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Stem Cells - Pavement to Periodontal Regeneration

Medical Science

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ABSTRACT

Periodontal regeneration is considered to be biologically possible but clinically unpredictable. Stem cells also known as "progenitor" or "precursors" cells are defined as clonogenic cells capable of both self-renewal and multi-lineage differentiation. Stem cells present a potentially unlimited capacity of autoreplication and they are capable of generating one or more cell lineages that are highly differentiated, depending on their replication potential. Sources of stem cells include: Adult dental pulp stem cells, Stem cells from dental follicle, Bone marrow derived mesenchymal stem cells, Stem cells from human exfoliated deciduous tooth, Periodontal ligament stem cells, Adipose derived stromal cells. This review provides a brief insight about stem cell basics, the state of art in human dental stem cell research and their potential role in periodontal regeneration.

INTRODUCTION:

Periodontitis is an inflammatory response in the periodontal tissues induced by microorganisms in dental plaque which contribute to tissue destruction, bone loss, and eventually tooth loss. The hallmark of inflammatory periodontal disease is connective tissue damage.

The goal of the treatment is to restore periodontal tissues affected by disease to their original architectural form and function. But, periodontium has a limited capacity for regeneration. Hence, therapeutic intervention becomes necessary to induce regeneration. Various conventional regenerative procedures have been pursued to regenerate lost tooth support such as bone autografts, allografts, or cell occlusive barrier membranes. However, these conventional regenerative procedures that are used either alone or in combination have limitations in attaining complete and predicable regeneration, especially in advanced periodontal defects.

Recent advances in stem cell biology and regenerative medicine have presented opportunities for tissue engineering as well as gene-based approaches in periodontal therapy.

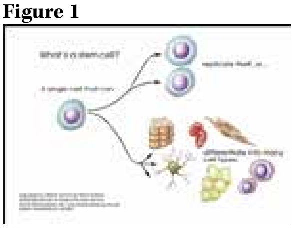
WHAT ARE STEM CELLS??

Stem cells are generally defined as clonogenic cells capable of both self renewal and multi-lineage differentiation. One daughter cell remains as a stem cell, while other becomes more committed to form a particular cell type (a "committed progenitor") by a process called asymmetrical cell division.

A cell must satisfy three main criteria to be classified as a stem cell:

The cell is not committed to differentiate into a single cell type It can divide without limit During cell division each daughter cell can choose whether to commit to differentiation into single cell type or to remain as a stem cell

Figure 1



STEM CELLS POTENCY

1.Totipotent: The capacity to differentiate into all cell types, including extra embryonic tissues.

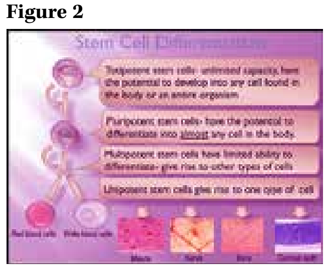
2.Pluripotent: The ability to differentiate into almost all cell types. These cells lack the capacity to contribute to extra embryonic tissues and therefore cannot develop into a fetal or an adult animal. .

3.Multipotent: The potential to give rise to cells from multiple but a limited number of lineages.

4.Oligopotent: The capacity to differentiate into a few cell types.

5.Unipotent: The ability to differentiate into one type of cell

Figure 2

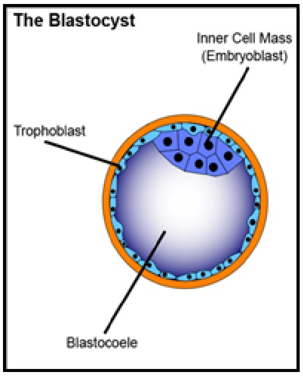


TYPES OF STEM CELLS

According to their origin and differentiation potential, stem cells are classified into embryonic stem cells and adult stem cells

1.EMBRYONIC STEM CELLS- derived from a four-or five-day-old human embryo, which is in the blastocyst phase of development. The stem cells from inner cell mass of blastocysts (embryoblast) are pluripotent and from outer cell mass (trophoblast) are totipotent. Human embryonic stem cells are unique as they can be maintained in an undifferentiated state in vitro for an indefinite period of time, while retaining their ability to differentiate into all types of specialized cells in the body. Though these cells have been demonstrated to produce approximately 220 different types of cells within the human adult body, its use has been restricted to the research field because of ethical concerns and the risk of tumorogenecity and teratoma formation.

Figure 3

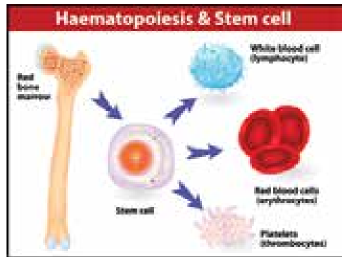


2.ADULT STEM CELLS (SOMATIC STEM CELLS) -Adult or somatic stem cells exist throughout the body after embryonic development and are found insight of different types of tissues. They remain in a quiescent or non-dividing state for years until activated by disease or tissue injury. Unfortunately, adult stem cells are present in miniscule quantities and this can present difficulty for identifying and isolating them in numbers great enough to use therapeutically. Because, adult stem cells are not as young as embryonic stem cells; they contain more DNA abnormalities acquired with age. They are generally multipotent stem cells. The most common source of adult stem cells is the bone marrow, which contains hematopoietic stem cells and bone marrow stromal cells or mesenchymal stromal/stem cells.

Hematopoietic stem cells (HSC_s)

These cells can be derived from various sources. Umbilical cord blood stem cells are stem cells collected from the umbilical cord at birth that can produce all of the blood cell in the body (hematopoietic).

Figure 4



Mesenchymal stem cell (MSC_s)

Mesenchymal stem cells called "Bone marrow stromal stem cells ($BMSC_s$) in 1998 by **Owen** and **Friedenstein** later coined the term "mesenchymal stem cells" (MSC_s) in 2001 by **Caplan.** Because of their differentiation potential, bone marrow mesenchymal stem cells have been used in various phases of clinical application. Mesenchymal stem cells have also been shown to form cementum, periodontal ligament and alveolar bone in vivo after implantation into periodontal defects in beagle dogs, suggesting that bone marrow may be a useful source of mesenchymal stem cells for periodontal regeneration.

SOURCES OF DENTAL STEM CELLS

The main differentiation potential of dental stem cells lies within the formation of dentin or periodontium associated tissues, whether these cells are derived from pulp, PDL or dental follicle.

DENTAL PULP STEM CELLS (DPS_s)	1st human dental stem cells. Isolated from dental pulp tissue of extracted third- molar teeth. More proliferative than $BMSC_s$. Odontoblastic differentiation potential is the important feature of pulp cells. The use of autologous $DPSC_s$ for the treatment of an alveolar bone defect following wisdom tooth extraction, showed consistently enhanced regeneration of the bone defect (d'Aquino R , Rosa A 2009).
STEM CELLS FROM HUMAN EXFOLIATED DECIDUOUS TEETH (SHED)	It contains multipotent stem cells. More proliferative than $BMSC_s$ and $DPSC_s$. Higher capability for osteogenic and adipogenic differentiation than $DPSC_s$ in vitro (Wang X, 2012). SHED cells induced surrounding recipient tissues to generate bone when they are transplanted into an immunocompromised mouse (Miura M, 2003).
STEM CELLS FROM APICAL PAPILLA (SCAP)	$SCAP_s$ are likely to be less differentiated than $DPSC_s$, Greater capacity for dentin regeneration than $DPSC_s$ In addition, they have the capability to form typical dentin pulp like complex when they are transplanted into immunocompromised mice in an appropriate carrier matrix.
PERIODONTAL LIGAMENT STEM CELLS ($PDLSC_s$)	Isolated from the root surface of extracted teeth. Differentiate into cells or tissues very similar to the periodontium. It contains a subpopulation of stem cells capable of differentiating into cementoblast/ cementocytes and collagen- forming cells in vivo. PDL stem cells transplanted into immunocompromised mice and rats demonstrated the capacity for tissue regeneration and periodontal repair. Transplanted human $PDLSC_s$ integrated into the PDL and attached to both the alveolar bone and cementum surfaces. These finding imply a potential functional role of human $PDLSC_s$ for periodontal regeneration. Autologous human progenitor cells form periodontal ligament may enhance tissue regeneration in patients with periodontitis (Fing F, Akiyama K, 2010).

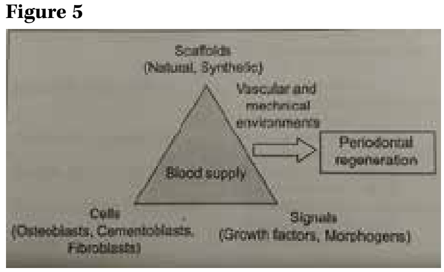
STEM CELLS AND TISSUE ENGINEERING

Tissue engineering is an interdisciplinary field of science based on principles of cell biology, development of biological substitutes that replace the damaged or lost tissues. The goal of tissue engineering is to promote healing, and ideally, true regeneration of tissues.

Tissue engineering triad

Conductive scaffold/ Extracellular matrix
Progenitor /stem cells
Inductive morphogenic signals

Figure 5



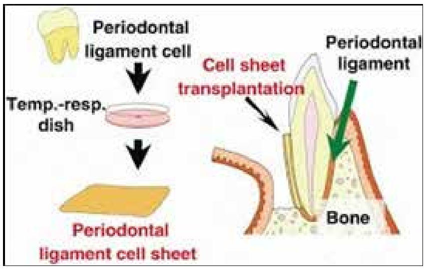
POTENTIAL APPLICATION OF STEM CELLS IN TISSUE ENGINEERING:

Cell transplantation using autologous cells (dental cell seeding attempts) have attempted to regenerate the periodontal tissues. The target tissue in the laboratory by culturing and proliferating mesenchymal cells together with scaffolds, before transplanting them into the body.

Developement of temperature responsive culture dishes by grafting a polymer poly (N- isopropylacrylamide) onto tissue culture graded polystyrene dishes by irradiation with an electron beam. This dish allowed intact cells with preserved extracellular matrix proteins and normal cell function to be harvested with just low temperature treatment (32 C fully hydrated). This has evolved novel strategy called " cell sheet engineering" which produces tissue without specific scaffold (Okano T, Bae YH 1990).

Authors	Conclusion
Akizuki T, Oda S 2005	Demonstrated periodontal regeneration after application of periodontal ligament cell sheet in beagle dogs.
Hasegawa M, Yamato M 2005	Assesed the ability of PDL cell sheets to regenerate the periodontal ligament tissue and demonstrated its usefulness in periodontal tissue regeneration.
Flores MG, Yashiro R 2008	Found that transplanted PDL cell sheet cultured with osteogenic induced periodontal tissue regeneration containing an obvious cementum layer and sharpey's fiber.
Huang SY, Zhang DS 2010	Set forward a hypothesis of transplanting PDL cell into the implant beds before inserting the implants.

Figure 6



CONCLUSION

The identification of stem cells in periodontal ligament with the ability to achieve new attachment formation in vivo holds promise to the development of novel, more effective approaches to periodontal regeneration and reconstructive therapy. In order to achieve this, studies on both embryonic stem cells and adult stem cells should continue as a part of collective effort to expand our knowledge on how cells function and what fails in the disease process. To summarize, the promise of stem cell therapy is an exciting one, but significant technical hurdles remain, which need to be overcome through years of intensive research.

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