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Stem Cells in Dentistry: "Where the Future Stands": A Brief Review

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Abstract

Stem cells are biological cells that possess two properties: self-renewal, i.e. the ability to go through unlimited cycles of cell division for the purpose of replenishing the cell pool, and potency, i.e. the capacity to differentiate into other cell types. Owing to the cells' proliferative capacity, the available pool of stem cells is not reduced when cells are transformed into other tissues and participate in the renewal of vital structures such as the bone marrow. Dental stem cells have been obtained from the pulp of the deciduous and permanent teeth, from the periodontal ligament, and from an associated healthy tooth structure in recent exciting findings in dentistry to treat a range of disorders. The goal of the current study of the literature is to go into more depth on the function of stem cells in dentistry.

Keywords: *Stem cell, Application in dentistry, Regeneration*

Introduction

Stem cells are defined as clonogenic cells capable of both self- renewal and multiline age differentiation since they are thought to be undifferentiated cells with varying degrees of potency and plasticity.[1]

Unspecialized cells called stem cells have the capacity to regenerate themselves and differentiate into a wide variety of other cell types.[2] Undifferentiated cells' ability to replicate indefinitely and be able to differentiate into any type of specialised cell is known as stemness. Microscopically, differentiation can be seen as morphological changes in cells and the presence of tissue-specific proteins in their cytoplasm.[3] Stem cells may remain dormant or silent over long periods of time until there is a physiological need for more cells to maintain tissues or they are activated by disease or tissue injury. Such self renewal or actively dividing and differentiating sites of tissue are known by the name "stem cell niches"[4] These tissues include the skin, adipose tissues, peripheral blood, hair follicles, bone marrow, brain, intestine, pancreas, and teeth. As a result, the primary function of adult stem cells is to maintain and repair the tissue in which they are found.[5] Stem cell science is the area of the health sciences that deals with the retrieval, culture, and harvesting of stem cells at the required site. Translational approaches, such as artificial skin therapies and target cell-based treatments for diabetes, atherosclerosis, and neurodegenerative illnesses in which stem cells are generated at the site of the disease, have been introduced and established as a result.[6]

Although not a novel idea, the idea of regeneration in medicine has substantially advanced with the discovery of stem cells, and more recently, it has found use in dentistry after dental stem cells were discovered. Currently, the only options for replacing teeth are conventional prostheses, such as fixed dental prostheses, detachable prostheses, or implants, together with any necessary preoperative bone augmentation. To replace severely damaged or missing teeth, or even specific tooth structures, new solutions may now be available thanks to advancements in stem cell biology and tissue engineering. Dental research is concentrating on stem cells due to the possibility of such treatments.7,8

Properties of Stem Cells [6]

1. They are undifferentiated cells, that is, they have not developed into a specialized cell types
2. They have the capability to undergo multiple cycles of cell division while maintaining their undifferentiated state
3. They have the ability to differentiate into specialized cell types.

Types of Stem Cells

1. Embryonic stem cells: Embryonic stem cells are derived from the blastocyst containing 50 to 150 cells. They are pluripotent and versatile and have the plasticity needed to differentiate into cells of all three germ layers.[9,10]

2. Adult stem cells: Adult stem cells are also called somatic or postnatal stem cells. They are multipotent and differentiate into a limited number of cell lines. Adult stem cells are easier to isolate and are not bound by the same legal and ethical constraints as embryonic stem cells. This, along with their rarer incidences of immune rejection and teratoma formation makes them suitable for use in most clinical practices.[11]

The history of research on adult stem cells began about 40 years ago. In the 1960s, researchers discovered that the bone marrow contains at least two kinds of stem cells. One population, called hematopoietic stem cells, forms all the types of blood cells in the body. A second population, called bone marrow stromal cells, was discovered a few years later. Stromal cells are a mixed cell population that generates bone, cartilage, fat, and fibrous connective tissue.[12]

Recent stem cell studies in the dental field have identified many adult stem cell sources in the oral and maxillofacial region. These cells are believed to reside in a specific area of each tissue, i.e., a ‘‘stem cell niche’’. Many types of adult stem cells reside in several mesenchymal tissues, and these cells are collectively referred to as mesenchymal stem cells or multipotent mesenchymal stromal cells (MSCs).[13]

3. Induced pluripotent stem cells: Induced pluripotent stem cells mimic embryonic stem cells in their potential to divide but are exempt from the ethical restraints since they are produced by transfecting genes found in embryonic stem cells into a donor cell with the help of vectors. Here, autologous somatic cells produce a patient specific embryonic stem cell equivalent and pave the way for treatments that are tailored to the needs of the individual. [14,15]

Table no 1: Various Sources of Adult Stem Cell

Haematopoetic Stem Cells	**Mesenchymal Stem Cells**
a) Bone marrow, b) Peripheral blood, c) Umbilical cord Stem cells i. Umbilical cord epithelium (UCE), from the amniotic membrane epithelium ii. Umbilical cord blood (UCB) d) Fetal liver	a) Muscle – muscle stem cell b) Synovium c) Dermal hairfollicle stem cell d) Nerve tissue – neuronal stem cell e) Liver – liver stem cells f) Gut epithelium g) Adipose tissue h) Amniotic fluid i) Pancreas – pancreatic stem cells j) Corneal limbal stem cells k) Mammary stem cells l) Salivary glands m) Heart n) Cartilage o) Blood vessels- mesangioblasts p) Lung **Dental Derived Adult Stem Cells** a) Permanent teeth – Dental pulp stem cells (DPSC): derived from third molar.

	b) Deciduous teeth – Stem cells from human-exfoliated deciduous teeth (SHED): stem cells are present within the pulp tissue of deciduous teeth. c) Periodontal ligament - Periodontal ligament stem cells (PDLSC). d) Stem Cells from apical papilla (SCAP). e) Stem cells from supernumerary tooth – Mesiodens. f) Stem cells from teeth extracted for orthodontic purposes. g) Dental follicle progenitor cells. h) Stem cells from human natal dental pulp- (hNDP)

Stem Cells in Dentistry [5,17]

Dental pulp stem cells (DPSC): The first dental stem cell to be isolated from human dental pulp—the pulp of the teeth—was known as dental pulp stem cells (DPSC). It has the capacity to promote chondrogenesis and osteogenesis. MSCs from dental pulp appear to be highly clonogenic when they are isolated. They can mature into odontoblast-like cells and osteoblasts to produce dentine and bone, and they can be separated from adult and foetal tissue (Bansal and Jain, 2015). Their best source is the third molar. DPSCs are an effective dental source for tissue engineering because of their cryopreservation capability, simple surgical accessibility, increased synthesis of dental tissue compared to non-dental stem cells, and anti-inflammatory properties. SHEDs proliferate at a faster rate than DPSCs. They divide into a larger number of cells, including brain cells. They have one important drawback: in vivo, they form a partial dentin-like complex. In vivo, DPSCs and SHED can create bone-like tissue, which is employed for periodontal, pulp regeneration, and dentin regeneration. Such neutral deficits can be treated with both DPSCs and SHED. DPSCs were investigated and employed satisfactorily for alveolar bone and mandible restoration.

Periodontal ligament stem cells (PDLSCs): It is utilised for PDL regeneration therapy since it is safe and effective. By splitting into important mesenchymal cell lineages, they can in vitro grow into cells that generate Sharpey's fibre, osteoblast-like cells, cementum tissue, and collagen. It is present on the root surfaces and the alveolar bone.

SCAP, or stem cells of the apical papilla: Immature roots contain these mesenchymal cells, which were identified from human immature permanent apical papilla. Odontoblasts come from SCAP, which causes apexogenesis. These cells can be implanted in a dish to produce neurons and odontoblast-like cells in vitro. SCAPs are a better candidate for tissue regeneration than DPSCs because they have a greater capacity for proliferation.

Dental follicle stem cells (DFCs): The tooth germ's surrounding loose connective tissue contains it. It has the capacity to differentiate into periodontal ligament cells, osteoblasts, and cementoblasts. It is taken out of the sac of a third molar. When DFCs link with the dentin matrix, they can produce tooth roots by forming a root-like tissue with a pulp-dentin complex.

Stem cells from human exfoliated deciduous teeth: These stem cells are highly proliferative and can be isolated from exfoliated deciduous teeth. They can cause the production of dentin and bone and differentiate into a variety of cell types, including osteoblasts, neural cells, adipocytes, odontoblasts, endothelial cells, myoblasts, and chondrocytes.

Application of Stem Cell in Dentistry

Endodontics: Regenerative Endodontics uses the basic logic that the patient specific tissue derived cell population called stem cells can be used for regeneration and revascularisation. This concept of regene-ration of pulp dentin complex dates to almost 50 years when it was first reported be Nygaard and Ostby.

Several case reports have documented revascularization of the necrotic root canal systems by disinfection followed by establishing bleeding into the canal system via over instrumentation. Use of intracanal irrigants (NaOCl and chlorhexdine) along with the placement of antibiotics (e.g., a mixture of ciprofloxacin, metronidazole, and minocycline paste), for several weeks, is a critical step, as it effectively disinfects the root canal systems and increases revascularization of the avulsed and necrotic teeth. The revascularization process offers negligible chances of immune rejection and pathogen transmission, as regeneration of the tissue takes place by the patient's own blood cells. However, some critical limitations of this technique entail that caution is required, as the source of regenerated tissue has not been identified and also the concentration and composition of cells trapped in the fibrin clot are unpredictable.**[9]**

Whole tooth regeneration: By planting various cell types on biodegradable scaffolds, tooth-like tissues have been produced. Cells are typically harvested, expanded, and differentiated in vitro, seeded onto scaffolds, and then implanted in the body. In other situations, the scaffolds are re-implanted into the jaw or an extracted tooth socket. Ikeda et al. (2009) described a successful adult mouse tooth replacement that was entirely functional thanks to the implantation of a bioengineered tooth germ into the alveolar bone near the site of the missing tooth. This method has been suggested as a prototype for upcoming organ replacement treatments.[18]

Uses in craniofacial repair during oral and maxillofacial surgery: The tissue engineering of a temporomandibular joint with a human-like form has made use of stem cells.

Stratified yet integrated layers of cartilage and bone were used by Alhadlaq and Mao to create an adult human mandibular condyle using MSC-derived cells enclosed in a polyethylene glycol diacrylate hydrogel. Immunodeficient mice received the osteochondral implants, modelled after human TMJs, for up to 12 weeks. The tissue-engineered mandibular joint condyles kept their shape and size after being harvested.[19]

Regeneration of alveolar bone: Mesenchymal condensation by aggregation of mesenchymal stem cells seen in the development of bone. It includes intra membranous and endochondral bone formation mechanisms. Bone has the intrinsic capability of regeneration during adulthood. In case of minor injuries regeneration takes place by the local cells like chondroblasts, osteoblasts, endothelioblasts and fibroblasts. In severe injuries self-healing alone can't repair the defect. So adequate supply of stem cells is required for the regeneration of efficient bone. Oral mesenchymal stem cells have more potential of bone regeneration.[20]

Regeneration of muscle tissue: Arminan et al. said that cardiomyocytes-like cells can be separated from dentin pulpal stem cells when cultivated with neonatal rat cardiomyocytes for about 4 weeks in vitro. Yang et al said that dystrophin producing muscle cells can be separated from dental pulp stem cells in cardiotoxin- paralyzed muscles in a mouse model and can be used as a treatment of choice for muscular dystrophy.[21]

Three-dimensional cell printing: The three-dimensional cell printing technique can be used to position cells so that they have the potential to generate tissue that imitates the natural tooth pulp tissue. Careful adaptation of the pulp tissue in the cleaned and shaped root canal systems should follow the apical and coronal anatomy. This procedure is the prime requisite for the success cant of the technique. However, research has yet to provide significant evidence that three-dimensional cell printing can create functional tissue in vivo.[6]

Alveolar bone defect repair: Orthodontic treatment includes extraction of premolars for correction of malocclusion. During surgical removal of teeth, accidentally buccal plates could be lost leading to alveolar bone defect. Such defects can be filled with stem cells to avoid the risk of dehiscence and periodontal damage after the spaces have been closed by retraction. Alveolar cleft osteoplasty can be successfully done with stem cells. [22,23]

Periodontal Regeneration: Periodontal regeneration is the total restoration of missing tissues to their original form and function by re-enacting the key wound healing processes that were involved in their formation. Such procedures are consistent with the idea that some mesenchymal cells persist in the periodontal ligament, maintain tissue homeostasis, and act as a source of replenishable progenitor cells throughout adulthood. It seems logical that PLSCs cultured within a suitable delivery scaffold, in conjunction with growth and differentiation factors present in autologous blood clots, will result in new periodontal tissue attachment via a tissue engineering approach because seeding to improve regeneration of other tissues appears to be successful.[24]

Conclusion

Stem cells have the capacity to replicate and produce cell lines that differentiate into multiple cell lineages. Stem cells may be harvested from various sites and are named adult stem cells or embryonic stem cells based on their origin. Owing to their self-renewing capabilities, they are used to correct large defects caused by diseases, trauma or surgery. Dental stem cells retain the property of differentiation into neurogenic, adipogenic and odontogenic components and are used in the reconstruction of orofacial structures. A multi-speciality approach involving cell biologists, pharmacologists and bioengineers is required to harness the vast potential of stem cell therapy and to obtain reliable treatment outcomes in the future.

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