogenic, and adipogenic than the parenchymal component. The regeneration of salivary gland function is still under investigation (Coppes RP *et al*., Rotter N *et al*.)[12,13]
j. STEM CELLS FROM MAXILLARY SINUS: It is derived from Schneiderian membrane of the maxillary sinus which has a higher expression of mesenchymal stem cells. It is used in the conventional maxillary sinus lifting and bone grafting prior to implant (Berberi A *et al*.).[14]

Applications of Stem Cells in the Orofacial Region

There are no available reports for stem cell therapy in dental hard tissue defects. However, the pulpal inflammation which can be treated by root canal treatment can use dental stem cells along with growth factors to regenerate dental pulp-like tissues (Rosa V *et al*.).[15] Periodontal diseases include gingivitis and periodontitis that leads to bone loss and loosening of teeth. The usual treatment involves scaling and root planning, guided tissue regeneration with graft materials for the bone loss, the dental stem cells have been used in periodontal regeneration in animal models and clinical trials and are proved to be safe (Menicanin *et al*.).[16] Major surgeries such as resection of tumor with replacement, skin grafts, or any congenital problems can be sorted out by application of stem cells as scaffolds along with the growth factors and calcium or phosphate-based bioactive ceramics. Before the application, identification and isolation of appropriate groups of stem cells is a crucial process and the quality of the stem cells has to be assessed before administering it in the clinicals (Yang B *et al*.).[17]

Stem Cell Bank

A stem cell bank is a platform for the large-scale population, preparation, storage, provision, and research of stem cells and called "life-bank" (Stacey *et al*.).[18] The stem cells should be stored following the principles which include "5C" that includes:

a. INFORMED CONSENT: The donors should voluntarily donate their organ or tissues. They should sign the informed consent and their information should be kept private (West CC *et al*.)[19]
b. CONFIDENTIALITY PRINCIPLE: The officials in the stem cell should not disclose the personal information of the donor at any cost
c. CONFORMITY PRINCIPLE: The conformity explains the guarantee of the stem cells for various research purposes, and hence, it should possess high quality. The stem cells have to be evaluated from the collection till its use in clinical applications (Barry J *et al*.)[20]
d. CONTAMINATION-FREE PRINCIPLE: The stem cells should be free from microbial contamination and contamination from cell lines. Clean containers, proper storage, and maintenance of liquid nitrogen sources are the few measures to avoid contamination and adulteration (Kono K *et al*.)[21]
e. COMMONWEAL PRINCIPLE: The donors should not be offered money or any forms of offerings for the stem cell donation as it might degrade the decorum of the principles in stem cell banking and the same should also be mentioned in the informed consent.

Conclusion

The oral cavity provides a rich source of stem cells and can be easily accessed and isolated; cryopreserved stem cells have also been used. The application of stem cells in the oral cavity has been broadly increased and this will create wonders in regenerative medicine. At the same time, the quality of the stem cells has to be

assessed and it must strictly follow the principles of stem cell bank before the clinical trials.

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Conflicts of interest

There are no conflicts of interest.

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