Stem Cells in Dentistry : An Overview

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Abstract

Stem cells are a booming field for the research and in dentistry, recent discoveries have isolated dental stem cells from the pulp of the deciduous and permanent teeth, from the periodontal ligament, and an associated healthy tooth structure, to cure number of diseases. This review highlights about the origin of stem cells, their properties, characteristics, different types with emphasis on their potential applications in field of dentistry.

Introduction

Stem cells are immature, undifferentiated cells that can divide and multiply for an extended period of time, differentiating into specific types of cells and tissues. They are defined as cells that self-replicate and are able to differentiate into at least two different cell types. Both criteria must be present for a cell to be called a 'stem cell'.[1]

When called into action following an injury, a stem cell self-renews undergoes cell division and gives rise to one daughter stem cell and one progenitor cell. A progenitor cell is an intermediate cell type formed before it achieves a fully differentiated state. It is regarded as committed to differentiating along a particular cellular developmental pathway of stem cells.

Stem cell → Stem cell + Progenitor cell → Differentiated cell[2]

Their self-renewal potential and unrestricted ability to generate new tissues make these cells an attractive cellular source for cell-based regenerative therapies.[3] Over the last few years, dentistry has begun to explore the potential application of stem cells and tissue engineering towards the repair and regeneration of dental structures. This review discusses the state of the science with regard to dental stem cells and presents a prospectus for the field of stem-cell based dentistry.

Characteristics of Stem-Cells

1. **Totipotency:** generate all types of cells including germ cells (ESC's)
2. **Pluripotency :** Generate all types of cells expect cells of embryonic membrane.
3. **Multipotency :** Differentiate into more than one mature cell(MSC).
4. **Self-renewal:** Divide without differentiation and create everlasting supply.
5. **Plasticity:** MSC's have plasticity i.e can expand beyond its potential irrespective of the parent cell from which it is derived and can undergo differentiation.

Historical Background

The term stem cell was proposed for scientific use by Russian histologist Alexander Maksimov in 1908. While research on stem cells grew out of findings by Canadian scientists in the 1960s.[4] In 1998 the first embryonic stem cell line was derived at university of Wisconsin-Madison.[5] In the year 2003 Dr. Songtao Shi who is a paediatric dentist discovered baby tooth stem cells by using the deciduous teeth of his six year old daughter, he was luckily able to isolate, grow and preserve these stem cells regenerative ability, and he named them as SHED (Stem cells from Human Exfoliated Deciduous teeth).[6] In 2006 Kerkis reported discovery of Immature Dental Pulp Stem Cells (IDPSC),[7] "a pluripotent sub-population of Dental Pulp Stem Cells (DPSC) using dental pulp organ culture. In 2007 DPSC conducted the 1st animal studies on bone regeneration[8-10] and dental end uses.[7,11,12]

Types of Stem Cells

In general, stem cells are broadly classified as embryonic stem cells (ESCs) and adult stem cells . Embryonic stem cells (ESC's) are derived from the inner mass of the blastocysts which is an early stage of an embryo. ASCs are present in adult tissues ,have restricted ability to proliferate .[13]

Embryonic Stem Cells (ESC's)[2]

They are totipotent cells virtually capable of differentiating into any type of cell and are considered immortal as they can be propagated and maintained in undifferentiated state indefinitely .But there is use is controversial due to the need to destroy an embryo to harvest them, thereby, raising moral and ethical concern. Further it is difficult to control their growth and pose risk of homogenecity and have only remained an excellent platform for research.

Adult Stem Cells

They are multipotent-capable of differentiating into more than one cell type but not all cell types.[14] They can be used later to regenerate tissue by transplantation into same (autologous transplant) or another individual (allogenic transplant). Depending on their origin, adult stem cells can be further classified as hemopoetic stem cells (HSC's) and mesenchymal stem cells (MSC's).[2]

Stem Cells in Dental Tissues

Stem cells have also been found in several dental tissues. One of the first tooth-related stem cells types was found in the pulp of permanent teeth and was named dental pulp stem cells.

Dental Pulp Stem Cells (DPSCs)

DPSCs were isolated from the human pulp tissue for the first time in 2000 by Gronthos et al.[15] The regenerative capacity of the human dentin/pulp complex enlightens scientists that dental pulp may contain the progenitors that are responsible for dentin repair. DPSC, generate a dentin, pulp like complex that is composed of mineralized matrix with tubules lined odontoblasts. Studies have shown that DPSCs also differentiate into adipocytes and neural like cells.[16]

Stem Cells From Human Exfoliated Deciduous Teeth (SHED)

Stem cells from human exfoliated deciduous teeth were isolated for the first time in 2003 by Miura et al who confirmed that they were able to differentiate into a variety of cell types to a greater extent than DPSCs, including neural cells, adipocytes, osteoblast-like and odontoblast-like cells, and can also be retrieved from a tissue that is disposable and readily accessible.[17] In vivo SHED cells can induce bone or dentin formation but, in contrast to dental pulp, DPSC failed to produce a dentin-pulp complex. The main task of these cells seems to be the formation of mineralized tissue, which can be used to enhance orofacial bone regeneration. Thus, they are ideally suited for young patients at the mixed dentition stage who have suffered pulp necrosis in immature permanent teeth as a consequence of trauma.[18]

Stem Cells from the Apical Papilla (SCAP)

Dental stem cells isolated from human teeth found at the tooth root apex are known as SCAP. SCAPs can only be isolated at a certain stage of tooth development ,but 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 .Because of their higher proliferative capacity, they are suitable for inducing roots. They can generate odontoblast like cells and produce dentin, thus help in formation of root dentine as in apexogenesis.[13]

Stem Cells to be Applied in Regenerative Strategies of the Endodontium

Two populations of stem cells involved in tooth formation are the epithelial stem cells and the mesenchymal stem cells; the latter required for pulp dentin regeneration. Mesenchymal stem cells located in a perivascular niche in the dental pulp, periodontal ligament, dental follicle and bone marrow may be potential sources for cell based therapies in regenerating the tooth.[18]

Amongst various mesenchymal stem cells, BMSCs have served as the standard of comparison regarding multipotentiality and are the most extensively studied mesenchymal stem cells. BMSCs have demonstrated good ability to form tooth supporting periodontal structures like cementum, periodontal ligament and alveolar bone suggesting their potential use for treating periodontal diseases.[19] However, because of their limited potential to generate odontoblasts, their use in pulp dentin regeneration may be limited and remains to be further explored.

Potential Applications in Dentistry

The regenerative potential of adult stem cells obtained from various sources including dental tissues has been of interest for clinicians over the past years and most research is directed toward achieving the following-

- Regeneration of damaged coronal dentin and pulp.
- Regeneration of resorbed root, cervical or apical dentin, and repair perforations.
- Periodontal regeneration.
- Repair and replacement of bone in craniofacial defects.
- Whole tooth regeneration.

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. 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.[2] Pulp tissue regeneration involves either delivery of autologous/ allogenic stem cells into the root canals or implantation of the pulp that is grown in the laboratory using stem cells. Both these techniques will have certain advantages and limitations that need further research.[20]

A landmark study conducted by Gronthos et al. demonstrated both in vitro and in vivo in animals that dental pulp stem cells (DPSCs) were capable of forming ectopic dentin and associated pulp tissue.[2]

Periodontal Regeneration

Due to the complex structure of the periodontium (consisting of hard and soft tissues), its complete regeneration has always remained a challenge. Kawaguchi et al. demonstrated that the transplantation of ex vivo expanded autologous MSCs can regenerate new cementum, alveolar bone, and periodontal ligament in class III periodontal defects in dogs. Going a step further, periodontal ligament cells cultured in vitro were successfully reimplanted into periodontal defects in order to promote periodontal regeneration by Hasegawa et al. A subsequent study by the same group reported a similar approach in humans. This study reported firm evidence that stem cells can be used to regenerate a tissue as complex as the periodontium.[21]

Repair & Regeneration of Bone in Craniofacial Defects

Use of autologous bone graft is considered the best option for repair of craniofacial defects, but it has the limitation of donor sites. Use of skeletal or dental stem cells may one day be used to repair craniofacial bone and may provide a promising alternative approach for reconstruction of craniofacial defects.[13]

Whole Tooth Regeneration

A therapeutic option that was unthinkable a few years ago seems an achievable goal today. Even to this day, the replacement of missing teeth has limitations. Although, implants are a significant improvement over dentures and bridges, their fundamental limitation is the lack of natural structural relationship with the alveolar bone (absence of periodontal ligament). They rely on direct integration of bone on tooth surface which is indeed an unnatural relationship as compared with the natural tooth. Further, they are also associated with a lot of aesthetic, functional, and surgical limitations that affect their prognosis.[2] Bioengineered tooth germ is regenerated from interactions between the dissociated epithelial and mesenchymal cells of the mice-derived molar tooth germ. Two means of regenerating teeth include conventional tissue engineering, in which the application of cells in a carrier material in vitro under the influence of a stimulus leads to tissue regeneration. The second process of tooth regeneration is using dental epithelium and mesenchymal cells in vivo after direct implantation, which is based on knowledge of general embryogenesis and physiological tooth development during childhood.[13]

Thus, stem cell therapy has considerable promise in dentin regeneration as well as whole tooth regeneration. Currently a huge amount of active medical research is underway for using these stem cells for therapy applications.

Conclusion

Stem cell-based regenerative therapies certainly hold much potential in the treatment of medical and dental conditions. In conclusion, stem cell-based dental tissue regeneration is a new and exciting field that has the potential to transform the way that we practice dentistry. Its future will depend on the understanding of the biology of the cells that will be used to regenerate tissues, and its boundaries will be demarcated by an in-depth knowledge of the potential risks and likely benefits associated with each regenerative procedure. The field of stem cell-based regenerative dentistry is complex and multidisciplinary by nature. Progress will depend on the collaboration between clinicians and researchers from diverse fields (e.g. biomaterials, stem cell biology, endodontics) working together toward the goal of developing biological approaches to regenerate dental and craniofacial tissues.

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