Boon in Dentistry - Stem Cells

Pallavi Singh[1], Meghna Mehta[2], Pranav Thakur[3]

[1]MDS 3rd Year Post Graduate Student in the Department of Public Health Dentistry, Babu Banarasi Das College of Dental Sciences, Lucknow, Uttar Pradesh, India, [2]MDS 3rd Year Post Graduate Student in the Department of Public Health Dentistry, Rama Dental College, Hospital and Research Centre, Kanpur, Uttar Pradesh, India, [3]MDS 2nd Year Post Graduate student, Department of Public Health Dentistry, Rama Dental College, Hospital and Research Centre, Kanpur, Uttar Pradesh, India

Corresponding Author: Dr. Pallavi Singh, Room No. 217, Babu Banarasi Das girls hostel, Babu Banarasi Das College of Dental Sciences, Faizabad Road, Lucknow, Uttar Pradesh. E-mail: pallavirolisingh@gmail.com

Abstract

Stem cells are undifferentiated biological cells those can be differentiated into specialized cells and can be divided through mitosis to produce more stem cells. These cells distinguished from other cell types by two important characteristics. Firstly, they are unspecialized cells capable of renewing through cell division even after long periods of inactivity. Secondly, under certain physiologic or experimental conditions, they can be induced to become tissue or organ specific cells with special functions. Because of their unique regenerative abilities, they have potentials for treating various diseases such as diabetes, heart disease, cancer, etc. Currently stem cell research now is one of the most fascinating and upcoming areas of biological sciences, but at the same time with many expanding fields of scientific inquiry, research on stem cells sometimes raises scientific questions as rapidly as it generates new discoveries.

Keywords: Craniofacial defect, Dental pulp, Stem cells, Tooth regeneration

INTRODUCTION

Stem cells are unique type of cells that have specialized capacity for self-renewal and potency, can give rise to one and sometimes many different cell types. "They are found in almost many of the multi cellular organisms and are characterized by the ability to renew through mitotic cell division while maintaining the undifferentiated state."[1] When a stem cell divides, each new cell has the potential either to remain a stem cell or become another type of cell with a more specialized function, such as a muscle cell, a red blood cell, or a brain cell.[2]

Stem cells are distinguished from other cell types by two important characteristics. First, they are unspecialized cells capable of renewing themselves through cell division, sometimes after long periods of inactivity. Second, under certain physiologic or experimental conditions, they can be induced to become tissue- or organ-specific cells with special functions. In some organs, such as the gut and bone marrow, stem cells regularly divide to repair and replace worn out or damaged tissues. In other organs, however, such as the pancreas and the heart, stem cells only divide under special conditions.[3]

Stem Cell Properties

A classic stem cell should possess two properties namely self renewal and potency.

- Self-renewal is the capacity of the cell to undergo numerous cycles of cell division maintaining the undifferentiated state. An ideal stem cell should have the capacity of self renewal beyond the "Hay licks" limit (the ability of the cell to proliferate to about 40-60 population doublings before it achieves senescence).[4]
- Potency means the differentiation capacity of the stem cell.[5]

Types of Stem Cell

Stem cells can be broadly divided into

1. Embryonic stem cell
2. Adult stem cell
   - Hematopoietic stem cell
   - Mesenchymal stem cell
3. Induced pluripotent stem cell.

Embryonic Stem Cell

They are totipotent cells capable of differentiating into virtually any cell type, as well as being propagated indefinitely in an undifferentiated state.[6]

Adult Stem Cell

Adult stem cells are multipotent stem cells. They have been harvested from different kind of tissues like bone marrow, umbilical cord, amniotic fluid, brain tissue, liver, pancreas, cornea, dental pulp, and adipose tissue. Adult stem cells are comparatively easier to isolate and do not have any ethical issues. Immune rejection and teratoma formation is also rare with adult stem cells. Adult stem cells are commonly used in current day practice.[7]

Haematopoietic Stem Cells

They are a somatic cell population with highly specific homing properties and are capable of self renewal and differentiation into multiple cell lineages. They can be obtained from bone marrow, peripheral blood, umbilical cord. Although these cells have unlimited potential in medical research, they have limited value in dental research. Dental research is mainly diverted to the other group of stem cells namely the non-haematopoietic stem cells or mesenchymal stem cells.

Non Haematopoietic Stem Cells or Mesenchymal Stem Cells

Non hematopoietic bone marrow derived Mesenchymal Stem Cells (MSCs), hereafter known as "MSCs"; are also known as Bone Marrow Derived Stem Cells (BMSCs), hereafter known as BMSCs", as described 3 decades ago. BMSCs can be isolated from single cell suspensions from bone marrow aspirates as they adhere to cell culture plates and display the characteristic of clonogenicity defined as the ability of a single cell to produce a colony when cultured at extremely low densities.

In recent time, dental cell therapies have been discussed by combining non dental mesenchymal stem cells and dental stem cells. Studies have demonstrated the positive effect of enamel matrix proteins on porcine BMSC differentiation into cementoblasts. Moreover, a recent study demonstrated that the use of MSCs in combination with platelet-rich plasma resulted in a reduction of probing depths by 4 mm and a clinical attachment gain of 4 mm, while bleeding and tooth mobility disappeared. Isolation of these cells thus offers potential applications for the treatment of mesenchymal tissue disorders, gene therapy, organ transplant rejection and treatment of autoimmune disorders.

Recent studies indicate that stem cells for cementum, dentin and periodontal ligament also exist. All of these cells can be expanded in vitro and embedded in a scaffold, inserted into defects to promote healing and tissue replacement. Mesenchymal stem cells like all stem cells, share at least two characteristics:

1. They can give rise to mature cell types that have characteristic morphologies and specialized functions.
2. The cells are capable of self renewal for the life time of the organism and are defined by their clonogenic potential.[8,9]

Induced Pluripotent Stem Cells

Induced pluripotent stem cells (IPS) is an evolving concept in which 3-4 genes found in the stem cells are transfected into the donor cells using appropriate vectors. The stem cells thus derived by culturing will have properties almost like embryonic stem cells. This path breaking discovery may have a major role in future stem cell therapy.[10]

Sources of Stem Cells

The oral and maxillofacial region can be treated with stem cells from the following sources

1. Bone marrow
2. Adipose tissue
3. Stem cells from oral and maxillofacial region.

Bone Marrow

Bone marrow stem cells (BMSCs) can be harvested from sternum or iliac crest. It is composed of both hematopoietic stem cells and mesenchymal stem cells (MSCs). The majority of oro-maxillofacial oral structures are formed from mesenchymal cells. The advantage of bone marrow is that it has a larger volume of stem cells and can be differentiated in to wide variety of cells. Isolation of BMSCs can be carried out only under general anesthesia with possible post operative pain.

Adipose Tissue

They can be harvested from the lipectomy or liposuction aspirate. Adipose derived stem cells (ADSCs) contain a group of pluripotent mesenchymal stem cells that exhibit multilineage differentiation. Advantage of adipose tissue is that it is easily accessible and abundant in many individuals.[11]

Stem Cells From the Oral and Maxillofacial Region

Stem cells from oral and maxillofacial region predominantly contain mesenchymal stem cells. In oral and maxillofacial area different types of dental stem cells were isolated and characterized. They include

- Dental pulp stem cells (DPSCs)
- Stem cells from exfoliated deciduous teeth (SHED)
- Periodontal ligament stem cells (PDLSCs)
- Stem cells from apical papilla (SCAP)
- Dental follicle progenitor cells (DFPCs).[12]

Stem Cells Storage and Transport

Tissue samples containing stem cells were placed in a screw top vial containing an appropriate media, which nourishes it during transport. The sample should reach the processing storage facility before 40 hours. In the laboratory the samples were trypsinized and passaged to yield colonies of stem cells. The required cell type can be manipulated by utilizing right inductive signals and appropriate growth factors to the stem cells.[13]

Stem Cell Markers and Scaffold

Cultured stem cells should be passed through stem cell markers like Oct4, Nanog, SSEA4, TRA-1-60 and TRA-1-81 before it is administered to patients to know the lineage of the cell. Compulsory endotoxin test should be subjected to the cultured stem cells to rule out any microbial contamination. Stem cells are loaded in an appropriate carrier called "scaffold" to close the defects or replace the organ. Scaffold can be of different shapes, pattern and biomaterials. Depending upon the necessity it can be made up of natural or artificial materials and can be biodegradable or non biodegradable. Materials such as poly lactic acid, polyglycolic acid (PGA), polyethylene terepthalate, polypropylene fumarate, hydroxyapatite/tricalcium phosphate, fibrin, alginates, and collagen are used.[13]

Stem Cells From Oral and Maxillofacial Region

Dental stem cells have been isolated from different soft tissues of the tooth. The tooth is mainly made of hard tissues which are connected to soft tissues. The hard tissues include the dentin which is covered by enamel in the crown and cementum in the root. The dentin encloses the dental pulp which is a richly innervated, highly vascularized soft (loose connective) tissue. The tooth is attached to its bony socket by another kind of soft (dense connective) tissue, the periodontal ligament (PDL).

In 2000, Gronthos et al. isolated the first MSC like cells from the human dental pulp. Subsequently, four more types of MSC-like cells have been isolated from dental tissues: pulp of exfoliated deciduous teeth, Periodontal ligament, apical papilla and dental follicle.[14,15]

The structures of interest in oral and maxillofacial region include the enamel, dentin, dental pulp, cementum, periodontal ligament, craniofacial bones, the temporomandibular joint, ligaments, skeletal muscles, tendons, skin, subcutaneous soft tissue, and salivary glands.

Dental Pulp Stem Cells

DPSCs were the first type of dental stem cells to be isolated. These cells were obtained by enzymatic digestion of the pulp tissue of the human impacted third molar tooth. DPSCs have a typical fibroblast-like morphology. They are clonogenic in nature and can maintain their high proliferation rate even after extensive subculturing. There is no specific biomarker to identify the DPSCs.

However, DPSCs express several markers including the mesenchymal and bone marrow stem cell markers, STRO-1 and CD146 as well as the embryonic stem cell marker, Oct4. Culturing DPSCs with various differentiation media demonstrated their dentinogenic, osteogenic, adipogenic, neurogenic, chondrogenic and myogenic differentiation capabilities.[16,17]

Following their transplantation in animal models, DPSCs were able to maintain their self renewal and to form pulp-like tissue, odontoblast-like cells, ectopic dentin as well as reparative dentin-like and bone-like tissues.[18]

The characteristic features and multilineage differentiation potential of DPSCs have established their stem cell nature and indicated their promising role in regenerative therapy.

Stem Cells From Human Exfoliated Deciduous Teeth (Shed)

In 2003, Miura et al. isolated cells from the dental pulp which were highly proliferative and clonogenic. The isolation technique was similar to those used in the isolation of DPSCs. However, there were two differences:

i) The source of cells was the pulp tissue of the crown of exfoliated deciduous teeth and
ii) The isolated SHEDs did not grow as individual cells, but clustered into several colonies which, after separation, grew as individual fibroblast-like cells.[15]

SHEDs have a higher proliferation rate and a higher number of colony forming cells than DPSCs. SHEDs were found to express early mesenchymal stem cell markers (STRO-1 and CD146). In addition, embryonic stem cell markers such as Oct4, Nanog, stage-specific embryonic antigens (SSEA-3, SSEA-4), and tumor recognition antigens (TRA-1-60 and TRA-1-81) were found to be expressed by SHEDs.[19]

Periodontal Ligament Stem Cells (Pdlscs)

The PDL does not only anchor the tooth, but also contributes to its nutrition, homoeostasis, and repair. PDL contains different types of cells including cells which can differentiate into cementoblast and osteoblasts. Heterogeneity and continuous remodeling of PDL is an indication for the presence of progenitor cells which can give rise to specialized cell types. In 2004, this speculation led to the discovery of the third type of dental stem cells which was referred to as PDLSCs.[20-23]

PDLSCs have a multilineage differentiation potential. They were able to undergo osteogenic, adipogenic and chondrogenic differentiation when they were cultured with the appropriate inductive medium.[24]

Dental Follicle Precursor Cells (Dfpcs)

The dental follicle (DF), is a loose connective tissue of an ectomesenchymal origin and it is present as a sac surrounding the unerupted tooth.[25] During tooth development it has been found that DF plays an important role in the eruption process by controlling the osteoclastogenesis and osteogenesis needed for eruption. It is also believed that DF differentiates into the periodontium as the tooth is erupting and becomes visible in the oral cavity. As the periodontium is composed of several cell types, it is reasonable to propose the presence of stem cells within the dental follicle which are able to give rise to the periodontium.[26,27]

Stem Cells of Apical Papilla (Scaps)

During tooth development, the dental papilla evolves into the dental pulp, and contributes to the development of the root. The apical part of the dental papilla is loosely attached to the developing root, and it is separated from the differentiated pulp tissue by a cell rich zone. It contains less blood vessels and cellular components than the pulp tissue and the separating cell rich zone.[3,26]

Regeneration of Craniofacial Defects

Stem cells can be useful in the regeneration of bone and to correct large craniofacial defects due to cyst enucleation, tumor resection, and trauma. The closure of a bone defect is commonly carried out with the transfer of tissue, which have disadvantages like- not able to restore the unique function of the lost part, donor site morbidity, accompanied by scarring, infection and loss of function. Adipose derived stem cells was used to treat the calvarial defect with severe head injury. Autologous adipose stem cells were extracted from gluteal region along with iliac crest bone graft. Autologous fibrin glue that holds the cells in place was prepared by cryoprecipitation. This successful technique has given new rays of hope that ADSCs (Adipose derive stem cells) can be used for difficult reconstructive procedures.

Stem cells isolated from dental pulp has a potential to differentiate into osteoblasts and are a good source for bone formation. Stem cells from oral and maxillofacial region can be combined with bone marrow stem cells to correct larger defects. Lagenbach et al. in their in vitro studies used microspheres (scaffold free tissue construct) to close the critical size bone defects. They found osteogenically differentiated microspheres with outgrowing cells can be used to ill up bone defects. This new procedure has added advantage of permitting the transplantation of more cells and better integrity compared with cell suspensions or gels.[28-31]

Dental Stem Cell Advantages

The advantages of stem cells from oral and maxillofacial region is that

1. Have high plasticity
2. It can be cryopreserved for longer period (Ideal for stem cell banking)
3. It showed good interaction with scaffold and growth factors
4. Stem cells transplantations can cause pathogen transmission and also need immunosuppression, so autologous stem cell source is the best option. Dental pulp stem cells will be better fitting tool due to easy surgical access, the very low morbidity of the anatomical site after the collection of the pulp.[32]

ONGOING RESEARCHES

Gingival Mesenchymal Stem Cells

GMSC (Gingival Mesenchymal Stem Cells) like other stem cells, have the ability to develop into different types of cells as well as affect the immune system. There are two types of GMSC: those that arise from the mesoderm layer of cells during embryonic development (M-GMSC) and those that come from cranial neural crest cells (N-GMSC). The cranial neural crest cells develop into many important structures of the head and face, and 90 percent of the gingival stem cells were found to be N-GMSC.

The two types of stem cells vary dramatically in their abilities. N-GMSC were not only easier to change into other types of cells, including neural and cartilage-producing cells; they also had much more of a healing effect on inflammatory disease than their counterparts. When the N-GMSC were transplanted into mice with dextrate sulfate sodium-induced colitis – an inflamed condition of the colon – the inflammation was significantly reduced. GMSCs suppress the inflammatory response by inhibiting lymphocyte proliferation and inflammatory cytokines and by promoting the recruitment of regulatory T-cells and anti-inflammatory cytokines.

The stem cells in the gingiva obtained via a simple biopsy of the gingival may have important medical applications in the future.[33]

Stem Cells Extracted From Urine

Pluripotent stem cells generated from human urine cells grow teeth-like structures in a group of mice. Pluripotent stem cells have the potential to develop into any type of body cell. These stem cells were then combined with early dental tissue obtained from mouse embryos and then transplanted into the bodies of mice.

The main advantage of using urine as a source is that it provides a much easier way to obtain stem cells compared to existing techniques (such as obtaining a sample of bone marrow). Scientists found that after three weeks, up to 30% of the mice developed ‘teeth-like structures’. Combining the human iPSCs with the mouse mesenchymal cells promote the development into tooth-like structures.

This will include more research to make sure that lab-grown teeth resemble and function like regular human teeth and whether lab-grown teeth are both safe and effective in the long-term.[34]

Tooth Regeneration

The regeneration of adult teeth will be possible in future with the newer advancement in stem cell therapy and tissue engineering. Regenerative procedures would be better fitting and alternative tool in place of dental implants. Experimental studies with animal models have shown that the tooth crown structure can be regenerated using tissue engineering techniques that combine stem cells and biodegradable scaffolds. Epithelial mesenchymal interactions are mandatory in tooth development. "These interactions are characterized by the reciprocal exchange of signals between these two naïve germ layer tissues and result in the emergence of unique terminal phenotypes with their supporting cells".

Tooth regeneration involves three key elements which include

- Inductive morphogenes
- Stem cells
- Scaffold

Steps involved in regeneration of tooth are

1. Harvesting and expansion of adult stem cells
2. Seeding the stem cells into scaffold which provides optimized environment
3. Cells are instructed with targeted soluble molecular signals spatially
4. Confirming the gene expression profile of the cells for next stage in odontogenesis.[35-37]

Harvesting Dental Stem Cells For Future Use

Harvesting stem cells and other tissues from human bodies and storing them for future procedures may sound like the work of a science fiction author, but scientists and researchers have found that these procedures are far from fictional. In reality, these cells have been proven quite beneficial in the treatment of a mind-blowing list of serious health conditions. From Parkinson's disease to cancer, stem cell harvesting has been shown to move us closer to the cure. Our baby teeth and also our wisdom teeth are known to be significant and valuable sources of the cells that have life-saving potential.[38]

Stem Cell Banking

Baby or deciduous teeth fall out naturally when a child is between 6 and 11 years of age. They contain stem cells that have the ability to develop into many different types of cells such as skin, nerve, muscle, fat, cartilage, and tendon. They can potentially be used to replace diseased and damaged tissues in the body without rejection. These teeth are by far the easiest and most natural, non-invasive source of stem cells.

Developing wisdom teeth have many "adult" stem cells. They share some of the same characteristics as embryonic stem cells, but:

- They can be obtained from teenagers having their wisdom teeth removed
- They can be preserved and "banked" like any other stem cell
- They can be used by their donor whenever their dentist, doctor or specialist requests them for a needed treatment.

Dental pulp stem cells extracted from wisdom teeth and deciduous teeth can be used to create stem cell banks. Having own "banked" stem cells is like having a back-up insurance policy. They are on hand when:

- The donor's dentist or doctor determines they are needed
- New stem cell-based treatments are developed by medical researchers.[39]

Role of Dental Stem Cells in Regenerative Medicine

The dynamic features of isolated dental stem cells revealed much potential for their use in regenerative medicine and tissue engineering.

Dental Pulp Regeneration

Since the discovery and isolation of the different types of dental stem cells, there have been many attempts to use them in the regeneration of the dental pulp tissue. Using a tooth slice model, pulp-like tissue was engineered using SHEDs seeded onto synthetic biodegradable scaffolds. SHEDs were able to differentiate into odontoblast-like cells, and also endothelial-like cells.

Bio-Root Engineering

Sonoyama et al. demonstrated the use of combined mesenchymal stem cell populations for root/periodontal tissue regeneration. They loaded root shaped hydroxyapatite/tricalcium phosphate (HA/TCP) block with swine SCAPs. They then coated the HA/TCP block with gelfoam containing swine PDLSCs and inserted the block in the central incisor socket of swine. Three months post-implantation, histological and computerized tomography scan revealed a HA/SCAP-gelfoam/PDLSC structure growing inside the socket with mineralized root-like tissue formation and periodontal ligament space.

Neural Regeneration

Cranial neural crest (CNC) cells represent an ideal source for neuronal differentiation and regeneration. The migrating CNC cells contribute to the formation of dental papilla, dental pulp, PDL and other tissues in the tooth and mandible. Therefore, it is reasonable to consider that the different types of dental stem cells are of CNC origin.

Cardiac Repair

It was found that DPSCs (Dental pulp stem cells) can help cardiac repair after myocardial infarction. In an experimental model of acute myocardial infarction, the left coronary artery was ligated in nude rats. Then DPSCs were transplanted to the border of the infarction zone. Four weeks after transplantation, evidence of cardiac repair was noted by improved cardiac function, increase in the number of vessels and a reduction in infarct size. The cardiac repair occurred in the absence of any evidence of DPSCs differentiation into cardiac or smooth muscle cells.[40-42]

CONCLUSION

The future dentistry will be more of regenerative based, where patients own cells can be used to treat diseases. Stem cell therapy has got a paramount role as a future treatment modality in dentistry. The ultimate goal of tooth regeneration is to replace the lost teeth. Stem cell-based tooth engineering is deemed as a promising approach to the making of a biological tooth (bio-tooth). Dental pulp stem cells (DPSCs) represent a kind of adult cell colony which has the potent capacity of self-renewing and multilineage differentiation. A bio-tooth made from autogenous DPSCs should be the best choice for clinical tooth reconstruction.

REFERENCES

1. Murray PE, Garcia-Godoy F, Hargreaves KM. Regenerative endodontics: a review of current status and a call for action. J Endod 2007; 33: 377-90.
2. Bluteau G, Luder HU, De Bari C, Mitsiadis TA. Stem cells for tooth engineering. Eur Cell Mater 2008; 16:1-9.
3. Jiang Y, Jahagirdar BN, Reinhardt RL, Schwartz RE, Keene CD, Ortiz-Gonzalez XR, et al. Pluripotency of mesenchymal stem cells derived from adult marrow. J Dent Res 2002; 418: 41-9.
4. Haylick L. The limited in vitro lifetime of human diploid cell strains. Exp Cell Res 1965;37:614-36.
5. Gurdon JB, Byrne JA. The first half-century of nuclear transplantation. Proc Natl Acad Sci USA 2003; 100:8048-52.
6. C Morsczeck, et al. Somatic stem cells for regenerative dentistry. Journal of Clinical Oral Investigations 2008;12(2):113-118.
7. Fortier LA. Stem cells, classifications, controversies and clinical applications. J Vet Surg 2005;34:415-23.
8. Song AM, et al: A study of enamel matrix proteins on differentiation of porcine bone marrow stromal cells into cementoblasts. 2007 (40): Journal of Clinical Oral Investigations. 381–39643.
9. Yamada Y, Ueda M, Hibi H, Baba S: A novel approach toperiodontal tissue regeneration with mesenchymal stem cells and platelet-rich plasma using tissue engineering technology: a clinical case report. Int J Periodontics and Restorative Dent 2006 (26): 363-369.
10. Takahashi K, Yamanaka S. Induction of pluripotent stem cells from mouse embryonic and adult fibroblast cultures by denied factors. Int J Periodontics and Restorative Dent 2006; 126:663-76.
11. Zuk PA, Zhu M, Mizuno H, Huang J, Futrell JW, Katz AJ, et al. Multilineage cells from human adipose tissue: Implications for cell- based therapies. Tissue Eng 2001;7: 211-28.
12. Seo BM, Miura M, Gronthos S, Bartold PM, Batouli S, Brahim J, et al. Investigation of multipotent postnatal stem cells from human periodontal ligament. J Periodontal Res 2004; 364:149-55.
13. Hutmacher DW, Goh JC, Teoh SH. An introduction to biodegradable materials for tissue engineering applications. Ann Acad Med Singapore 2001; 30:183-9.
14. Gronthos S, Mankani M, Brahim J, Robey PG, Shi S. Postnatal human dental pulp stem cells (DPSCs) in vitro and in vivo. Proc Natl Acad Sci 2000; 97:13625-30.
15. Miura M, Gronthos S, Zhao M, Lu B, Fisher LW,Robey PG, et al. SHED: stem cells from human exfoliated deciduous teeth. Proc Natl Acad Sci USA 2003; 100: 5807-12.
16. Laino G, d'Aquino R, Graziano A, Lanza V, Carinci F, Naro F, et al. A new population of human adult dental pulp stem cells: a useful source of living autologous fibrous bone tissue (LAB). J Bone Miner Res 2005; 20: 1394-402.
17. Zhang W, Walboomers XF, Shi S, Fan M, Jansen JA. Multilineage differentiation potential of stem cells derived from human dental pulp after cryopreservation. J Periodontal Res 2006; 12: 2813-23.
18. Batouli S, Miura M, Brahim J, Tsutsui TW, Fisher LW, Gronthos S, et al. Comparison of stem-cell mediated osteogenesis and dentinogenesis. J Dent Res 2003; 82: 976-81.
19. Kerkis I, Kerkis A, Dozortsev D, Stukart-Parsons GC, Gomes Massironi SM, Pereira LV, et al. Isolation and characterization of a population of immature dental pulp stem cells expressing OCT-4 and other embryonic stem cell markers. J Periodontal Res 2006; 184: 105-16.
20. Gould TR, Melcher AH, Brunette DM. Migration and division of progenitor cell populations in periodontal ligament after wounding. J Periodontal Res 1980; 15: 20-42.
21. McCulloch CA, Melcher AH. Cell density and cell generation in the periodontal ligament of mice. Am J Anat 1983; 167: 43-58.
22. McCulloch CA, Bordin S. Role of fibroblast subpopulations in periodontal physiology and pathology. J Periodontal Res 1991; 26(3 Pt 1): 144-54.
23. Isaka J, Ohazama A, Kobayashi M, Nagashima C, Takiguchi T, Kawasaki H, et al. Participation of periodontal ligament cells with regeneration of alveolar bone. J Periodontol 2001; 72: 314-23.
24. Gay IC, Chen S, MacDougall M. Isolation and characterization of multipotent human periodontal ligament stem cells. Orthod Craniofac Res 2007; 10: 149-60.
25. Cahill DR, Marks SC, Jr. Tooth eruption: evidence for the central role of the dental follicle. J Oral Pathol 1980; 9: 189-200.
26. Wise GE, Frazier-Bowers S, D'Souza RN. Cellular, molecular, and genetic determinants of tooth eruption. Crit Rev Oral Biol Med 2002; 13: 323-34.
27. Diekwisch TG. The developmental biology of cementum.Int J Dev Biol 2001; 45: 695-706.
28. d'Aquino R, De Rosa A, Lanza V, Tirino V, Laino L, Graziano A, et al. Human mandible bone defect repair by the grafting of dental pulp stem/progenitor cells and collagen sponge biocomplexes. Eur Cell Mater 2009; 18:75-83.
29. Lendeckel S, Jödicke A, Christophis P, Heidinger K, Wolff J, Fraser JK, et al. Autologous stem cells (adipose) and fibrin glue used to treat widespread traumatic calvarial defects: Case report. J Craniomaxillofac Surg 2004; 32:370-3.
30. Alhadlaq A, Tang M, Mao JJ. Engineered adipose tissue from human mesenchymal stem cells maintains predefined shape and dimension: Implications in soft tissue augmentation and reconstruction. J Oral Pathol 2005; 11:556-66.
31. Langenbach F, Naujoks C, Kersten-Thiele PV, Berr K, Depprich RA, Kübler NR, et al. Osteogenic differentiation inluences stem cell migration out of scaffold-free microspheres. J Craniomaxillofac Surg. 2010; 16:759-66.
32. Graziano A, d'Aquino R, Laino G, Papaccio G. Dental pulp stem cells: A promising tool for bone regeneration. J Clin Pediatr Dent 2008; 4:21-6.
33. Casagrande L, et al: Stem cells in dental practice: perspectives in conservative pulp therapies. J Clin Pediatr Dent 2006 Fall; 31(1): 25-7.
34. Cai J, Zhang Y, Liu P, et al. Generation of tooth-like structures from integration-free human urine induced pluripotent stem cells. J Oral Pathol. Published online July 30 2013.

35. Honda MJ, Fong H, Iwatsuki S, Sumita Y, Sarikaya M. Toothforming potential in embryonic and postnatal tooth bud cells. Med Mol Morphol 2008;41:183-92.
36. Nakahara T, Ide Y. Tooth regeneration: Implications for the use of bioengineered organs in irst-wave organ replacement. J Clin Pediatr Dent 2007; 20:63-70.
37. Thesleff I, Sharpe P. Signalling networks regulating dental development. J Mech Dev 1997; 67:111-23.
38. Bell CS, Dingwerth DJ et al. Harvesting dental stem cells for future use. J Craniomaxillofac Surg November 4, 2013.
39. Yamada Y, Ito K, Nakamura S, Ueda M, Nagasaka T. Promising cell-based therapy for bone regeneration using stem cells from deciduous teeth, dental pulp, and bone marrow. J Clin Pediatr 2011; 20: 1003-1013.
40. Cordeiro MM, Dong Z, Kaneko T, Zhang Z, Miyazawa M, Shi S, Smith AJ, Nor JE. Dental pulp tissue engineering with stem cells from exfoliated deciduous teeth. J Endod 2008; 34:962-9.
41. Ruffins S AK, Bronner-Fraser M. Early migrating neural crest cells can form ventral neural tube derivatives when challenged by transplantation. Dev Biol 1998; 203: 295-304.
42. Chai Y, Jiang X, Ito Y, Bringas P, Jr., Han J, Rowitch DH, Soriano P, McMahon AP, Sucov HM. Fate of the mammalian cranial neural crest during tooth and mandibular morphogenesis. J Endod 2000; 127: 1671-9.

How to cite this article: Singh P, Mehta M, Thakur P. Boon In Dentistry- Stem Cells. Int J Sci Stud 2014;2(4):59-65.

Source of Support: Nil, **Conflict of Interest:** None declared.