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Biobanking in Dentistry

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Abstract

Tissue Engineering has proven to be one of the latest technology for maintaining the tissue viability and organ integrity. Over the recent years, tooth tissue /stem cell engineering has gained maximum popularity and has thought to be a promising way to replace, and or regenerate the diseased tooth. Dental pulp due to its high vascularity and regenerating capacity, establishes evidence to be a source of stem cells. Scientific advancements in the regenerative technology, with the inclusion of dental pulp stem cells, tissue scaffolds and cell signaling molecules and harvesting of dental stem cells from sources like extracted teeth, periodontal ligament, deciduous teeth, etc. Biobanking provides the basis for the introduction of latest advancements in dentistry. The purpose of this article is to highlight the use of dental stem cells in biological procedures to develop the regenerative procedures in field of medicine and dentistry.

Keywords: Stem Cells, Tooth Banking, Cryopreservation

INTRODUCTION

Stem cells can be defined as cells that self-replicate and are able to differentiate into at least two different cell types. Stem cells (SC) are undifferentiated cells capable of self-renewal and differentiation into multiple functional repair and tissue regeneration. These cells are widely used in the injury repair and tissue regeneration. [1] Adult Stem cells have been harvested from other tissues like hair follicles, bone marrow, etc. Not long ago, dental- derived stem cells have been made accessible and proved to be a source for the tooth regeneration. These cells are named according to the source from where they have been extracted, and are characterized by their SC markers, colony-forming ability, and dental regenerative function. [2]

These dental stem cells (DSC) have shown real promise in the field of regenerative medicine because of its accessibility, plasticity and higher proliferative ability. Moreover, unlike other mesenchymal stem cells, DSC does not have the any ethical issues associated with its harvesting. Hence harvesting and storage of the individuals DSC for future medical needs will soon become a modus operandi. Therefore the purpose of this article is to describe the various dental stem cells that can be harvested and the method of banking these SC for future use as well as to highlight the possible clinical applications of the stored dental stem cells. [2]

Types and sources of stem cells

- *Embryonic/fetal* - Embryonic stem cells are derived from the inner cell mass of a developing blastocyst and are considered as pluripotent cells as they are able to form, all the body's cell lineages.[3]
- *Adult/postnatal* - Post-natal stem cells (derived from specific tissues or organs) are considered multipotent as they can form multiple lineages that constitute an entire tissue or tissues. Also known as somatic (from Greek, "of the body") stem cells and germline (giving rise to gametes) stem cells, they can be found in children, as well as adults.[3,4] These can be either haematopoietic stem cells (HSCs) or mesenchymal stem cells (MSCs).[3]

According to Cell Plasticity and Source of the stem cell [4] the stem cells can be divided as per their plasticity as shown in Table 1.

Table 1: Stem cell type based on its' plasticity

Stem cell type	Cell plasticity	Source of stem cell
Totipotent	Each cell transforms into a new individual	Cells from early (1-3 days) embryos
Pluripotent	Cells proliferates into various other cell types (over 200)	Some cells of blastocyst (5-14 days).
Multipotent	Cells differentiated, but can form a number of other tissues	Fetal tissue, cord blood and postnatal stem cells including dental pulp stem cells

Stem cells can also be categorized according to their source as: [4]

i. *Autologous postnatal stem cells* –These stem cells involve a single donor system, where the extraction and implantation of cells take place into the same individual. Harvesting of one's bone marrow stem cells and instilling back to the same donor provides an exemplification of autologous postnatal stem cells. The other sources for stem cells include amniotic fluid, umbilical cord, fetal tissue, as well as dental stem cells.

ii. *Allogenic postnatal stem cells* - These cells are acquired from the donor of identical species. These cells are ten deposited in a cell bank, making them available for future use depending upon the requirement.

iii. *Xenogenic cells* - These cells are extracted from donors of different species. Animal models are commonly used. Dental pulp stem cells from animals are believed to produce tooth like structures in humans.

Various sources of dental stem cells

Dental SC isolated from various tissues can be categorized into dental mesesnchymal SCs and dental epithelial SCs. Mesenchymal Stem cells from human dental tissues include dental pulp SCs in human permanent teeth, SCs from human exfoliated deciduous teeth (SHED), periodontal ligament stem cells (PDLSCs), and dental follicle SCs (DFSCs) from human third molars. [5]

Dental Epithelial Stem Cells: Enamel of the tooth is the highly mineralized and the strongest tissue of the body. The deposition of enamel matrix causes the ameloblasts to migrate peripherally and form a conical projection which outlines the crown of the tooth, marks the formation of enamel. Human enamel cannot rejuvenate by itself. Dental epithelial SCs found in the mouse cervical loop helps in forming the apical bud. The apical bud is a condensed SC area which is held responsible for the growth of dentition when it combines with mesenchymal cells. [4,6]

Stem cells from Human Exfoliated Deciduous teeth (SHED): The dental pulp embodies a collection of stem cells, termed as pulp stem cells or, in case of young exfoliating teeth, they are named as stem cells from human exfoliated deciduous teeth (SHED). SHED cells multiply rapidly and grow much faster than adult stem cells, suggesting that they are less mature, so they have the potential to develop into a wider variety of tissue types. [7]

Adult Dental Pulp Stem Cells (DPSC): Dental pulp stem cells (DPSCs) can be isolated from the dental pulp. It has been shown that adult dental pulp contains precursors capable of forming odontoblasts under appropriate signals like calcium hydroxide or calcium phosphate materials. Tooth repair is a lifetime process, thus suggesting that MSC might exist in adult dental pulp. The in vivo therapeutic targeting of these adult stem cells remains to be explored. [6]

Stem Cells from the Apical Papilla (SCAP): These mesenchymal stem cells found in the apical papilla of the incompletely developed teeth are proven to be a great source of stem cells. SCAP are the primary source of odontoblasts that are responsible for the formation of the root dentin. Dental papilla is derived from ectomesenchyme induced by the overlying dental lamina during development. It develops gradually into dental pulp after being wrapped in dentin. Apical papilla is apical to the epithelial diaphragm, and there are cells located both in dental pulp and apical papilla.[8] Apical papilla has the advantage of collateral circulation, which helps in its survivalat the time of pulp necrosis. [8]

Periodontal Ligament Stem Cells (PDLSC): Periodontal tissues are able to reconstruct themselves after injury. In the early 1970s, researchers hypothesized that PDLSCs might be the reason for the periodontal repair. PDLSCs were first extracted by Seo et al, and had the capability of proliferating into cementoblast-like cells,adipocytes and collagen-forming cells. [9]

Dental Follicle Stem Cells (DFSC): Dental follicles are derivedfrom the ectomesenchymal tissue surrounding the developing tooth germ. [2] Human dental follicles arecollected fromthe wisdom tooth after extraction, and help in playing avital role in tooth eruption by stimulating osteoclasts and osteoblasts for the genesis. After tooth eruption, the dental follicle metamorphoses into cells of the periodontium, osteoblasts of alveolar bone, the PDL, fibroblasts and cementoblasts.

Advantages and disadvantages of Dental Stem Cells [7]

The various advantages of DSC over other sources of postnatal stem cells are given in Table 2.

Table 2: Advantages and disadvantages of Dental stem cells

Advantages	**Disadvantages**
Provides guaranteed matching of donors	Small number of cells available for isolation
Saves cells before their damage	No proper research on side effects
Simple and Painless procedure	
Less expensive compared to cord blood storage	
Lesser ethical issues	

Therapeutic applications of Dental Stem Cells [3,6,10,11]

The DSC can be made to differentiate into a particular phenotype by either controlling or restricting the differentiation pathways with specific culture medium with specific cytokines, growth factors, amino acids, other proteins as well as active ions, and co-culture with a specific cell type or tissue. The possible applications dental derived stem cell scan range from dental pulp regeneration to the treatment of paralysis. **(Table 3)**

Table 3: Potential Clinical Applications of Dental Stem Cell Therapy

Dental oriented	Medical oriented
Continued root formation	Cardiomyocyte differentiation of the dental pulp stem cells
Pulp healing and regeneration	Differentiation into muscular tissue
Replantation and transplantation	Corneal reconstruction with dental pulp stem cells
Pulp/dentin tissue engineering and regeneration	Vasculogenic transformation of dental pulp stem cells (treatment of ischemia)
Bioroot engineering	Osteogenic proliferation of dental pulp stem cells

Dental Biobanking: a preparatory step for future bioengineering

With advancements in tooth tissue engineering, dental SCs can regenerate into odontoblasts, dentin/ pulp-like structure, and dentin. In addition, dental SCs can further differentiate into constituent cells like adipocytes and neurons, and stimulate the multiplication of visceral neural cells. Besides, it is also postulated that dental SCs could be an aid in the treatment of diseases like myocardial infarction and liver dysfunction in the near future. Thus, the benefits of dental SCs are not just confined to dental use but are also proving to be a boon for regenerative therapy.[12]Dental Stem cells with its amazing benefits and preserving them for a cause, came into demand. With the preservation of dental SCs, the term "tooth bank" was first embossed in 1966. Dental stem cells and its analogues have been reported to be become a major source of stem cells today. However, the appropriate preservation methods for teeth and/ or dental SCs are still not clear. With the rapid development of advanced cryopreservation and micro-freezing technologies, National Hiroshima University in Japan developed the first tooth bank as a venture company. [4] Numerous tooth banks are developed in the recent years due to an increasing demand for the preservation of the teeth for stem cells and its analogues.[13]

Some of the licensed tooth stem cell banks, Internationally and in India, used for cryopreservation and isolation are as follows [6,14]

1. In Japan, the first tooth bank was established in Hiroshima University and the company was named as 'Three Brackets'(SuriBuraketto).
2. BioEden (Austin, Texas), StemSave, and Store-a-Tooth
3. The Norwegian tooth bank.
4. In India, Stemade Biotech Pvt. Ltd. (Delhi, Chennai, Chandigarh, Pune, and Hyderabad).

Steps in Biobanking

Various methods have been used to isolate and preserve DSC by different investigators as shown in **Table 4**. The fundamental steps in dental biobanking are given in **Figure 1**.

Figure 1: Fundamantal steps in dental tooth banking [2,6,7,10,15,16]

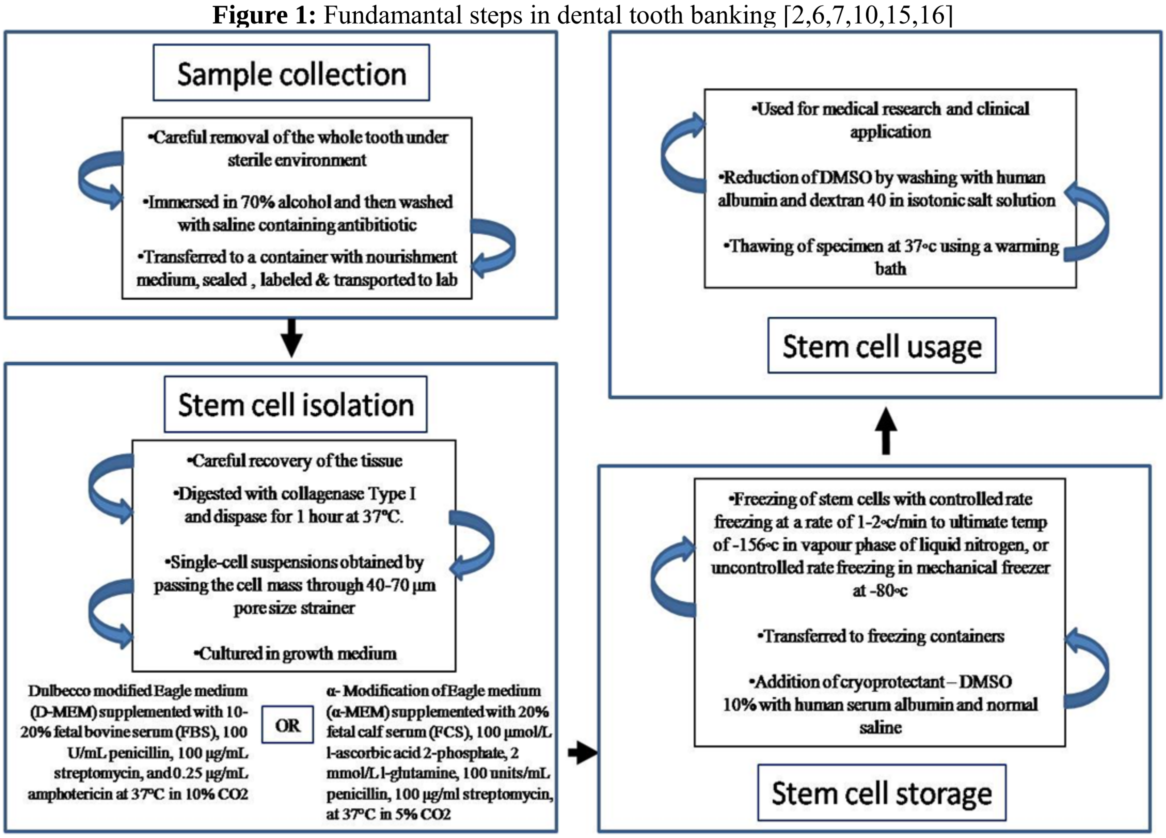

Table4: Tooth Banking methods [15]

Investigators	Indication	Preservation method
Malekfar A et al. [21](2016)	Isolation of DPSC from teeth with irreversible pulpitis	Solution : 10% DMSO 90% FBS Control temperature : 4°c Storage temperature : -80° c
Lindemann et al.[22] (2014)	Isolation and Characterization of DPSC of intact deciduous teeth	Solution: 10% FBS (1:9), 10% DMSO Control temperature : 4° c Storage temperature: -196 °c
Lee, et al. (2012) [23]	Magnetic cryopreservation for dental pulp stem cells	Serum free cryopreservation medium containing 3% DMSO, Programmable freezer (ABI), in the presence of a 0.01 mT magnetic field Control temperature: 4°C until placed in this freezer at - 5°C; Storage temperature: - 150°C
Chang PC, et al.(2010)[24]	Autotransplantation DPSC isolation PDLSC isolation	Solution: BAMBANKER 2, 10% DMSO Control temperature: Programmable Freezer (ABI Corp Ltd.)75mA electric current to generate a magnetic field -5 °c for 15 min. 0.5 c/min to -30° c Storage temperature: -150 °c
Oh YH et al. (2005) [25]	PDL cell viability	Solution: DMEM:F= 3:1 10% FBS 10% DMSO Control temperature: −196°C Storage temperature: −196°C (LN)
Schwartz O. et al. (1986) [26]	Autotransplantation Replantation	Solution: DMEM culture medium 10% human serum; 10% DMSO Control temperature: 1.2°C/min to −40°C; 6°C/min to −100°C Storage temperature: −196°C

DMSO=dimethyl sulfoxide;
LN=liquid nitrogen;
PDL=periodontal ligament;
FBS= fetal bovine serum;
DPSC= dental pulp stem cells;
PDLSC=periodontal ligament stem cells;
DMEM= Dulbecco's Modified Eagle's medium

CONCLUSION

Stored cryopreserved cells or tissue used for future therapies becomes an integralpart of biobanking.As the usage of dental stem cells is gaining popularity in other areas of medicine, research on stem cell is in vogue.Since the dental stem cells has the ability to form in to other cell lineages and as they are easy to handle, they have proven to be a promising source of stem cells in both medical and dental field. The dental stem cells harvested can be be stored as a biological insurance for the individual or blood relatives until certain disease requires its usage. Cryopreservation proves to be anefficacious method for biobanking of tooth and dental pulp. However, considerable research is required to prove the above statement. Tooth banking for dental stem cell preservation can be considered as a preventive treatment plan.[17]

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