*Journal of Applied Dental and Medical Sciences*
*NLM ID: 101671413 ISSN:2454-2288*
*Volume 2 Issue 1 January - March 2016*

**Review Article**

# Stem cells: A new paradigm in dentistry

**B. K. Motwani[1], Manmohit Singh[2], Gurpreet Kaur[3], Sanjeev Singh[4], Pritesh O. Gangde[5]**

*[1]Professor, HOD Department of Prosthodontics, Chhattisgarh Dental College and Research Institute, Rajnandgaon, Chhattisgarh (India)*
*[2]Reader, Department of prosthodontics,Bhojia Dental College, Baddi, Himachal Pradesh.*
*[3]Reader, Department of Orthodontics.Himachal Dental College, Sundernagar, Himachal Pradesh.*
*[4]Reader, Department of Prosthodontics, Chhattisgarh Dental College And Research Institute, Rajnandgaon, Chhattisgarh (India).*
*[5]Post Graduate Student, Department of Prosthodontics, Chhattisgarh Dental College And Research Institute, Rajnandgaon, Chhattisgarh (India).*

ARTICLE INFO

Keywords:
Stem cells, dental pulp, periodontal ligament, dental follicle, apical papilla.

ABSTRACT

Stem cell (SC) therapy has a promising future for tissue regenerative medicine. However, because SC technology is still in its infancy, interdisciplinary cooperation is needed to achieve successful clinical applications. Dental SCs have drawn attention in recent years because of their accessibility, plasticity, and high proliferative ability. Based on their ability to rescue and/or repair injured tissue and partially restore organ function, multiple types of stem/progenitor cells have been speculated. Growing evidence demonstrates that stem cells are primarily found in niches and that certain tissues contain more stem cells than others. Among these tissues, the dental tissues are considered a rich source of mesenchymal stem cells that are suitable for tissue engineering applications.Several types of dental SCs have been identified, including dental pulp SCs from adult human dental pulp, SCs from human primary exfoliated deciduous teeth, periodontal ligament SCs, and dental follicle SCs from human third molars. Similar to mesenchymal SCs, these dental SCs can undergo self-renewal and have multipotent differentiation ability, but do not have the ethical issues associated with other sources of SCs.This review describes new findings in the field of dental stem cell research and on their potential use in the tissue regeneration.

## Introduction

The regenerative abilities of certain animals have always been a fascination for man. Regeneration is a remarkable physiological process in which remaining tissues organize to reform a missing body part but mammals appear to have lost this ability, perhaps for more proficient wound healing ability. Most tissue repair events in mammals are dedifferentiation-independent events resulting from the activation of pre-existing stem cells or progenitor cells. Stem cells or progenitor cells are the common denominator for nearly all types of regeneration which are either already pre-existing.[1]

The human body is made up of three basic categories of cells: germ cells, somatic cells and stem cells. The materials required for tissue engineering include stem cells, morphogens (or growth factors) and a scaffold to guide cell growth. Scientific study into cell-based therapies has identified tremendous potential for the use of these stem cells to treat a number of diseases and disorders.

It is now accepted that progenitor/stem cells reside within orofacial region. Stem cells residing in the orofacial region have been classed as the Mesenchymal stem cells (MSCs) /Adult stem cells (ASCs) / Tissue stem cells (TSCs).[2] Studies have identified several niches of multipotent mesenchymal

* *Corresponding author:* ***Dr. Pritesh Onkar Gangde ,Postal Address: Chaitanyawadi, Choti Umri, Nr. S. B. I. colony no. 5, Akola, Maharashtra, India. Pin Code: 444005 Mobile No: 08871534649, 07387610776 Email Address : pritesh29095@gmail.com***

progenitor cells, known as dental pulp stem cells, which have a high proliferative potential for self-renewal. These progenitor stem cells are now recognized as being vital to the dentine regeneration process following injury. More recently, researchers have discovered that stem cells harvested from deciduous teeth may be a source of tissue regeneration and repair.[3] Five different types of dental stem cells isolated from dental soft tissues are dental pulp, apical papilla, dental follicle and periodontal ligament.

The characteristic features of these cells express various arrays of biomarkers including those specific for mesenchymal and/or embryonic stem cells. In vitro and in vivo studies have revealed that these stem cells varied in their proliferation and differentiation potential.[2] Thus it is imperative to know about the various sources of stem cells in dental region their characteristics and possible clinical applications before harnessing their full potential towards the field of Dentistry.

According to Columbia Encyclopedia Stem cells are defined as "unspecialized human or animal cells that can produce mature specialized body cells and at the same time replicate themselves."[4] When a stem cell divides, the daughter cells can either enter a path leading to the formation of a differentiated specialized cell or self-renew to remain a stem cell, thereby ensuring that a pool of stem cells is constantly replenished in the adult organ. This mode of cell division characteristic of stem cells is asymmetric and is a necessary physiological mechanism for the maintenance of the cellular composition of tissues and organs in the body (Figure 1)[1].

**Effectiveness of the stem cells:**

A stem cells *Potency* its capacity or efficiency specifies to differentiate into different cell types (Figure 2, 3) and accordingly the cells can be divided into several categories of efficiency

- Totipotent stem cells: These cells are produced from the fusion of an egg and sperm cell. Cells produced by the first few divisions of the fertilized egg are also totipotent. Totipotent stem cells can differentiate into embryonic and extraembryonic cell types. Such cells can construct a complete, viable, organism.
- Pluripotent stem cells are the descendants of totipotent cells and can differentiate into nearly all cells, i.e. cells derived from any of the three germ layers.
- Multipotent stem cells can differentiate into a number of cells, but only those of a closely related family of cells.
- Oligopotent stem cells can differentiate into only a few cells, such as lymphoid or myeloid stem cells.
- Unipotent cells can produce only one cell type, their own, but have the property of self-renewal which distinguishes them from non-stem cells (e.g. muscle stem cells).[5]

**Sources of the Stem Cells in Orofacial Region:**

Mesenchymal stem cells (MSCs) are a prospective source of adult stem cells (with mesodermal and neuroectodermal origin) for regenerative medicine as they are extraordinarily plastic and when expanded into colonies, retain their multilineage potential.

MSCs are able to differentiate into cells of mesodermal origin like adipocytes, chondrocytes or

osteocytes, as well as give rise to representative lineages of the three embryonic layers.[6, 7] MSCs are also found within the dental pulp (DP), an extremely rich site for stem cell collection: owing to its peculiar formation, it acts as ''sealed niche'' and may explain why it is possible to find a rather large number of stem cell there.[7, 8] The first type of dental stem cell was isolated from the human pulp tissue and termed dental pulp stem cells (DPSCs).[9] Subsequently, four more types of dental-MSC-like populations were identified:

- Stem Cells from Exfoliated Deciduous Teeth (SHED),[9]
- Periodontal Ligament Stem Cells (PdlSCs), [6-9]
- Stem Cells from Apical Papilla (SCAP).
- Dental tissue from human third molar.

These dental stem cells are derived from the neural crest, and thus have a different origin from bone marrow-derived MSCs, which are derived from mesoderm.

In teeth, two different stem cell niches have been suggested: the cervical loop of rodent incisor for epithelial stem cell and a perivascular niche in adult dental pulp for MSC. In addition to the dental pulp MSC, other MSC populations have been isolated from human dental tissues such as the periodontal ligament and the dental follicle but nothing is known about the existence of a niche in these tissues. In the dental pulp, MSCs are thought to reside in a perivascular niche, but little is known on the exact location and molecular regulation of this niche.[10, 11]

DPSCs, on the other hand, are thought to be arising from two different sources: ectomesenchyme of the neural crest or ectoderm of the dental lamina and thus possess two different cell lines.

The comparison of the osteogenic and adipogenic potential of MSC from different origins shows that, even if cells carry common genetic markers, they are not equivalent and are already committed toward a specific differentiation pathway.[12, 13] Commitment could arise from conditioning of stem cells by their specific microenvironment or stem cell niche. A brief account of different sources of stem cells in orofacial region and their properties is as follows**:** [3-19]

**Dental Pulp Stem Cells (DPSC):**

Their source is dental pulp mesenchyme (neural crest mesenchyme). They are slow cycling cells having restricted potential and represent mature adult pulp stem cells. They have better immunologic/host acceptance. In vitro they formed odontoblasts, osteoblasts, endothelial cells, adipocytes, chondrocytes, neurons and smooth muscle cells while in vivo, various directions like odontogenic, myogenic, adipogenic, angiogenic and osteogenic are found and were able to form complete dentin pulp complex. It's in vitro developmental capability and in vivo therapeutic targeting is yet to be explored.

**Stem Cells From Human Exfoliated Deciduous Teeth (SHED):**

Their source is human exfoliated deciduous teeth (coronal pulp). They are multipotent cells with very high proliferative potential and higher cell doublings. In vitro they can differentiate odontogenically, osteogenically, adipogenically, chondrogenically, or neurally. In vivo they can form neurons, adipocytes, odontoblasts, and osteoinductive and endothelioid cells. But they failed to form complete dentin pulp complex in vivo.

**Periodontal Ligament Stem Cells (PDLSC):**

They can be extracted from periodontal ligament of the roots of the extracted teeth. They are the primary source for treatment of periodontal disease. These cells are multi-potential. In vitro, PDLSCs differentiate into osteoblasts, cementoblasts, and adipocytes.In vivo, after transplantation into mice, structures resembling bone, Cementum, cartilage, and periodontal ligament have been found. They can contain multiple stem cells lineages. But their utility is yet to be explored.

**Dental Follicle Stem Cells (DFSC):**

They are extracted from dental follicle of the impacted teeth and possess multiple potentialities. They have lesser ability to form adipocytes and their potential yet to be identified for forming odontoblasts, neural cells and other tissues.

**Stem Cells from Apical Papilla (SCAP):**

They are taken from extraction sites of third molars or other teeth. They are easily accessible and have a higher proliferative potential than PDLSC. In vitro, SCAPs can differentiate osteogenically, odontogenically and adipogenically. In vivo, SCAPs have been found to differentiate into odontoblasts and osteoblasts. Differentiation potential of apical papilla progenitor cells has not been established yet. The nature of all embryonic dental papilla, mature dental pulp and apical papilla progenitor cell populations remain to be characterized further.

**Bone Marrow Stem Cells (BMSC):**

They are derived from bone marrow of mandible/maxilla. They have lower odontogenic potential than DPSCs and are a secondary source for periodontal disease. Orofacial BMSCs are less adipogenic than BMSCs from other sources. Collectable amount of cells from orofacial region is much less than from other sites so safe cell expansion techniques are to be used.

**Epithelial Stem Cells (EpSC):**

These stem cells developed from third molars of newborn or juvenile animals or from the cervical loop of rodent incisors. They possess clonogenicity and are unipotent. Stem cells from third molars are promising for tooth formation/ regeneration. Cells from cervical loop can only be used to study characterization of dental epithelial stem cells and analyses of dental epithelial tissue. Their clinical application is difficult as it requires tooth donation from children. Cells from cervical loop of rodent incisor cannot be used for treatment as it would need introduction of rodent cells in mouth.

**Induced Pluripotent Stem Cells (IPSC):**

Adult human cells are reprogrammed to form embryonic stem like cells called Induced pluripotent stem cells. These are immunologically more acceptable and an attractive alternative source. Oral fibroblasts are able to form IPS cells in lab applicable for future use. However, the downside is that some of the transcription factors used is well known oncogenes. Viruses used in the technique have intrinsic risk in regard to cell transformation.

**Immature Dental Pulp Stem Cells (IDPS):**

They can be extracted from pulp of primary teeth. They co-express mesenchymal and embryonic stem cell markers and present the capacity to differentiate into derivative cells of the three germinal layers. In vitro, these cells can be induced to undergo uniform

differentiation into smooth and skeletal muscles, neurons, cartilage, and bone under chemically defined culture conditions. After in vivo transplantation of these cells into immunocompromised mice, they showed dense engraftment in various tissues and they can be used for corneal reconstruction. Their applications need to be further explored.

**Oral Epithelial Stem Cells (OESCs):**

They are derived from oral epithelial progenitor cells from basal layer of oral mucosa. They are unipotent stem cells and possess clonogenicity. They can form highly stratified and well organized graft. But they cannot differentiate into mesenchymal cell lineage.

**Gingiva derived MSCs (GMSCs):**

These cells are derived from lamina propria of gingiva. They possess clonogenicity, self-renewal and multipotent differentiation capacity similar to BMSCs and proliferate faster than BMSCs, displaystable morphology after extended passages. These cells exhibit adipogenic, osteogenic and chondrogenic potential along with immuno-modulatory effect on lymphocytes. Their applications further need to be explored.

**Tooth Germ Progenitor Cells (TGPCs):**

They are the stem cells in the mesenchyme of the third molar tooth germ and possess very high proliferative activity. They can differentiate into lineages of three germ layers including osteoblasts, neural cells and hepatocytes. Their applications further need to be explored.

**Salivary gland stem cells (SGSCs):**

They are derived from the stromal tissue of salivary glands. They are useful for regeneration of salivary gland damaged from irradiation and can be guided to osteogenic, chondrogenic and adipogenic differentiation. It is difficult to isolate salivary gland stem cells from the collection of stromal cells.

**Perisoteum derived Stem Cells (PSCs):**

They lie in theinner membrane of periosteum. They undergo preferential osteogenic differentiation and possess mesenchymal multipotentiality. They can differentiate into osteoblasts, adipocytes and chondrocytes. But, they have limited potential for cell differentiation.

**Dental Applications of Stem Cells**

Stem cells from dental sources have found applications in treatment of various diseases and defects which involves craniofacial regeneration, dentin regeneration, periodontal regeneration, cementum regeneration, pulp regeneration, cleft lip and palate, salivary gland regeneration, tmj reconstruction, whole tooth regeneration, cancer therapy, cancer models for biology of cancer, oral mucosa models for studying oral biology , cell and organ models for studying molecular physiology behind processes like tooth eruption, forensic dental profiling, correlation and collection of ante-mortem and postmortem data.

**Challenges of stem cell therapy:**

A major difficulty with stem cell therapy is to identify the stem cells within a culture of real fabric. The cultures contain many different cells and are a challenge to identify specific cell types. When stem cells are identified and then isolated from tissues,

appropriate solutions must be created to trigger these cells into the desired cell types.

Finally, even though the cells may be identified, isolated and grown, there are supplementary issues like immune response and efficiency. A person's immune system can identify the transplanted cells as foreign bodies and that it can generate an immune reaction that results in refusal of the new cells.[20]

**Conclusion:**

The prospective of stem cell therapy to ease the suffering of human beings and to dramatically influence disease has provoked scientists to investigate ways to augment current therapies for stem cell and develop new ones. Dental stem cells can grow not only dental tissues but other non-dental tissues as well. They are not only being investigated in the field of Medicine have found their place in the field of Dentistry as Forensic Odontology as well opening newer insights and avenues for research in this hitherto less ventured arena of Forensic dental investigations using stem cells. Dental stem cell banking will be an easy way to store one's own stem cells. Nevertheless, challenge for the dental professional in the anticipated era of stem cells and tissue engineering is imminent.

**References:**


1. Bongso A, Richards M. Best Practice & Research Clinical Obstetrics and Gynaecology 2004;18:827–842.
2. Jamal M, Chogle S, Goodis H, Karam SM. Dental Stem Cells and Their Potential Role in Regenerative Medicine. J Med Sci 2011;4:53-61.
3. Sloan AJ, Waddington RJ. Dental pulp stem cells: what, where, how? International Journal of Paediatric Dentistry 2009; 19: 61–70.
4. Stem cell. http://www.answers.com/ Accessed 14,2011.
5. Stem Cell – Wikipedia, the free encyclopedia. http://www.en.wikipedia.org/wiki/stem-cell. Accessed 14,2011.
6. Suchanek J, Soukup T, Visek B, Ivancakova R, Kucerova L, Mokry J. Dental pulp stem cells and their characterization. Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub. 2009;153:31-5.
7. Fares Zeidán-Chuliáa, MamiNoda. "Opening" The Mesenchymal Stem Cell Tool Box Eur J Dent. 2009; 3:240–49.
8. D'aquino R, De Rosa, A, Laino G, Caruso F, Guida L, Rullo R, Checchi V, Laino L, Tirino V, Papaccio G. Human dental pulp stem cells from biology to clinical applications. J Exp Zool 2008;312:408–15.
9. Miura M, Gronthos S, Zhao M, Lu B, Fisher LW, Robey PG, Shi S . SHED: stem cells from human exfoliated deciduous teeth. Proc Natl Acad Sci USA 2003;100:5807-5812.
10. Bluteau G, Luder HU, Bari CD, Mitsiadis TA. Stem cells for tooth engineering. Eur cell Mater 2008;16:1-9.
11. Suchánek J, Soukup T, Ivančaková R, Karbanová J, Hubková V, Pytlík R et al. Human Dental Pulp Stem Cells – Isolation and long term cultivation. Acta Medica (Hradec Kralove) 2007;50:195–201.
12. Musina RA, Bekchanova ES, Belyavskii AV, Sukhikh GT. Differentiation potential of

mesenchymal stem cells of different origin. Bull Exp Biol Med 2006;141:147-151.

13. Musina RA, Bekchanova ES, Sukhikh GT. Comparison of mesenchymal stem cells obtained from different human tissues. Bull Exp Biol Med 2005;139:504-9.
14. Egusa H, Sonoyama W, Nishimura M, Atsuta I, Akiyama K. Stem cells in dentistry – Part I: Stem cell sources. J Prosthodont Res 2012;56:151–65.
15. Peng L, Ling Y, Zhou X. Mesenchymal Stem Cells and Tooth Engineering. International Journal of Oral Science2009;1:6-12.
16. Ulmer FL, Winkel A, Kohorst P, Stiesch M. Stem Cells: Prospects in Dentistry. Schweiz Monatsschr Zahnmed 2010;120:860-72.
17. Monteiro BG, Serafim, Melo RC, Silva GB, Lizier MCP, Maranduba et al. Human immature dental pulp stem cells share key characteristic features with limbal stem cells. Cell Proliferation 2009;42:587–94.
18. Izumi K, Tobita T, Feinberg SE. Isolation of human oral keratinocyte progenitor/stem cells. J Dent Res 2007;86:341–6.
19. Giannobile WV, Helms JA, Hollister SJ, Krebsbach PH, Shi S. Craniofacial Tissue Engineering by Stem Cells. J Dent Res 2006;85:966-79.
20. Importance of stem cells. http://www.stemcellmlm.com/index. Accessed 14,2011.