Indian Journal of Dental Sciences.
October 2012 Supplementary Issue
Issue:4, Vol.:4

www.ijds.in

Review Article

Indian Journal of Dental Sciences

E ISSN NO. 2231-2293 P ISSN NO. 0976-4003

Stem Cell Applications In Denistry And Medicine

[1] Arora Arvind
[2] Sharma Vineet
[3] Singh Jyotkiran
[4] Singh Gurpreet

[1] Professor
[2,3] Reader
Dept. of Conservative Dentistry & Endodontic
[4] Sr. Lecturer
Dept. of Medicine.
Luxmi Bai Institute of Dental Sciences & Hospital

Address For Correspondence:
Dr. Arora Arvind
Professor,
Dept. of Conservative Dentistry & Endodontic,
Luxmi Bai Institute of Dental Sciences & Hospital

Submission : 17th December 2011
Accepted : 24th June 2012

Quick Response Code

Abstract

While the regeneration of a lost tissue is known to mankind for several years, it is only in the recent past that research on regenerative medicine/dentistry has gained momentum. Initial existence from pioneering studies has documented the likely breakthrough that stem cells offer for various life threatening diseases that have so far defeated modern medicine care. This review takes you on a sojourn of origin of stem cells, their properties, characteristics, current research and their potential applications.

Key Words
Stem cells, Multipotent, Embryonic stem cells

Introduction

Stem cells are unspecialized cells with an extraordinary ability to self-renew, capable of differentiating into one or more specialized cell type playing a crucial role in hemostasis and tissue repair. When called into action following injury.

Stem cells

(Cells division)

Stem cell + progenitor cells (intermediate cell type)

Differentiating cells

Types Of Stem Cells

1. Embryonic stem cells (ESCs)
    - Derived from embryos that are 2-11 days old called blastocyts.
    - Are totipotent cells
    - Have the highest potential to regenerate are repair[1]

ESCs are not so far used therapeutically as- owing to the belief that the process of extraction of stem cells from an embryo destroys the embryo itself and some view this as taking life so, raising ethical and moral concerns. It is difficult to control the growth and differentiation of embryonic stem cell posing risk of tumourogenicity and teratoma formation.

2. Advent Stem Cells
    - Are multipotent
    - Are found in most adventtissues.

They are of two types:

i. Hemopoetic Stem Cells (HSCs) - are obtained either from cord blood or peripheral blood.
ii. Mesenchymal Stem Cells (MSCs) - are obtained from mesodermal layer of fetus and in advent from bone marrow, dermal stem cells, etc.

Characteristics of Stem Cells

1. Totipotency: generate all types of cells including germ cells (ESCs)
2. Pluripotency: generate all types of cells except cells of the embryonic membrane.
3. Multipotency: differentiate into more than one mature cell (MSC)
4. Self-renewal: divide without differentiation and create everlasting supply.
5. Plasticity: MScs have plasticity and can undergo differentiation. The trigger for plasticity is stressing of tissue injury which upregulates the stem cells and releases chemoattractants and growth factors.

Source Of Stem Cells

1. Bone Marrow Stem Cells- The most commonly known procedure involving stem cells is the bone marrow transplant. Bone marrow transplants are used for the treatment of diabetes, crohn's disease, bone defects or cartilage injury.[2]
2. Cord Blood Stem Cells- Obtained from umbilical cord blood. Used to treat blood relates diseases. In treatment of leukemia, myocardial infarction, diabetes mellitus and neurological disorders.[3]
3. Adipose Tissue Stem Cells- MSCs can be isolated from adipose tissue obtained from liposuction aspirates or abdominoplasty procedures and are being studied for repairing tissue defects resulting from traumatic injury, tumor resection and congenital defects, calvarial defects following severe head injury and in dentistry for repair of jaw bone.[4],[5]
4. Embryonic Stem Cells- In 1998 scientists derived cells from frozen human embryos to generate human embryonic stem cells for the first time.[6]
5. Dental Stem Cells- A new source of readily available MSCs-teeth-was discovered in 2000 by scientists at the NIH stem cells can be collected from
    - Deciduous teeth when they naturally exfoliate between 6-11 years.
    - From teeth that are surgically

removed such as premolars for orthodontic.
- Extraction of 3rd molars.

Niches Of Dental Stem Cells

Dental stem cells reside in multiple niches of deciduous and permanent teeth.

a. From dental follicle of unerupted 3rd molar (DFCs).
b. Stem cells from human exfoliated deciduous teeth (SHED).
c. Periodontal ligament stem cells (PDLSC)
d. Stem cells from apical papilla (SCAP)

Clinical Applications For Dental Stem Cells

Alveolar bone regeneration: Defects of at least 1.5 cm in the alveolar ridge of 17humans were filled with a construct of stem cells collected from third molars and seeded onto a collagen matrix. One year later in many cases, the gap was filled with bone[7].

Periodontal ligament: Due to the complex structure of the periodontium. Its complete regeneration has always remained a challenge. All the current regenerative techniques such as autologous bone grafts, allografts or alloplastic materials have limitations and cannot be used in all clinical situations. Therefore, a cell mediated bone regeneration technique will be a viable therapeutic alternative. Periodontal ligament cells cultured in vitro were successfully reimplanted into periodontal defects in order to promote periodontal regeneration by Hasegaura et al[8].

Regeneration of damaged coronal dentin and pulp- To this date, no restorative material has been able to mimic all physical and mechanical properties of tooth tissue. Furthermore, we have not been successful in providing an ideal solution to certain situations such as an immature tooth with extensive coronal destruction and reversible pulpitis. If the regeneration of tooth tissue is possible in these situations, it facilitates physiological dentin deposition that forms an integral part of the tooth thereby restoring structural integrity, minimizing interfacial failure, microleakage, and other consequent complications. Similarly, young permanent teeth that require apexogenesis or apexification are prefect candidates for regeneration of pulp as they allow completion of both vertical and lateral root development, improving the long term prognosis. However, pulp regeneration in fully formed teeth may not be of great benefit, although there is sufficient evidence to say that a restored vital tooth serves longer than a root canal treated one.

Pulp tissue regeneration involves either delivery of autologous/allogenic stem cells into the root canals or implantation of pulp that is grown in the lab, using stem cells. Both these techniques will have certain advantage and limitations that need further research[9],[10],[11].

Third Dentition (Bioengineered Teeth)

A method has been developed to regenerate tooth buds in a single procedure by combining dental pulp and bone marrow on a scaffold and implanting this into surgically created defects. After a number of months, the construct led to organized dentin, enamel, pulp, cementum and periodontal ligament surrounded by regenerated alveolar bone, suggesting a method that could translate directly to humans[12].

Application In Medicine:

A. CORNEA- Based upon similarities of human dental stem cells with limbal cells in the eye, human dental stem cells were used to successfully treat an animal model for cornea damage by chemical burn[13].
B. LIVER DISEASE- Stem cells from third molars were differentiated into hepatocytes in cell culture and in an animal. Model of liver disease, they prevented liver fibrosis and increased levels of albumin and bilirubin[14].
C. MYOCARDIAL INFARCTION (HEART ATTACK) - Human dental stem cells injected intramyocardially into a rat model of acute myocardial infarction showed an increase in angiogenesis, improvement in cardiac function, and a reduction in infarct size[15].
D. MUSCULAR DYSTROPHY - Animal studies have been done on the golden retriever for treating muscular dystrophy.
E. DIABETES - Dental stem cells have been shown to produce insulin[16] and to modulate the immune system by suppressing T-cells response in laboratory and animal testing[17],[18].
F. STROKE - Neuronal stem cells from human third molars were used to treat a rat model of middle cerebral artery exclusion[19].
G. SPINAL CORD INJURY AND OTHER NEUROLOGICAL DISEASES/DISORDERS - Neurons have been generated from dental stem cells[20], including from PDLSC[21], DPSC[22], DFSC[23], and SHED[24].

Summary:

Research has shown that teeth are a source of high quality stem cells that may be used for the treatment of medical and dental diseases. The discovery that odontogenic tissues are a source of adult stem cells has opened up a new role for dentist in the field of medicine. Dentists are positioned to become one of the key providers of stem cells, and as a result, their linkage with the medical field will become very intimate.

References:

1. Keller GM. In vitro differentiation of embryonic stem cells. Curr opin cell boil 1995;7:862-9
2. Thomas ED, Lochte HL Jr., Lei WC et at. Intravenous infusion of bone marrow in patients receiving radiation and chemotherapy. N.Enge J med 1957;257:491-496
3. Reimann V, Creutzig U, Kogler G. stem cells derived from cord blood in transplantation and regenerative medicine. Dtsh Arztebl Int 2009;106:831-836
4. Lendeckel S, Iodicke A, Christophis P et at. Autologous stem cells (adipose) and fibrin glue used to treat widespread traumatic calvarial defects: case report J. caniomaxilla fac surg. 2004;32:370-373
5. Mesimaki K, Lindros B, Tornwall J et al. novel maxillary reconstruction with ectopic bone formation by GMP adipose stem cells. Int. j oral maxillofac surg 2009;38:201-209
6. Thomson JA, itskovitz- Eldor J, Shapiro SS, et al. Embryonic stem cell lines derived from human blastocysts. Science. 1998; 282;1145-1147.
7. D' Aquino R, De Rosa A, lanza V, et al. human mandible bone defects repair by the grafting of dental pulp stem/proginetor cells and collagen sponge biocomplexes. Eur cell mater 2009;18:75-83
8. Hasegaura M, Yamato M, Kikuchi A, Okano T, Ishikawa I, Human periodontal ligament stem cell sheets can regenerate periodontal ligament

tissue in athymical rat model. Tissue eng 2005;11:469-77
9. 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
10. Doyon GE, Dunsha T, Von Frauhofer JA. Fracture resistance of human root dentin exposed to intracanal calcium hydroxide J. Endod 2005;31:895-7
11. Caplan DJ, Cai J, Yin G, White BA. Root canal filled versus non root canal filled teeth: a retrospective comparisonof survivaltimes J. Public health Dent 2005;65:90-6
12. Zhang W, Abukawa H, Troulis MJ, etal. Tissue engineered hybrid tooth-bone constructs. Methods, 2009;47:122-128
13. Monterio BG, Serafim RC, Melo GB, et al. Human immature dental pulp stem cells sharer key characteristic features with limbal stem cells. Cell prolif. 2009;42:587-594
14. Ikeda E, Yagi K, Kojima M, et al. multipotent cells from the human third molar: feasibility of cell based therapy of liver disease. Differentiation. 2008;76:495-505
15. Gandia C, Arminan A, Garcia-Verdugo JM, et al. human dental pulp stem cells improve left ventricular function, induce angiogenesis and reduce infarction size in rats with acute myocardial infarction. Stem cells. 2008;26:638-645
16. Haung CY, Pelaez D, Dominquez-Bendala J, et al. plasticity of stem cells derived from adult periodontal ligament. Regen Med. 20098;4:809-821
17. Pierdomenico L, Bonsi L, Calvitti M, et al. Multipotent mesenchymal stem cells with immunosuppressive activity can be easily isolated from dental pulp. Transplantation 2005;80:836-842
18. Yamaza T, Kentaro A, Chen C, et al. immunomodulatory properties of stem cells from human exfoliated deciduous teeth. Stem cells Res Ther 2010;1:5
19. Yang KL, Chen MF, Liao CH, et al. A simple and efficient method for generating Nurr-1 positive neuron al stem cells from human wisdom teeth (tNSC) and the potential of tNSC for stroke therapy cytotherapy 2009;11:606-617
20. Nosrat IV, Smith CA, Mullally P, et al. Dental pulp stem cells provide neurotrophic support for dopaminergic neurons and differentiate into neurons in vitro; implications for tissue engineering and repair in the nervous system. Eur J Neurosic 2004;19:2388-2398
21. Widera D, Grimm WD, Moebius JM, et al. highly efficient neural differentiation of human somatic stem cells, isolated by minimally invasive periodontal surgery. Stem cells dev. 2007;16:447-460
22. Arthur A, Rychkov G, Shi S, et al. adult human dental pulp stem cells differentiate toward functionally active neurons under appropriate environment cues. Stem cells. 2008;26:1787-1795
23. 24. M orsczecke C, Vollner, Saugspier M, et al. comparison of human dental follicle cells (DFCs) and stem cells from human exfoliated deciduous teeth (SHED)P after neural

Source of Support : Nill, **Conflict of Interest** : None declared