Journal of Applied Dental and Medical Sciences
NLM ID: 101671413 ISSN:2454-2288
Volume 2 Issue3 July- September 2016

Review Article

STEM CELLS IN DENTISTRY: A NEAR FUTURE

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ARTICLE INFO

Keywords:
Stem cells, undifferentiated cells, dental pulp, apical papilla, regenerative dentistry

ABSTRACT

Stem cells are undifferentiated cells that retain the ability to continuously divide and produce progeny cells that can differentiate into various other types of cells. In human body, there are many sources from which the stem cells are derived such as eye, brain, blood from umblical cord, bone marrow, skin and teeth. These stem cells can be derived from embryonic and adult tissues and cultured to form other different cells for regenerative and therapeutic purpose. Five different types of dental stem cells have been isolated from dental soft tissues: dental pulp, apical papilla, dental follicle and periodontal ligament. This article summarizes information available on the different types of dental stem cells and discusses their potential use in regenerative Dentistry.

Introduction

The human body has a remarkable capacity for regeneration. Cells in tissues such as blood and epithelia divide rapidly, and are regenerated continually throughout life; whereas cells in most other tissues turn over more slowly and respond only to specific biologic signals. Their fate is decided by the cell cycle. The cell cycle consists of four distinct phases: G_1 phase, S phase (synthesis), G_2 phase and M phase (mitosis). The G1, G2 and M phase are collectively known as interphase. Cells that have temporarily or reversibly stopped dividing are said to enter a state of quiescence called G_0 phase.[1]

Differentiated cells are the ones which are specialized in their function, which they can perform in a certain organ or tissue and cannot undergo the process of repair or regeneration. They lose their regenerative ability, as they enter the quiescent G_0 stage from G_1 stage and remain so for long period of time. On the contrary, undifferentiated cells retain their regenerative capacity throughout life. Several tissues of the body like blood, skin, GIT have regenerative ability and undergo rapid renewal because they contain undifferentiated cells that help in this process. These undifferentiated, regenerative cells are termed as **stem cells**.[1, 2]

Discussion

There are two broad categories of stem cells; embryonic and adult stem cells.

Embryonic stem cells are harvested from embryos and are derived from the inner cell mass of the blastocyst. These cells form the three germ layers (ectoderm, mesoderm and endoderm), and are capable

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of developing into more than 200 cell types. In 1998, the first human embryonic stem cell line was derived at University of Wisconsin-Madison.[3]

Adult stem cells are derived from mature tissue. These are undifferentiated cells found among differentiated cells in a tissue or an organ which can renew themselves and can differentiate to yield major specialized cell types of the tissue from which they originated.[4]

Dental Sources of Adult Stem Cells [5, 6]

They are divided into two groups with respect to their major differentiation potential.

- First group is associated with the **dental pulp** and consists of
  - Dental Pulp Stem Cells (DPSC)
  - Stem Cells from Human Exfoliated Deciduous Teeth (SHED)
  - Stem Cells From Root Apical Papilla (SCAP)
- Second group is related to the **periodontium** and contains
  - Periodontal Ligament Stem Cells (PDLSC)
  - Dental Follicle Progenitor Cells

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The existence of stem cells in teeth is a robust phenomenon and required for odontogenesis. Early in fetal development, teeth arise from the neural crest through a series of interactions between neural, mesenchymal, and epithelial tissues.[7] The developed tooth can be thought of as an encapsulated population of quiescent stem cells. [8] The finding of stem cells in natal teeth, supernumerary teeth, and odontoma reinforces the concept that stem cells play a key role in organogenesis of every tooth. It has also been shown that the pluripotency of dental stem cells may be a function of the age of the tooth or the age of the donor.[11]

Dental Pulp Stem Cells (DPSC)

The undifferentiated cells of the oral ectomesenchyme are not entirely lost after tooth eruption in human. In the 1990s, precursor cells from the dental pulp were experimentally isolated.[12] Later, dental ectomesenchymal stem cells were isolated from the dental pulp (DPSCs) of extracted wisdom teeth. These cells exhibit similar features as bone-marrow-derived mesenchymal stem cells. The ectomesenchymal stem cells of human exfoliated deciduous teeth (SHEDs) were isolated from the dental pulp of exfoliated incisors. These cells could be cultivated either as fibroblast-like, adherent cells, or like neural stem cells as neurospheres. SHEDs are capable of differentiation into odontoblast, adipocytes and neural cells. They induced bone formation and produced dentin under in vivo conditions; and they were able to survive and migrate in murine brain after transplantation into immunocompromised animals. [13, 14]

Stem Cells from Human Exfoliated Deciduous Teeth (SHED)

Stem cells from human exfoliated deciduous teeth (SHED) were identified as a novel population of stem cells capable of differentiating into a variety of cell types including neural cells, odontogenic cells, and adipocytes. The most significant difference between

SHED and adult dental pulp stem cells (DPSCs) is that SHED are able to induce bone formation when implanted into immunocompromised mice subcutaneously using hydroxyapatite/tricalcium phosphate as a carrier vehicle, while DPSCs generated a dentin/pulp-like structure. Importantly, SHEDs are derived from a readily accessible tissue source, human deciduous teeth that are expendable and routinely exfoliated in childhood with little or no morbidity to the patient.

Stem Cells from Root Apical Papilla (SCAP)

A new class of dental stem cells was isolated from the dental papilla of wisdom teeth or incisors of 4 month old mini-pigs (SCAP, stem cells from apical papilla).[15] The dental papilla is an embryonic-like tissue that becomes the dental pulp during maturation and formation of the crown. Therefore, SCAPs can only be isolated at a certain stage of tooth development. However, SCAPs have a greater capacity for dentin regeneration than DPSCs because the dental papilla contains a higher number of adult stem cells compared to the mature dental pulp. In addition, SCAPs' are likely to be less differentiated than DPSCs, as they originate from an embryonic-like tissue. Also, only a combination of SCAPs and PDL stem cells induced the formation of a dental connective tissue, namely, the attachment of an artificial tooth crown in the alveolar bone.

Periodontal Ligament Stem Cells (PDLSC)

Another class of dental ectomesenchymal stem cells are Periodontal Ligament Stem cells, which were isolated from the root surface of extracted teeth. These cells could be isolated as plastic-adherent, colony-forming cells, but display a low potential for osteogenic differentiation under in vitro conditions. PDL stem cells differentiate into cells or tissues very similar to the periodontium.[16]

Dental follicle precursor cells

The PDL-stem cells are capable of differentiation toward periodontal cells; however, the dental follicle, which plays a crucial role in tooth development, contains precursors of the periodontium as well. The dental follicle is separated from developing dentin by epithelial cell layers (Hertwig's epithelial root sheath) during early steps of periodontal development. The human dental follicle is a tissue of the tooth germ, which can easily be isolated after wisdom tooth extraction. Likewise, bovine dental follicles, cells of the human dental sac develop into the mature periodontium consisting of alveolar bone, the PDL and cementum. The dental follicle contains ectomesenchymal cells which are derived from the neural crest.

Non-Hematopoietic Mesenchymal Stem Cells

Today, there is an abundance of adult stem cells available for possible cell-based therapies. Since a long time, bone marrow-derived mesenchymal stem cells have been studied and discussed for research and therapeutics. These cells are in close vicinity to hematopoietic stem cells, which have successfully been used to treat certain types of leukemia for many years. Non-hematopoietic bone marrow- derived mesenchymal stem cells are also known as "bone marrow stromal cells (BMSCs)", as described decades ago.[17] 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.[18] Mesenchymal stem cells are capable of differentiating into osteoblasts, chondrocytes or retinal cells, which means a trans differentiation into cells of at least two different germ layers.[19]

APPLICATIONS IN DENTISTRY [20, 21]

Regrowing Dental Enamel From Cultured Cells

The regeneration of enamel is clearly more problematic than that of dentin and bone. The basic structural unit of enamel is enamel rod, which is tightly packed and mechanically adherent to other rods, providing high resistance to stress fractures. The interwoven architecture of enamel crystals provides both strength and protection for the tooth. The enamel organ epithelium, including the ameloblasts (progenitor cells), remains as a protective layer on the tooth crown only until eruption, as they undergo apoptosis while elaborating the enamel matrix and are lost by the time the enamel is fully formed. Therefore, in contrast to dentin, enamel does not regenerate after traumatic injury because the progenitor cells are no longer present.

Regeneration Of Dentin

Dentin is mineralized tissue having great deal of similarity to bone. It does not turn over throughout life, as bone but has limited repair capacity maintained by a precursor population, associated with pulp tissue that has ability to mature into odontoblasts. Dental pulp stem cells (DPSC's) were transplanted with hydroxyapatite in immunocompromised mice; they generated dentin like structure with collagen fibers running perpendicular to the mineralizing surface and also contained dentin sialophosphoprotein. This newly formed dentin was lined with odontoblast like cells which surrounded an interstitial tissue i.e. reminiscent of pulp with respect to the organization of the vasculature and connective tissue.[22]

Formation Of Cementum And Regeneration Of Root

Cultures of primary human cementum derived cells (HCDC's) have been established from healthy teeth using a collagenase pretreatment, with these cells discrete colonies containing cells with fibroblast like morphology are formed and when these colonies become sufficiently large, cells from individual colonies were isolated and cultured. The presence of cementoblast progenitors in cultures of bovine dental follicle cells has been reported and their differentiation capacity has been demonstrated. Bovine dental follicle cells (BDFC) obtained from tooth germs by collagenase digestion were compared with bovine alveolar bone osteoblasts (BAOB) and bovine periodontal ligament cells (BPDL) in vitro and in vivo. To elucidate the differentiation capacity of BDFC in vivo, cells were transplanted into severe combined immunodeficiency (SCID) mice and analyzed after 4 weeks.

NEAR FUTURE OF DENTAL STEM CELLS[23]

Pulp Regeneration—The use of stem cells to regenerate dental pulp tissues is being studied as an alternative method to conventional root canal treatment.

Cranial Defects—Human dental stem cells isolated from deciduous teeth were useful for correcting large cranial defects in rats, providing a promising model for reconstruction of large cranial defects in craniofacial surgery.

Long-Term Prospect- *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.

ETHICAL CONCERNS [11]

Stem cell research is controversial not because of its goals, but because of the means of obtaining some of its cells. Research involving most cells, such as derived from adult tissues and umbilical cord blood, is uncontroversial, except when its effectiveness as an alternative to embryonic stem cells is debated. The crux of debate centers on embryonic stem cells, which enables research that may facilitate the development of medical treatments and cures but require the destruction of an embryo to derive the stem cells. In addition, because cloning is one method of producing embryos for research, the ethical issues surrounding cloning are also relevant. The American Association for the Advancement of Science (AAAS) and the Institute for Civil Society (ICS) recognize that there are varied social, political, ethical and religious viewpoints to be considered in discussions about the scientific use of tissue from human embryos and fetuses.

CONCLUSION

Making an entire tooth with enamel and dentin structures *in vivo* is a reality and not a utopia. Recently, a new approach has been proposed for growing teeth in the mouse mandible in which epithelial and mesenchymal cells were sequentially seeded into a collagen gel drop and then implanted into the tooth cavity of adult mice. With this technique the presence of all dental structures such as odontoblasts, ameloblasts, dental pulp, blood vessels, crown, periodontal ligament, root and alveolar bone could be observed. Thus, the implantation of these tooth germs in the mandible allowed their development, maturation and eruption, indicating that stem cells could be used in the future for the replacement of missing teeth in humans.

REFERENCES

1. www.stemcells.nih.gov/info/basics/pages.aspx (Last accessed on 20-11-2013).

2. Smith A. A glossary for stem-cell biology. Nature 2006; 441: 1060.

3. Thomson JA, Itskovitz-Eldor J, Shapiro SS, et al. Embryonic stem cell lines derived from human blastocysts. Science 1998; 282:1145–1147.

4. www.sciencedaily.com/terms/adult stem cells.htm (Last accessed on 20-11-2013)

5. Karaöz E, Doğan BN, Aksoy A, et al. Isolation and in vitro characterisation of dental pulp stem cells from natal teeth. Histochem Cell Biol. 2010; 133:95-112.

6. Huang AH, Chen YK, Lin LM, et al. Isolation and characterization of dental pulp stem cells from a supernumerary tooth. J Oral Pathol Med. 2008; 37:571-574.

7. Baksh D, Song L, Tuan RS. Adult mesenchymal stem cells: characterization, differentiation and application in cell and gene therapy. J Cellular and Molecular Med 2004; 8 :301-6

8. 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 USA 2000; 97:13625–13630.

9. Kerkis I, Kerkis A, DozortsevD, Stukart-ParsonsGC, MassironiSM, Pereira LV, Caplan AI, Cerruti HF (2006) Isolation and characterization of a population of immature dental pulp stem cells expressing OCT-4 and other embryonic stem cell markers. Cells Tissues Organs 184:105–116.

10. Miura M, Gronthos S, Zhao M, Lu B, Fisher LW, Robey PG, Shi S.SHED: stem cells from human exfoliated deciduous teeth. ProcNatlAcadSci U S A. 2003 May 13; 100 (10):5807-12. Epub 2003 Apr 25.