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Stem Cells: A Step Ahead in Regenerative Dentistry with Accent on Orthodontics

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Author's contribution

The sole author designed, analyzed and interpreted and prepared the manuscript.

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ABSTRACT

Stem cells are undifferentiated cells that can give rise to different cell types for performing several specialized functions or remain undifferentiated. They have provided an upfront in various fields of dentistry. In Orthodontics, they provide a step ahead in the field of craniofacial research and development. This article provides an insight into the various aspects of stem cells including their advantages, disadvantages and future perspectives.

Keywords: Stem cells; bioroot engineering; bone regeneration; orthodontics.

1. INTRODUCTION

The term "stem cell" has roots as far back as 1868 in the works of German biologist Haeckel. Wilson coined the term stem cell. Russian Histologist Alexander Maksimov proposed the term Stem cell in 1908. Gronthos et al. [1] identified odontogenic progenitor population in adult dental pulp in 2000. Human exfoliated deciduous teeth (SHEDS) were discovered by Dr. Songtao Shi in 2003. Dr. Kerkis reported discovery of immature dental pulp stem cells (IDPSC) in 2006. Stemcells are generally defined as clonogenic cells with the capacity to both self-renew and give rise to differentiated cells [2].

Stem cell therapy provides an unique platform for research in terms of craniofacial defects,

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temporomandibular disorders, tissue engineering and most importantly the stem cell based therapies to treat the damage caused by congenital deformities, trauma, cancer, caries and periodontal disease.

2. PROPERTIES

There are few properties of stem cells that make them unique:

1. **Proliferation:** Stem cells have the unique ability of replicating themselves into millions of cells.
2. **Blank Cells:** Stem cells are basically unspecialized cells that have the capacity to give rise to specialized cells like heart, nerve, muscle e.t.c.
3. **Differentiation:** It is the property of stem cells to differentiate into specialized cells through various signaling processes.

3. CHARACTERSTICS OF STEM CELLS [3]

1. **Totipotency:** Produce all types of cells as well as germ cells (ESCs).
2. **Pluripotency:** Produce all types of cells apart from cells of the embryonic membrane.
3. **Multipotency:** More than one adult cell (MSC) is distinguished.
4. **Unipotency:** Produce one particular cell type.

3.1 Types

Stem cells are of two types.

3.1.1 Embryonic stem cells

In the year 1998, the first human embryonic stem cells were isolated. These are derived from embryos that have been fertilized in in vitro fertilization clinics and donated for research purpose. It is difficult to control it's growth due to their high expression of telomerase. In 1998, James Thompson of the University of Wisconsin-Madison proved that embryonic stem cells can be sustained indefinitely in the laboratory, creating hundreds of generations of identical stem cells.

3.1.2 Adult stem cells

These are multipotent cells that can give rise to specialized cells; nerve, cardiac e.t.c. They are immune by nature. These stem cells are sited in positions called NICHES. They are regulated by a protein BMI-1, Notch pathway, Sonic Hedgehog and the Wnt developmental pathway. They can be classified as:

a. Haematopoietic Stem cells
b. Non Haematopoietic Stem cells/ Mesenchymal cells.

3.2 Stem Cell Markers

Stem cells can be derived from deciduous, permanent and wisdom teeth.

STRO-1, a trypsin-resistant cell-surface antigen, is a commonly used dental stem cell marker for all dental mesenchymal stem cells [4].

3.3 Dental Implications

Stem cell lines are implicated in various craniofacial defects. The mesenchymal stem cells can be identified in human dental pulp as Dental pulp stem cells (DPSC), in exfoliated human primary teeth as stem cells from human Exfoliated deciduous teeth (SHED), and periodontal ligament as Periodontal ligament stem cells (PDLSC).

These cells have higher growth potential which can be employed for various tissue engineering strategies:

3.3.1 Dental Pulp Stem Cells (DPSC)

Dental Pulp Stem Cells can be derived from bone marrow stromal / stem cell [1,5]. These cells can be isolated by various methods:

3.3.1.1 Size sieved isolation

It is carried out by enzymatically treating the whole dental pulp tissue containing cells between 3 and 20 μm diametre in a solution of 3% collagenase Type I for one hour at 37℃. Then the cells are filtered and obtained for further culture and amplification.

3.3.1.2 Stem cell colony cultivation

It is carried out by enzymatic digestion of the dental pulp tissue is containing 50 or more cells that is further amplified for experiments.

3.3.1.3 Magnetic activated cell sorting (MACS)

It is an immune-magnetic method used for separation of stem cell populations based on their surface antigens (CD271, STRO-1, CD34, CD45, and c-Kit).

3.3.1.4 Fluorescence activated cell sorting (FACS)

It is a method of isolation of stem cells from cell suspension based on cell size and fluorescence.

3.3.2 Apical papilla derived stem cells (APDCS, also stem cells from apical papilla/SCAP)

Abe et al. first reported these cells from immature tip of the dental papilla of human developing third molars [6,7]. These cells can serve as a source of primary odontoblasts for root dentin formation [8,9].

3.3.3 Periodontal ligament stem cells

These cells can serve as a source of cementoblast like cells. They help in periodontal tissue regeneration [10].

3.3.4 Dental follicle progenitor cells

In 2002, these cells were first reported [11,12]. They serve as a source of cementoblast, osteoblast, periodontal ligament, adipogenic, osteogenic, neuronal lineage and periodontal tissue regeneration [13,14].

3.3.5 Stem cells from exfoliated deciduous teeth

These cells can serve as a source of neural cells, adipocytes, and odontoblasts [15-17].

4. METHOD OF STEM CELL GROWTH

The tooth is examined and ruled out for any infection. It is rinsed with antibiotics/saline solution and transferred to transportation tube/kit. Saline solution is added and the waiting period is 5 minutes. Before 48 hours, tube is sealed and transported under room temperature.

The steps in the laboratory as follows:

1. Dental curette is used to remove the pulp from the prepared tooth.
2. Markers are used to identify stem cells. Viable cells are separated by centrifugation process, later cryopreserved and retrieved.

Cell alive system (CAS) is the newer method of magnetic freezing where evens a weak magnetic field to water or cell tissue would lower the freezing point of the body by up to 6-7℃.

5. IN ORTHODONTICS

The application in Orthodontics ranges as:

1. **Repair of Alveolar Bone Defect:** Orthodontic treatment warrants extraction of premolars for correction of malocclusion [18]. During extractions, accidentally buccal plates can be lost leading to alveolar bone defect. These defects can be filled with stem cells to avoid the risk of dehiscence and periodontal issues after the spaces have been closed by retraction. Alveolar cleft osteoplasty can be successfully done with stem cells [19].
2. **Remodelling and Regenerating Oral Tissues:** Remodelling of the alveolar bones is important in regenerating tissues [20]. Stem cells play a pivotal role in controlling this phenomenon coupled by local signaling/growth factors and systemic hormones [21].
3. **Distraction Osteogenesis:** Stem cells can induce mobilization of osteoblastic and osteoclastic cells [22,23]. Stem cells can accelerate bone regeneration in the distraction gap and enhance consolidation [24,25].
4. **Temporomandibular Defects:** Degenerative bone diseases including TMJ defects can be bioengineered with stem cells [26,27]. Cells from various sources like articular cartilage cells, fibroblasts, mesenchymal stem cells have been used to reconstruct TMJ [28,29].
5. **Bioroot Engineering:** It is the amalgamation of stem cells from apical papilla (SCAP) and Periodontal ligament stem cells (PDLSCs).

5.1 Advantages in Orthodontics

5.1.1 Shorter treatment time

Embryonic stem cells have been differentiated into cartilage cells and implanted on artificially created cranial osseous defects [30].

Mesenchymal stem cells (MSCs) express and secrete various factors like (SDF‑1), (VEGF), (bFGF), (MMPs), and other cytokines that are important for angiogenesis. Various bioactive factors are secreted by the stem cells that suppress the local immune system, inhibit fibrosis, stimulate mitosis. Thus, by increasing the rate of healing and regeneration, treatment time can be reduced [31].

5.1.2 Periodontal health consideration

Orthodontic treatment is successful when the periodontium is healthy without any signs of diseases and defects [32]. Human PDLSCs get attached to the surfaces of the alveolar bone and tooth root when integrated into the PDL tissue [33].

Dental pulp stem cells (DPSCs) have the highest osteogenic potential among bone marrow mesenchymal stem cells (BMMSCs) and periosteal cells [34].

5.1.3 Lesser root resorption

External apical root resorption is the most common and undesirable sequelae of Orthodontic treatment [35]. Various derivatives of stem cells may be used prior to the treatment, to prevent root resorption or post treatment to repair the damage [36,37].

5.1.4 Patient benefits

Bone marrow mesenchymal stem cell (BM‑MSC)–treated wounds exhibit significantly accelerated wound closure, with increased re‑epithelialization, cellularity, and angiogenesis [38,39].

6. FUTURE PERSPECTIVES

6.1 Periodontal Regeneration

Periodontium can be regenerated successfully by transplantation of ex vivo prolonged autologous MSCs as shown by Kawaguchi et al. It is also confirmed by Hasegawa et al, that periodontal defects can be managed by reimplantation of these cells [40].

6.1.1 Regeneration of pulp and damaged coronal dentin

Dental Pulp Stem Cells (DPSCs) can form ectopic dentin and related pulp tissue as demonstrated by Gronthos et al. [41,42].

6.1.2 Tooth regeneration [43,44]

Three key elements are involved in tooth regeneration which include:

- Inductive morphogenes
- Stem cells
- Scaffold

Regeneration of tooth can be carried out by the following steps [45-47]:

First, the adult stem cells are harvested. Stem cells are arranged into a scaffold that provides provides optimized environment. Cells are instructed with targeted soluble molecular signals spatially and gene expression is read.

6.2 Replantation and Transplantation

It can be carried out via stem cell therapy.

6.3 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.

6.4 Stem Cell Banks

Cryopreservation or banking of stem cells maintains the viability of cells indefinitely. “During cryopreservation, the cells are put to sleep through a process called vitrification, in which the tissue is placed in liquid nitrogen at a temperature of –196 degrees Celsius. The cryopreservation process stops all cellular metabolism involving both cell growth and cell death [48,49]. The cells preserved today can be applied to future regenerative therapies.

7. CONCLUSION

Stem cells play an important role starting from embryonic development through adulthood. Their potential needs to be unlocked as stem cell therapies are employed to cure diseases.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Author has declared that no competing interests exist.

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