REVIEW ARTICLE

Stem Cells from Human Exfoliated Deciduous Teeth- A Boon to Dentistry

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ABSTRACT

Stem cells have a property of self renewal and replication. Dental stem cells are considered as an important and valuable source of stem cells which can be collected from healthy pulp. Stem cells from human exfoliated deciduous teeth (SHED) has now attracted scientist and researchers as it has important role in regeneration and tissue engineering of the lost or damaged tissues. Mesenchymal stem cells (MSCs) are multipotent stem cells having the capacity to divide and differentiate into a variety of cell types. MSCs mainly include Stem cells from human exfoliated deciduous teeth (SHED), periodontal ligament stem cells (PDLSC), dental pulp stem cells (DPSC), stem cells from apical papilla (SCAP), dental follicle stem cells (DFSC) and bone marrow derived mesenchymal stem cells (BMSC). The current review focuses on all the possible details, advances and clinical application of stem cell from human exfoliated deciduous teeth.

KEYWORDS: Stem cells, Stem Cells From Human Exfoliated Deciduous Teeth, Culture, Regeneration

INTRODUCTION

Stem cells are one of the most promising treatment modality for many diseases because of its ability to replicate and produce cells of different types as per the requirement.[1] They are helpful in repairing of the injured tissue as well as its regeneration. Stem cells of dental origin have also been proven to be successful in such type of injuries. Their nomenclature is according to the site from where they are isolated. Dr. Songtao Shi in 2003 discovered stem cells from deciduous teeth of his six years old daughter and after that referred it as stem cell from human exfoliated deciduous tooth. In living organisms, stem cells are important for many reasons. Stem cells form a reservoir for repairing of the cells throughout the life span of a particular organism.[2]

TYPES OF STEM CELLS

Stem cells mainly can be grouped under following heads:

a. **Mesenchymal type of stem cells:** It is useful for repairing of the spinal cord injuries. Stem cells derived from the oral and maxillofacial regions mainly belong to the mesenchymal type of stem cells. These mainly include stem cells like SHED, PDLSC (periodontal ligament stem cells), DFSC (dental follicle stem cells), DPSC (Dental pulp stem cells) and SCAP (stem cells from apical papilla).[3]

According to the position in the tooth, stem cells are named as:

- Stem cells from human exfoliated deciduous teeth (SHED)[4]
- Periodontal ligament stem cells (PDLSC)[5]
- Dental pulp stem cells (DPSC)[6]
- Stem cells from apical papilla (SCAP)[7]
- Dental follicle stem cells (DFSC)[8]
- Bone marrow-derived mesenchymal stem cells (BMSC)[9]

b. **Human adipogenic type of stem cells:** these are the derivatives of embryonic mesoderm and are capable of formation of bone, cartilage, muscles, etc. they are useful in treating various cardiovascular conditions because of its angiogenic properties. Similarly, it has been proven to be successful in healing the chronic wounds.[1,10]

c. **Osteoblastic type of stem cells:** Human adipogenic type of stem cells differentiates into Osteoblasts that could help in healing and repair of malunion or non union type of fractures. Lee et al. in his study the concluded that bone formation occurs due to the differentiation of the human adipogenic type of stem cells due to osteoblastic lineages.[10,11]

d. **Chondrocyte stem cells:** These stem cell possess a similar kind of mechanism of action as that of an osteoblastic type of stem cells. They are useful in the growth of bone as well as cartilages.[1]

PROPERTIES OF SHED

SHED is considered to be a unique and distinctive type of

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cell present in the human body with an ability to develop into several different type of cells. When a stem cell divides, each new cell has the potential to either remain a stem cell or become another type of cell with a more specialized function.[12] Stem cells have the following three general properties:

- Stem cells are unspecialized type of cell
- Stem cells have a capacity to divide itself
- Stem cells can renew themselves for long periods of time
- Stem cells can become specific specialized cell types of the body.
- Lineage property- Differentiation into different cell types by adult stem cells is unusual from the cells expected predicted lineage.[12]

SCREENING AND COLLECTION OF SHED

The technique involved in the collection of SHED is relatively easy and a noninvasive procedure.

1. **A collection of the tooth:** Immediate placement of the exfoliated teeth in the normal saline solution, followed by referral to the dentist working with the bank. The pulp of the tooth exfoliated may be of two different colors. Red color which may suggest normal blood flow in the pulp up to the time of its removal which may indicate a proper viability of the cells. On the other hand, gray color pulp is an indicative of insufficient, nonviable recovery of stem cells. The contraindications for the collection of the stem cells include the teeth associated with a cystic lesion, tumors or pulpal or periapical abscess. The samples containing stem cells should be placed in a screw tight vial with appropriate media during transportation.[1]

2. **Transportation:** The pulp tissue is transported in a solution which should provide sufficient nutrients as well as maintaining the stem cells in its original form and prevent it from drying. The appropriate solution which may fulfill the above criteria is "hypotonic phosphate buffered saline".[1]

Stem cells are very sensitive to temperature and time. Hence attention should be kept for transportation of the tooth. Transportation of avulsed teeth for maximum recovery of stem cells is done in Store-A-Tooth device from the dental clinic to the laboratory. Within 40 hours the sample should reach the storage facility.[13]

3. **Isolation of the stem cells:** Steps that are followed for isolation involves:
   a. Washing with PBSA - Dulbecco's Phosphate Buffered Saline solution.
   b. Povidone Iodine- for disinfection.
   c. Washing again with PBSA.
   d. Centre of the tooth rich in stem cells can be collected with the forceps (sterile) or can be flushed out.
   e. Collagenase Type I, Dispase or Trypsin- EDTA at 37ºC are used for tissue digestion for about an hour. Cells are passed through 70 micrometer filter for obtaining a single cell suspension.
   f. Cultivation and culture of the cells can be done in mesenchymal stem cell medium.[1]

4. **Storage of the stem cell:**
   a. CRYOPRESERVATION (cryo – cold): It is considered to be a very effective method for maintaining the viability of the transported stem cells by cooling to subzero temperatures, typically –196°C (*neelampari)* where the biological activity concludes leading to cell death. Procedure involves slow cooling at 1 to 2 °C/min in the presence of a cryoprotectant, Dimethyl SulphOxide (DMSO) to avoid the damaging effects of intracellular ice formation is considered standard.[1]
   b. MAGNETIC FREEZING: in this method, a weak magnetic field is applied to the water and tissues thereby lowering the freezing point of body up to 6-7° C. It ensures distributed low temperature without the cell wall damage resulted by ice expansion and nutrient drainage due to capillary action, as caused by conventional freezing methods. Magnetic freezing is considered to be more reliable as well as relatively cheaper as compared with cryopreservation.[14]

CLINICAL APPLICATIONS OF STEM CELLS

a. **Bone regeneration**: Stem cells have been scientifically proven to have a capacity of bone regeneration. This property helps in correction of the craniofacial anomalies and defects. Also conditions such as Parkinson's disease, autoimmune diseases, musculoskeletal disorders etc. can be successfully treated. SHED have a property of pulpal regeneration within the injured tooth. In a rat study carried out by Costa A et al. in 2008 concluded that the stem cells recovered from the human pulp could successfully reconstruct the cranial defects.[1,15]

b. **Tissue Regeneration**: Stem cells are also useful in dentin and pulpal regeneration. A study carried out by Bohl et al. in 1998 investigated the pulpal cells cultivated on PGA polyglycolic acid resulted in a tissue of higher density similar to the native pulp.[16] Nor et al. in 2006 concluded that seeding SHED on synthetic scaffolds placed in pulpal chamber gave rise to odontoblast like cells in immunocompromized mice. These findings suggested that pulp and dentin generation might also occur in the pulpless teeth.[15]

c. **Root formation**: Stem cells from apical papilla have also contributed in the continued root formation. Inspite of the intact pulp tissue in the canal, surgical removal of apical papilla in minipigs model resulted in incomplete root development. Further research is required to confirm the role of apical papilla in continued root formation.[15]

d. **Replantation and Transplantation**: In a study conducted by Andreasen et al. in 1995 and Kling et al. in 1986 investigated the alveolar bone and PDL ingrowth in the inner dentinal wall in a tooth with arrested root formation after replanting avulsed maxillary incisor suggesting the role of stem cells in replantation. Clinical studies conducted by Tsukiboshi et al. in 2002 have observed that transplanted tooth with minimal root formation will have minimum further root development after transplantation. Also in cases where a small amount of root is formed, it may continue or lead to its completion after transplantation.[15]

e. **Bio root engineering:** Stem cells from periapical follicle isolated from apical end of developing root of human third molars evaluated the application of these cells in PDL regeneration/cementum regeneration as well as for bio root engineering.[15]

LICENSED CORD BLOOD BANKS IN INDIA

There are number of Licensed Cord Blood Banks in India such as [17] Cordlife Sciences and Cryobanks International, Reliance Life Sciences- Delhi, Histostem- South Korea, Life cell- Chennai.

CONCLUSION

Human stem cells have a major effect in the development of human bodies. SHED are the stem cells obtained from exfoliated deciduous teeth which have an ability to divide and develop into a different type of stem cells. Stem cells represent an important and inseparable part of regenerative dentistry and medicine. Further research along with a long-term follow-up of the patient is warranted.

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