Review Article

JRAD Journal of Research and Advancement in Dentistry

J Res Adv Dent 2017;7:1:173-177.

Stem Cells in Dentistry

Gitanjali Mago[1*] Ajay Gupta[2] Vijay Prakash[3] Puneet Sharma[4] Nikhil Reddy[5] Wasim Hussain[6]

[1]Post Graduate Student, Department of Prosthodontics, Divya Jyoti College of Dental Sciences and Research, Modinagar, UP, India.
[2]Professor and Head, Department of Prosthodontics, Divya Jyoti College of Dental Sciences and Research, Modinagar, UP, India.
[3]Professor, Department of Prosthodontics, Divya Jyoti College of Dental Sciences and Research, Modinagar, UP, India.
[4]Post Graduate Student, Department of Prosthodontics, Divya Jyoti College of Dental Sciences and Research, Modinagar, UP, India.
[5]Post Graduate Student, Department of Prosthodontics, Divya Jyoti College of Dental Sciences and Research, Modinagar, UP, India.
[6]Post Graduate Student, Department of Prosthodontics, Divya Jyoti College of Dental Sciences and Research, Modinagar, UP, India.

ABSTRACT

Background: Stem cells provide new strategies to regenerate missing tissues. Stem cells are offering treatment to various diseases because of their self renewal and multipotent properties. With the better understanding of modern sciences, there are advances ongoing in the field of stem cells for fixing various biological problems. There is a revolution in the tissue engineering due to the continued improvements in the application of mesenchymal stem cells (MSCs). This article focuses on the various types of stem cell sources and also provides an overview of the different applications of stem cells in dental sciences.

Keywords: Dental pulp stem cells, tissue engineering, regenerative medicine, mesenchymal stem cell.

INTRODUCTION

Ability of the tissues to undergo renewal or regeneration due to trauma or disease makes the human body perform variety of functions essential for its survival and healthy existence. This ability of tissues to regenerate is possible due to the presence of unique set of cells known as stem cells.[1] Stem cells are mesenchymal spindle shaped cells with the potential of clonogenic proliferations.[2] These are defined as an unspecialized cells capable of perpetuating itself through cell divisions and have the potential to give rise to differentiated cells with specialized functions.

With the development taking place in the field of stem cell research, the science of tissue engineering and regeneration is also attracting much attention with its new therapeutics techniques.[1] Tissue engineering / regeneration is an interdisplenery field which utilizes scaffold matrices to fill the tissue voids to provide structural support and to deliver the growth factors that have the ability to form tissues within the body upon transplantation.[3] 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.[4]

HISTORY

Russian histologist Alexander Maksimov, first proposed the term stem cells in 1908.[5] Stem cells have a very long and interesting history which is stretched over a century beyond. It was discovered in mid 1800s that stem cells has the ability to generate different types of cells and are considered as the building blocks for life. In early 1900s, it was observed that some cells have the capability to generate into blood cells and attempts were made in the direction of in vitro fertilisation of human eggs.[6] The concept of regeneration in the medical field is although not new but has

Received: Oct. 17, 2017: **Accepted:** Dec. 17, 2017
*Correspondence Dr. Gitanjali Mago.
Department of Prosthodontics, Divya Jyoti College of Dental Sciences and Research, Modinagar, UP, India.
Email: dr.gitanjalimago123@gmail.com

pISSN 2278-0076
eISSN 2321-9270

significantly advanced post the discovery of stem cells and in recent times it has found its application in dentistry due to the identification of dental stem cells. Although, the concept of tooth regeneration was initially not accepted but the ground-breaking work by stomatologist G. L. Feldman (1932) showed evidence of regeneration of dental pulp under certain optimal biological conditions. This work introduced the biological-aseptic principle of tooth therapy to achieve pulp regeneration using dentine fillings as building material for stimulating pulp regeneration. Nevertheless subsequent researchers further improved this work. Major breakthrough in dental history was achieved in year 2000 when Gronthos *et al*. identified and isolated odontogenic progenitor population in adult dental pulp. These cells were referred to as dental pulp stem cells (DPSCs).[7] Since this discovery several researchers have reported on the different varieties of dental stem cells.

SOURCES OF STEM CELLS

There are several sources of stem cells. Pluripotent stem cells can be isolated from human embryos that are a few days old. Cells from these embryos can be used to create pluripotent stem cell "lines" —cell cultures that can be grown indefinitely in the laboratory. Pluripotent stem cell lines have also been developed from fetal tissue (older than 8 weeks of development).

Primary sources of stem cells are mainly, adult stem cells and embryonic stem cells.[6]

A. Adult stem cells

Adult stem cells are found throughout the body in different tissues like bone marrow, brain, blood vessels, liver, skin etc. These cells are known to reside in a specific area of each tissue called stem cell niche.[5] Different types of adult cells reside in several mesenchymal tissues and these are collectively referred to as mesenchymal stem cells or multipotent mesenchymal stromal cells.

1. Mesenchymal stromal cells – these are multipotent stromal cells and can differentiate into various types of cells. MSCs when grown in a defined microenvironment in vitro have the capability to differentiate into at least 3 cell lineages: osteogenic, chondrogenic and adipogenic and can also be in other cell lineages which are odontogenic in origin. These mesenchymal stromal cells depending upon their site of origin they are differentiated as:

a. Bone marrow derived MSCs –

The bone marrow stroma contains mesenchymal stem cells (MSCs), also known as marrow stromal cells which are multipotent stem cells. These multipotent stem cells are heterogeneous and possess a high replicative capability to differentiate into various connective tissue cells and are an optimum source of bone regenerative therapy.

b. Dental stem cells –

Development of tooth is the result of coordinated interactions between oral epithelial ectodermal cells that form the enamel organ and cranial neural crest derived mesenchymal cells which give rise to dental papilla and dental follicle as well as other components of the tooth such as dentin, pulp, or cementum etc. Different dental stem cells have been recognised which are described as follows:

i. Dental pulp stem cells –

These were first isolated from human permanent third molars and are clonogenic and highly proliferative. They are capable of generating dentin and pulp like tissues when transplanted. Studies have confirmed that dental pulp stem cells can differentiate into osteoblast, chondroblast and myloblast. These play a significant role in inflammation or repair during pulp exposures.

ii. Stem cells from exfoliated deciduous teeth (SHED cells) –

These highly proliferative multipotent cells were isolated from exfoliated deciduous teeth. These cells can induce dentin and bone formation as they are highly proliferative and are capable of differentiating into osteoblasts, neural cells, adipocytes and odontoblasts.[8, 9]

iii. Stem cells from apical papilla (SCAP cells)-

These cells were first collected from the human third molars in the apical papilla of developing teeth in the junction of apical papilla and dental pulp at the apices of the teeth.

iv. Stem cells from periodontal ligament (PDLSCs)-

These cells were obtained from third molar teeth and have the capability to differentiate into fibroblasts that secretes collagen type I, adipocytes and cementoblastslike cells and they can promote the differentiation of the Hertwig's epithelial root sheath cells.

v. Dental follicle precursor or progenitor cells (DFPCs)-

These cells are isolated from dental follicle of third molar and exhibit a greater plasticity than other dental stem cells. These cells are the progenitor for the periodontal ligament cells, cementoblasts and osteoblasts.

vi. Induced pluripotent stem cells-

These cells were recovered from the pulp of deciduous teeth and from third molar. In regenerative therapeutic applications these cells are of great interest as they also have the memory of the somatic tissues from which they are derived.

B. Embryonic stem cells -

Embryonic cells are produced from the undifferentiated inner cell mass of the blastocyst at an early stage of embryonic development. These cells are of an utmost importance as they can differentiate into all the stomatic lineages and can also be differentiated into male and female germ cells. This is the major reason why moral and ethical questions arises on the use of human embryonic stem cells.[10]

USES OF STEM CELLS IN TISSUE REGENERATION

In regenerative medicine, cell-based therapies are the most common approaches. Applying this approach clinically has some challenges like to identify methodologies to induce cell proliferation and differentiation, to maintain cell survival, and to remove unwanted cells.
Stem cells possess a remarkable potential to differentiate into many different cell types to form the desired organ. These cells hold a great promise for regenerative therapy. The progeny remain as unspecialized progenitors which serve as an internal source of repair and replenishment, or may differentiate into specialized cells to form the desired tissue. The most commonly used stem cells are (1) ES cells, (2) somatic or adult stem cells, and (3) induced pluripotent stem cells.[11]

SCAFFOLDS IN TISSUE ENGINEERING

Stem cells will require different types of scaffolding material to generate specific tissues which is an area of great interest. There are two basic methods for tissue engineering (1) top-down approach, and (2) bottom-up approach.

The top-down approach is a more traditional method in which the cells are seeded in a preformed three dimensional scaffold made from polymer, natural porous materials, or decellularized native extracellular matrix.[7]

Whereas in the bottom-up approach, various methods have been used to aggregate cells to form distinct subunits that could eventually be used as building blocks to engineer whole organs.[11]

TISSUE ENGINEERING OF DENTAL STRUCTURES AND PERIODONTIUM USING dMSCs

In tissue regeneration, the relevance of dMSCs lies in their potential to form different dental and dentofacial structures. There are four distinct categories of tissue regeneration for dental and periodontal structures, the underlying rationale, and current status of clinical translation. The first and simplest means of dental tissue regeneration is reparative dentine formation in dental pulp following direct pulp capping (DPC). Second, pulp revitalization allows for disinfection of necrotic, immature root canals and restoration of pulp-like tissues and pulp vitality. Third, pulp tissue engineering which is aimed at regeneration of the pulp–dentin complex using exogenous dMSCs, biocompatible scaffolds, and growth factors.[12]

APPLICATION OF STEM CELLS IN DENTISTRY

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.[12] Using a tooth slice model, pulp-like tissue was engineered using SHEDs seeded onto synthetic biodegradable scaffolds.[3] SHEDs were able to differentiate into odontoblast-like cells, and also endothelial-like cells.[2]

Bio-Root Engineering

Sonoyama et al. demonstrated the use of combined mesenchymal stem cell populations for root/ periodontal tissue regeneration.[18] They loaded root shaped hydroxyapatite/ tricalcium phosphate 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.[8] 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.[13-15]

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.[15- 18]

Cardiac Repair

It was found that DPSCs (Dental pulp stem cells) can help cardiac repair after myocardial infarction.[15] 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.[5] The cardiac repair occurred in the absence of any evidence of DPSCs differentiation into cardiac or smooth muscle cells.[4]

FUTURE PROSPECTS

There is a great excitement in the scientific community about the stem cells and dental regenerative medicine which has showed the feasibility of not only stem cell transplantation but also organ replacement but it is yet to be known more about this branch of medicine. Stem cell transplantation and the formation of whole teeth has become a promising field by the use of stomatic dental tissue or the progenitor cells.

The bioengineering technologies developed for tooth regeneration will make substantial contributions to encourage the future organ replacement by regenerative therapies in a wide variety of organs such as the liver, kidney and heart.[19]

CONCLUSION

Stem cells of the pulp appear to hold the key to various cell-based therapies in regenerative medicine, but most avenues are in experimental stages and many procedures are undergoing standardization and validation. The advancement of science has transformed our lives in such a way that would have been unpredictable about half century ago. Whether stem cell research will have a similar effect remains to be determined but the promise is so great that bit seems wise to consider seriously how best to further continue the research in such a manner that is sensitive to public sensibilities and disease interventions.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

REFERRENCES

1. Nakao K, Tsuji T. Dental regenerative therapy: Stem cell transplantation and bioengineered tooth replacement. *Jpn Dent Sci Rev* 2008; 44(0): 70-75.

2. Peng L, Ye L, Zhou XD. Mesenchymal stem cells and tooth engineering. *International J Oral Sci* 2009; 1(1):6-12.

3. Sandhu SS, Nair M. Stem Cells: Potential Implications for tooth regeneration and tissue engineering in Dental Science. *People's J of Sci Res* 2009; 2(1): 41-45.

4. Amireddy R, Kumar SD, Murthi S. Stem cells: A window to regenerative dentistry. *Indian J Dent Adv* 2010; 2(3): 264-267.

5. Ranganathan K, Lakshminarayanan V. Stem cells of the dental pulp. *Indian J Dent Res* 2012; 23(4): 558-563.

6. Egusa H, Sonoyama W, Nishimura M, Atsuta I, Akiyama K. Stem cells in dentistry – Part I: Stem cell sources. *J Prosthodont Res* 2012; 56(0): 151–165.

7. Egusa H, Sonoyama W, Nishimura M, Atsuta I, Akiyama K. Stem cells in dentistry – Part II: Clinical applications. *J Prosthodont Res* 2012; 56(1): 229–248.

8. Marawar PP, Mani A, Sachdev S, Sodhi NK, Anju A. Stem cells in dentistry: an overview. *Pravar Med Rev* 2012; 4(2):11-15.

9. Sedgley MC, Botero MT. Dental Stem Cells and their sources. *Dent Clin N Am* 2012 ; 56(2) : 549-561.

10. Kim SG, Solomon C, Suzuki T, Jiang N. Effect of growth factors on dental stem/progenitor cells. *Dent Clin N Am* 2012 ; 56(2) : 563-575.

11. Horst VO, Jheon HA, Klein DO. Stem cell and Biomaterials research in dental tissue engineering and regeneration. *Dent Clin N Am* 2012; 56(2): 495-520.

12. Kim HR, Kang KM. Therapeutic potential of mesenchymal stem cells for oral and systemic diseases. *Dent Clin N Am* 2012; 56(2): 651-675.

13. Goodis EH, Kinaia MB, Kinaia MA. Regenerative endodontics and tissue engineering: what the future holds? *Dent Clin N Am* 2012; 56(2): 677-689.

14. Masthan KMK, Sankari L, Babu NA, Gopalakrishnan T. Mystery inside the tooth: the dental pulp stem cells. *J Clin Diagn Res* 2013; 7(5):945-947.

15. Kabir R, Gupta M, Aggarwal A, Sharma D, Sarin A, Kola MZ. Imperative role of dental pulp stem cells in regenerative therapies: a systematic review. *Niger J Surg* 2014; 20(1): 1-8.

16. Singh H, Bhaskar DJ, Rehman R, Jain CD, Khan M. Stem cells: an emerging future in dentistry. *Int J Adv Health Sc* 2014; 1(2): 17-23.

17. Liu J, Yu F, Sun Y, Jiang B, Zhang W, Yang J, Xu GT, Liang A, Liu S. Characteristics and potential applications of human dental tissue-derived mesenchymal stem cells. *Stem Cells* 2015; 33(1): 627–638.

18. Singh P, Mehta M, Thakur P. Boon in dentistry - stem cells. *Int J Scient Stud* 2014; 2(4): 59-65.

19. Asatrian G, Pham D, Hardy WR, James AW, Peault B. Stem cell technology for bone regeneration: current status and potential applications. *Stem Cells and Cloning* 2015; 8(01): 39-48.