Tissue Engineering : A Breakthrough in Endodontics

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Pulpal regeneration after tooth injury is difficult to accomplish the reason why infected pulp requires root canal therapy or tooth extraction. Tissue engineering aims at the regeneration of affected or lost pulp tissue using stem cell therapy.

The dental pulp contains progenitor/stem cells, which can proliferate and differentiate into dentin-forming odontoblasts . Damaged odontoblasts can be replaced by newly generated populations of odontoblasts derived from stem cells from pulp. Following physiological stimulation or injury, such as caries and operative procedures, stem cells in pulp may be mobilized to proliferate and differentiate into odontoblasts by morphogens released from the surrounding dentin matrix. Tissue engineering with the triad of dental pulp progenitor/stem cells, morphogens,and scaffolds may provide a useful alternative method for pulp-capping and root canal treatment .

In stem cell therapy, the technique for manipulation of the growth of the isolated pulp progenitor/stem cells and induction of three-dimensional tissue formation invitro needs to be developed.

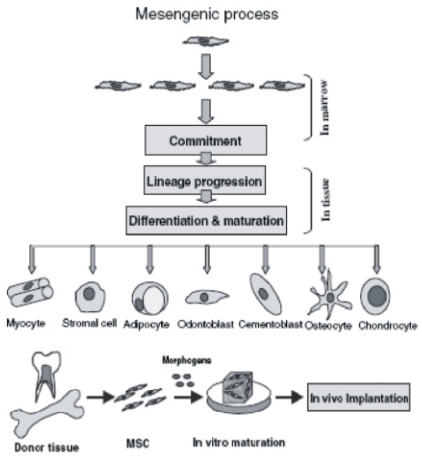
Stem Cells

Stem cells are primal undifferentiated cells that retain the ability to divide and differentiate into other cell types. Stem cells differ from other kinds of cells in the body.

All stem cells regardless of their source have three general properties: they are capable of dividing and renewing themselves for long periods; they are unspecialized; and they can give rise to specialized cell types.

There are Two Types of Stem Cells

1. Embryonic stem cells, as their name suggests, are derived from embryos. Specifically, embryonic stem cells are derived from embryos that develop from eggs that have been fertilized in vitroin an in vitro fertilization clinic and then donated for research purposes with informed consent of the donors. They are not derived from eggs fertilized in a woman's body.



2. Adult stem cell is an undifferentiated cell found among differentiated cells in a tissue or organ, can renew itself, and can differentiate to yield the major specialized cell types of the tissue or organ. The primary roles of adult stem cells in a living organism are to maintain and repair the tissue in which they are found.

Goals of Stem Cell Therapy in Tissue Engieering

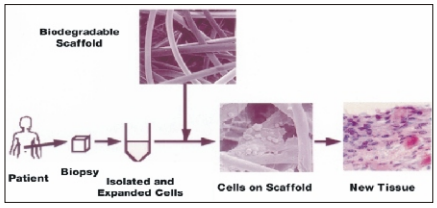
- Proliferate extensively and generate sufficient quantities of tissue.
- Differentiate into the desired cell type(s).
- Survive in the recipient after transplant.
- Integrate into the surrounding tissue after transplant.
- Function appropriately for the duration of the recipient's life.
- Avoid harming the recipient in any way.

Source of Pulp Stem Cells

The source of odontoblastoid cells that repair dentinal bridges has proved to be controversial. Initially, the replacement of irreversibly injured odontoblasts by predetermined odontoblastoid cells that do not replicate DNA after induction was suggested, researchers proposed that the cells within the subodontoblast cell rich layer of Hohl adjacent to odontoblasts differentiate into odontoblastoids. The purpose of these cells seem to be limited to an odontoblast supporting role, however because the survival of these cells is linked to the survival of the odontoblasts, and no proliferative or regenerative activity was observed.

Stem Cell Therapy

Stem cell therapy is one of the most promising area s of tissue engineering because the transplantation of the materials that contain pulp stem cells grown in the laboratory provides an an inductive means to regenerate new tooth tissues. The transplantation of odontoblastoid stem cells into teeth accomplish regeneration removes the problem of delivering growth factors and genes into host target cellsand waiting for the target cells to differentiate. Recent studies focused on evaluating the use of human odontoblastoid stem cells transplantation for regeneration of oraltissues in conjunction with in vitro tissue engineering to produce regenerative biomimetic materials.



Tissue Regeneration Using Stem Cell Therapy

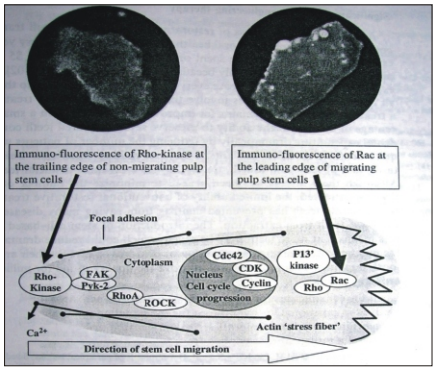


Figure: The molecular regulation of pulpal stem cell migration. The migration of dental pulp stem cells seems to be controlled by a balance in the Rac/Rho kinase activation. When Rac is activated, the cell migrates forward. When Rho kinase is activated, the cell remains fixed in position. The signaling pathways of Rac/Rho Kinase are shown here.

A major focus of contemporary studies in developmental biology has been to delineate the biological cues that drive stem cell proliferation and differentiation. Four signaling protein families that govern patterning and morphogenesis have been identified:

- Fibroblast growth factors,
- Hedgehog proteins,
- Bone morphogenetic proteins,
- Wingless- and int-related proteins (Wnts).

Proteins from each of these families are now being evaluated for their utility for stem cell based engineering of craniofacial defects. Recently, these applications have been extended to treat the diseases of endodontic origin.

Naturally derived collagen or synthetic materials such as polyglycolic acid (PGA) are used as a scaffold for attachment and guidance of cells. The pulp derived fibroblasts adhering to the PGA fibers can proliferate and form a new tissue similar to that of native pulp The synthetic matrices, however, must undergo degradation simultaneously with the new tissue formation by the cultured cells.

Bone morphogenetic proteins (BMPs) have been implicated in tooth development, and the expression of BMP2 is increased during the terminal differentiation of odontoblasts. Beads soaked in human recombinant BMP2 induce the mRNA expression of Dspp, the differentiation marker of odontoblasts after implantation onto dental papilla in organ culture. BMP2 also induces a large amount of reparative dentin on the amputated pulp in vivo (Nakashima, 1994a). It has been suggested that BMP2 may regulate the differentiation of pulp cells into odontoblastic lineage and stimulate reparative dentin formation (Nakashima and Reddi, 2003).

Future Directions

The last decade has proved to be an exciting time for pulp biology and has led to rapid advances in our knowledge of repair in this tissue. At the start of a new millennium, the use of biological molecules for the development of novel restorative treatment modalities in clinical dentistry is in sight. These approaches have potential applications in unexposed cavity preparations for protection of the pulp from harmful effects of dental materials by increasing the residual dentin thickness through reactionary dentinogenesis, as well as in exposed pulp situations for restoration of the structural integrity of the dentin wall by reparative dentinogenesis. In the severely compromised pulp, it may even be possible to use biological approaches in endodontic therapy to seal the root canal.

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