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Dental stem cells the magical cells - current application and the future with review of literature

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Abstract: With increase in the understanding of stem-cell behavior, their application has extended well beyond not only regenerative medicine but also dentistry. The breakthrough of stem cells has produced new possibilities in the regeneration of different organs and tissues. In past few years many studies and revelations have been conducted in dentistry which indicate that stem cells and tissue engineering together are a unit have given rise to so called "Regenerative Dentistry". The tooth (permanent teeth and deciduous teeth) is the natural store house for these stem cells. These are capable of reproducing themselves and can be voluntarily recovered at the time of an intended dental procedure. Besides dental stem cells have lot of medical benefits in the progress of new medical therapies. Like regenerative diseases and cancer therapy. This article highlights the research in dental field on Stem cells their current applications and what can be done and achieved in the future.
Keywords: Stem Cells, Dentistry, regeneration, Applications, Future.

Introduction

Stem cells are clonogenic, undifferentiated biological cells which are capable of self-renewal and are classified according to their potency. This is directly related to the stages of cell division and differentiation of the human embryo during different stages of development. In fact; they can differentiate into each of the more than 200 cell types of the adult body [1]. The stem cell therapy has the potential in treatments for major degenerative diseases, by providing healthy cells to replace diseased tissues and organs. Also they have the potential to differentiate into specialized cells and can divide to produce extra stem cells.

Research into stem cells initiated with the discovery of dental pulp stem cells (DPSCs). Later on researchers recognized the mesenchymal type of stem cell inside dental pulp. Which have the potential to differentiate into a various type of other cells. The odontoblasts which form major part of dentin may carry on mild injury, such as early caries or attrition, and exude a reactionary dentin matrix? This reparative dentin a 'bridge' of mineralized tissue instantly below the extensively broken tissue, in order to protect pulp vitality. Now researchers are trying out the possible applications of stem cells for restoring and regeneration of dental and dent facial structures [2].

Classification

Based on the Cell type/ tissue of origin:

1) Somatic Stem Cells (SSCs) are self-renewable population of cells present in all tissues and described as multi potent cells. They exist in mature tissues such as hematopoietic, neural, gastrointestinal, and mesenchymal tissues. For instance, a multi potent blood stem cell is a hematopoietic cell that can differentiate into several types of blood cell types (such as neutrophils and lymphocytes) but cannot differentiate into brain cells, bone cells or other non-blood cell types.
2) Embryonic Stem Cells (ESCs) are derived from pre-implantation embryos before differentiation of trophoectoderm and inner cell mass, capable of giving rise to the entire organism and extra embryonic tissues. They are described as "pluripotent".
3) Induced Pluripotent Stem Cells (IPSCs) are capable of differentiation into ectodermal, mesodermal and endodermal

cells and are "reprogrammed," to become pluripotent.

Stem Cells and Dental Pulp:

Stem cells can be separated from the three types of teeth, they are:

(a) *Deciduous Teeth:* The healthy pulps of deciduous teeth are a rich source of viable Stem Cells.
(b) *Wisdom Teeth:* The healthy pulp from wisdom teeth is an exceptional source for workable stem cells. Entire or sectioned divisions of third molars containing healthy pulp which gets exposed at the time of sectioning can be recovered at the time of their removal.
(c) *Permanent teeth:* Healthy pulp from all the permanent teeth is potential resource of stem cells. Bicuspids or the premolars, and even 3rd molar teeth requiring to be removed for orthodontic suggestions are an example of this.

Different Types of Tooth Stem Cells:

1. *Adipocytes:* They have successfully been utilized to repair injured cardiac muscle caused by severe heart attack. There is also initial data to point out that they can be used to treat cardiovascular diseases, orthopedic problems and spine, , congestive heart failure, and also used in plastic surgery. [2]
2. *Chondrocytes and Osteoblasts:* These types of stem cells have effectively been used to grow cartilages and bones suitable for transplant and to develop intact teeth in animals.
3. *Mesenchymal:* These stem cells have successfully been used to restore spinal cord damage and to recall feelings and progress of movement in paralyzed patients. Since they can figure neuronal clusters they have been used to treat neuronal degenerative disorders such as Parkinson's diseases and Alzheimer's, cerebral palsy. [2]

According to Khazaei, et al stem cells in dentistry are broadly classified into two categories. [3]

a. *Stem cells of Dental origin:* They include, Dental pulp stem cells (DPSCs), Stem cells from human exfoliated deciduous teeth, Stem cells from apical papilla, periodontal ligament SC, Dental follicle, progenitor cells, Tooth germ
b. *Stem cells of non dental origin:* Oral mucosa derived Stem Cells, bone derived mesenchymal Stem Cells, and salivary gland derived stem cells. The oral cavity harbors various types of multi-potent stem cells such as PDLSC (periodontal ligament stem cell), SCAP (stem cells from apical papilla) and dental follicle stem cells. Al though bone marrow stem cells are well-established and are considered the gold standard for research targeting stem cells therapies, the oral cavity can provide stem cells with simple and less invasive procedures (especially compared to bone marrow aspiration), under local anesthesia and without esthetic damage [3-4]. Additionally, dental pulp stem cells (DPSC) and stem cells from human exfoliated deciduous teeth (SHED) can be found in the dental pulp of permanent and deciduous teeth, respectively. As the latter are retrievable from naturally exfoliated teeth, which are one of the only disposable post-natal human tissues, the interest towards SHED has increased [4]. In fact, primary teeth offer a second chance to those parents who have not opted to save the umbilical cord for possible future needs. Due to its ability to cross line age boundaries, stem cells from dental pulp are also being investigate daimingat cardiac repair and the regeneration of the central nervous system [5-6].

Stem Cell Cryopreservation:

Extracted permanent and primary (including exfoliating) teeth can be conserved for future use with cryopreservation at temperature as low as -196° C. Research has confirmed that stem cells obtained from the dental pulp and the periodontal ligament of extracted third molars hold on to the ability to differentiate into numerous cell types following defrosting after cryopreservation using liquid [7-8].

Applications of Stem Cells in Dentistry and Medical sciences [6]:

Stem cell t therapy has received attention from medical field, regenerative medicine and

dentistry for treating various diseases. Dental and non dental SCs serve are being used for clinical applications to improve damages of various diseases Such as injuries to the nervous system heart infarcts and muscular dystrophy disorders and to regenerate bone tissue [9-13].

1. Dental pulp stem cells (DPSCs) loaded on collagen sponge scaffold were used to restore human mandibular bone defects [14].
2. Periodontal ligament stem cells (PDLSCs) derived from PDL serve as the most suitable sources of SCs used for periodontal Therapy. The successful regenerative effect of PDL cells have not only been observed in several animal models but clinical experiments on human shave also presented evidence on the strong potential of application of autologous PDL cells in the treatment of periodontitis and regeneration of the periodontium [15].
3. Yang et al showed the positive role of Dental Stem Cells in tooth root regeneration and formation. DPSCs can generate pulp-like tissues with odontoblast like cells. [16-17].
4. Dental stem cells have been reported to be applied in the regenerative medicine for regeneration of non dental tissues like muscle and neural tissues, induction of angiogenesis, and treatment of liver diseases [2] *In vivo* studies show that induced stem cells from exfoliated deciduous teeth (SHED) is able to form smooth and skeletal muscle cells besides it also Improve the muscular dystrophy in animal models [8].
5. DPSCs differentiate into neurons *in vitro* and when injected into the cortical lesions in the brain of rats exhibited properties similar to neurons, indicating the potential of Dental pulp stem cells (DPSCs) in neurogenesis and gliogenesis 18].
6. Neurodegenerative diseases such as in Parkinson's and Alzheimer's disease stem cells have raised a new hope. Tooth germ progenitor cells have shown their neuroprotective effects in Alzheimer's and Parkinson's diseases through the application of angiogenic, antiapoptotic, and antioxidativemechanisms [19].
7. Dental stem cells have shown to inhibit the progression of liver fibrosis and improveliver function in animal studies with liver injury [20].
8. Dental stem cells are able to form the corneal epithelium following corneal injury. Reconstruction of the corneal epithelium was also reported *via* transplantation of SHED, containing tissue-engineered cell sheet, into animal models [21].
9. Recently scientists have been investigating analternative approach to treating HIV-1/AIDS, based on the creation of a disease-resistantimmune system through transplantation of autologous, gene-modified (HIV-1-resistant) hematopoietic stem and progenitor cells (GMHSPC) [22].
10. Human Stem cells are currently being used to test new drugs. Cancer cell lines, for example, are used to screen potential anti-tumor drugs. The stem cells have been used since many years in immune-reconstitution following cancer development or following cancer treatments Clinical trials are underway to explore the low immunogenic properties of stem cells and their possible use for treatment of problems with an overactive immune system seen with allergies and autoimmune disorders [6].

Short comings:

In spite of various advantages of Stem cells in dentistry and regenerative medicine, scientists have recently reported that human Dental Stem Cells cultured in vitroexhibit different karyotypicabnormalities such as polyploidy, aneuploidy, and ring chromosomes as well as high frequency of chromosomal mutations. These results suggest that cultured Dental Stem Cells are cryogenically instable and must be carefully analyzed before use in clinical therapy [22].

Conclusion

The science of stem cells therapies has the potential to lead to treatments for major degenerative diseases, by providing healthy cells to replace diseased tissues and organs. Regeneration of the dental tissues offers an eye-catching alternative to more conventional restorative approaches because the infected tissue is replaced by natural tissue, which forms an essential part of the tooth.

Complementary studies are suggested to be conducted to identify the novel aspects of application of DSCs in dentistry and regenerative medicine in particular. To summarize, the promise of stem cell therapies is an exciting one, but significant. Technical hurdles remain that will only be overcome through years of intensive research.

References

1. Rosan V. What and where are the stem cells for Dentistry? *Singapore Dental* 2013; 34:13-18.
2. Singh H, Bhaska DJ, Rahila R, Chatainya DJ, Mohsin K. Stem Cells: An Emerging Future. *Dentistry International Journal of Advanced Health Sciences,* 2014; 1(2):17.
3. Khazaei M, Bozorgi A, Khazaei S, Khademi A. Stem cells in dentistry, sources, and applications. *Dental Hypotheses,* 2016; 7: 27-31
4. Rosa V, Botero TM, Nor JE. Regenerative endodontics in light of the stem cell paradigm. *Int. Dental J.* 2011; 61 (Suppl. 1):23-28.
5. Gandia C, Arminan A, Garcia-Verdugo JM, Lledo E, Ruiz A, Minana MD et al. Stem Cells and emerging trends in medical sciences. *Journal of Resesrch and Sciences,* 2008; 26:638-645.
6. Young F, Sloan A, Song B. Dental pulp stem cells and their potential roles in central nervous system regeneration and repair. *J. Neurosci. Res.* 2014; 2(2): 16-21.
7. Tammanvar P. Dental Pulp Stem Cells Scope in Dentistry a Review. *IOSR Journal of Dental and Medical Sciences*, 2013; 8(1):38-41.
8. Seo BM, Miura M, Sonoyama W, Coppe C, Stanyon R, Shi S. Recovery of stem cells from cryopreserved periodontal ligament. *J Dent Res*. 2005; 84:907-912.
9. Nosrat IV, Widenfalk J, Olson L, Nosrat CA. Dental pulp cells produce neurotrophic factors, interact with trigeminal neurons *in vitro*, and rescue motoneurons after spinal cord injury. *Dev Biol* 2001; 238:120-132.
10. Armiñan A, barenhof J. Role of Human dental pulp stem cells in ventricular defects and cardiac infarction. *Journal of Clinical Medicine and Applied Sciences,* 2006; 02:124-128.
11. Kerkis I, Ambrosio CE, Kerkis A, Martins DS, Zucconi E, Fonseca SA *et al*. Early transplantation of human immature dental pulp stem cells from baby teeth to golden retriever muscular dystrophy (GRMD) dogs: Local or systemic. *J Transl Med* 2008; 6:35.
12. Graziano A, d'Aquino R, Cusella-De Angelis MG, De Francesco F, Giordano A, Laino G, *et al*. Scaffold's surface geometry significantly affects human stem cell bone tissue engineering. *J Cell Physiol* 2008; 214:166-172.
13. Graziano A, d'Aquino R, Laino G, Papaccio G. Dental pulp stem cells: A promising tool for bone regeneration. *Stem Cell Rev* 2008; 4:21-26.
14. 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. *Euro Cell Mater* 2009; 18:75-83.
15. Feng F, Akiyama K, Liu Y, Yamaza T, Wang TM, Chen JH *et al*. Utility of PDL progenitors for *in vivo* tissue regeneration: A report of 3 cases. *Oral Dis* 2010; 16:20-28.
16. Yang B, Chen G, Li J, Zou Q, Xie D, Chen Y *et al*. Tooth root regeneration using dental follicle cell sheets in combination with a dentin matrix-based scaffold. *Biomaterials*, 2012; 33:2449-2461.
17. Lee JH, Lee DS, Choung HW, Shon WJ, Seo BM, Lee EH *et al*. Odontogenic differentiation of human dental pulp stem cells induced by preameloblast-derived factors. *Biomaterials* 2011; 32:9696-9706.
18. Király M, Kádár K, Horváthy DB, Nardai P, Rácz GZ, Lacza Z *et al*. Integration of neuronally pre differentiated human dental pulp stem cells into rat brain *in vivo*. *Neurochem Int* 2011; 59:371-381.
19. Yalvaç ME, Yarat A, Mercan D, Rizvanov AA, Palotás A, Şahin F. Characterization of the secretome of human tooth germ stem cells (h TGSCs) reveals neuro-protection by fine-tuning micro-environment. *Brain BehavImmun*, 2013; 32:122-130.
20. Ikeda E, Yagi K, Kojima M, Yagyuu T, Ohshima A, Sobajima S *et al*. Multipotent cells from the human third molar: Feasibility of cell-based therapy for liver disease. *Differentiation*, 2008; 76:495-505.
21. Gomes JA, Geraldes Monteiro B, Melo GB, Smith RL, Cavenaghi Pereira da Silva M, Lizier NF et al. Corneal reconstruction with tissue-engineered cell sheets composed of human immature dental pulp stem cells. *Invest Ophthalmol Vis Sci* 2010; 51:1408-1414.
22. Duailibi MT, Kulikowski LD, Duailibi SE, Lipay MV, Melaragno MI, Ferreira LM, et al. Cytogenetic instability of dental pulp stem cell lines. *J Mol Histol* 2012; 43:89-94.

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