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Review Article

Stem Cell in Dentistry-A Review

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Abstract

The numerous tissues of the creature body go through normal physiological regeneration. The renewing tissues have relatively limited abilities to restore harm due to disease or trauma. Stem Cells (SCs) are undifferentiated cells competent of self-renewal and differentiation into numerous functional cell types. Stem Cell (SC) therapy has a encouraged future for tissue regenerative medicine. However, Stem Cell technology is still in its primary years, interdisciplinary cooperation is essential to attain successful clinical applications. Dental Stem Cells have good accessibility, plasticity, and high proliferative ability. Some types of dental Stem Cells have been recognized from adult human dental pulp, human primary exfoliated deciduous teeth, periodontal ligament and dental follicle. Dental stem cells have also proven their use in Forensic dental investigation and anthropology which is an stimulating new area of research. This article pitches light on various sources of stem cells, processing techniques in the orofacial region and its clinical uses.

Keywords: Exfoliated Deciduous Teeth, Regenerative Medicine, Renewal, Proliferative, Stem Cells, Transplantation, Periodontal Ligament

Introduction

The regenerative abilities of numerous animals have always been an enthrallment for humans. Regeneration is a amazing physiological process in which lasting tissues categorize to reorganize a missing body part. Most tissue repair events in mammals are autonomous events resulting from the activation of pre-existing stem cells or progenitor cells. Stem cells or progenitor cells are the straight denominator for nearly all types of regeneration [1]. The human body is made up of three basic categories of cells: germ cells, somatic cells and stem cells. The materials required for tissue engineering include stem cells, morphogens (or growth factors) and gallows to guide cell growth. Scientific study has identified fabulous potential for the use of these stem cells to treat a number of diseases. It is now accepted that progenitor/stem cells reside within orofacial region. Stem cells residing in the orofacial region have been classified as the Mesenchymal Stem Cells (MSCs) /Adult Stem Cells (ASCs) / Tissue Stem Cells (TSCs) [2]. According to the study multipotent mesenchymal progenitor cells known as dental pulp stem cells who have high proliferative potential for self-renewal. These progenitor stem cells are now documented as being vital to the dentine regeneration process succeeding injury. More recently researchers have revealed deciduous teeth may be a source of tissue regeneration and repair. There are five different types of dental stem cells isolated from dental soft tissues which are dental pulp, apical papilla, dental follicle and periodontal ligament. The characteristic features of these cells express various arrays of biomarkers including those specific for mesenchymal and/or embryonic stem cells [3].

According to Columbia Encyclopedia Stem cells are defined as "unspecialized human or animal cells that can produce mature specialized body cells and at the same time replicate themselves [4]. When a stem cell divides, the daughter cells can either enter a path leading to the formation of a differentiated specialized cell or self- renew to remain a stem cell, thus ensuring that a pool of stem cells is regularly replenished in the adult organ. This mode of cell division feature of stem cells is asymmetric and is a essential physiological mechanism for the preservation of the cellular composition of tissues and organs in the body [1].

Stem Cell Types

1.1. **Embryonic stem cell**

a) Totipotent stem cell

b) Pluripotent stem cell

1.2. **Adult stem cell**

c) Hematopoietic stem cell

d) Mesenchymal stem cell

Induced Pluripotent Stem Cell Effectiveness of the Stem Cells [5].

A stem cells strength is its capacity to differentiate into different cell types and accordingly the cells can be divided into several categories which are.

Totipotent Stem Cells

These cells are formed from the fusion of an egg and sperm cell. Cells produced by the first few divisions of the fertilized egg are also totipotent. Totipotent stem cells can differentiate into embryonic and extraembryonic cell types. Such cells can construct a complete, viable, organism.

Pluripotent Stem Cells

These are the offspring totipotent cells and can differentiate into nearly all cells, i.e. cells derived from any of the three germ layers.

Multipotent Stem Cells

It can discriminate into a number of cells, but only those of a closely related family of cells.

Oligopotent Stem Cells

These are differentiating into only a few cells, such as lymphoid or myeloid stem cells.

Unipotent Cells

These can produce only one cell type, their own, but have the property of self- renewal which distinguishes them from non-stem cells (e.g. muscle stem cells).

Sources of the Stem Cells in Orofacial Region

Mesenchymal Stem Cells (MSCs) are potential source of adult stem cells for regenerative medicine as they are amazingly synthetic and when extended into colonies, they maintain their multilineage potential. MSCs are able to distinguish into cells of mesodermal origin like adipocytes, chondrocytes or osteocytes [6,7]. MSCs are also found within the Dental Pulp (DP), a tremendously rich site for stem cell collection [8,9] These dental stem cells are derivative from the neural crest, and have a different origin from bone marrow-derived MSCs, which are derived from mesoderm. In amassing to the dental pulp MSC, other MSC populations have been secluded from human dental tissues such as the periodontal ligament and the dental follicle [10,11].

Dental Pulp Stem Cells (DPSCs) are considered to be arising from two sources: first one is from ectomesenchyme of the neural crest or ectoderm of the dental lamina. The evaluation of the osteogenic and adipogenic potential of MSC from diverse origins shows that, yet if cells carry familiar genetic markers, they are not alike and are previously committed toward a specific differentiation pathway [12,13]. Commitment could arise from conditioning of stem cells by their specific microenvironment or stem cell niche.

Dental Pulp Stem Cells (DPSC)

DPSC is dental pulp mesenchyme. They are slow cycling cells having limited potential and it signify mature adult pulp stem cells. They have enhanced immunologic/host acceptance [14].

Stem Cells from Human Exfoliated Deciduous Teeth (SHED)

SHED is exfoliated from deciduous teeth. They are multipotent cells with very high proliferative potential and superior cell doublings.

Periodontal Ligament Stem Cells (PDLSC)

They can be obtained from periodontal ligament of the roots of the extracted teeth. They are the primary source for treatment of periodontal disease and these are multi- potential cells.

Dental Follicle Stem Cells (DFSC)

They are extracted from dental follicle of the impacted teeth and possess multiple potentialities. They have minor ability to form adipocytes and their potential yet to be recognized for forming odontoblasts, neural cells.

Stem Cells from Apical Papilla (SCAP)

SCAP is obtained from third molars or other teeth. They are easily accessible and have a higher proliferative potential.

Bone Marrow Stem Cells (BMSC)

They are derivative from bone marrow of mandible or maxilla. Orofacial BMSCs are less adipogenic than BMSCs from other sources.

Epithelial Stem Cells (EpSC)

These stem cells developed from third molars of newborn. They have clonogenicity and are unipotent. Stem cells from third molars are capable for tooth formation/ regeneration.

Induced Pluripotent Stem Cells (IPSC)

Adult human cells are reprogrammed to obtain embryonic stem like cells called Induced pluripotent stem cells. These are immunologically extra satisfactory and an attractive alternative source. Oral fibroblasts are able to form IPS cells in laboratory.

Immature Dental Pulp Stem Cells (IDPS)

IDPS are obtained from pulp of primary teeth. They co- express mesenchymal and embryonic stem cell markers and present the capacity to differentiate into derivative cells of the three germinal layers.

Oral Epithelial Stem Cells (OESCs)

They are derivative from oral epithelial progenitor cells from basal layer of oral mucosa. They are unipotent stem cells and have clonogenicity. They can form highly stratified and well-ordered graft.

Gingiva Derived MSCs (GMSCs)

These cells are resultant from lamina propria of gingiva. These cells show adipogenic, osteogenic and chondrogenic probable along with immuno-modulatory effect on lymphocytes.

Tooth Germ Progenitor Cells (TGPCs)

They are the stem cells in the mesenchyme of the third molar tooth germ and possess very high proliferative activity. They can differentiate into lineages of three germ layers including osteoblasts, neural cells and hepatocytes.

Salivary Gland Stem Cells (SGSCs)

They are derived from the stromal tissue of salivary glands. They are helpful for renewal of salivary gland broken from irradiation and can be guided to osteogenic, chondrogenic and adipogenic differentiation.

Perisoteum Derived Stem Cells (PSCs)

They are extracted from inner membrane of periosteum. They can discriminate into osteoblasts, adipocytes and chondrocytes.

Collection, Isolation, And Preservation of Dental Stem Cells

Step 1: Tooth collection

The extracted tooth is immediately transferred into vial which contain hypotonic phosphate buffered saline solution. Then the vial is carefully sealed and placed into thermite, after which the carrier is placed into an insulated metal transport vessel. Thermette along with insulated transport vessel maintains the sample in a hypothermic state during transportation. This procedure is described as sustentation. The time from harvesting to coming at processing storage facility should be approx. 40 hours [15,16,17].

Step 2: Stem cell isolation

The Tooth surface is washed and cleaned thrice with Dulbecco's phosphate buffered saline without Ca2+ and Mg2+. Disinfection is done and again washed with PBSA. Pulp tissue is extracted from the pulp chamber and is placed in a sterile Petri dish, washed thrice with PBSA. The tissue digestion is done with collagenase Type I and dispose for 1 h at 37°C [18]. Isolated cells are passed through a 70um filter to attain single cell suspensions. Then the cells are refined in a MSC medium. Usually, isolated colonies are visible after 1 day.

Stage 3: The stem cell storage includes: (a) Cryopreservation (b) Magnetic freezing.

a) Cryopreservation

It is the procedure of preserving cells by cooling them to sub-zero temperatures. Liquid nitrogen vapor is used to conserve cells at a temperature of <-150°C [19,20-23].

b) Magnetic Freezing

This technology is referred to as cells alive system (CAS), which work on this principle by applying a weak magnetic field to water or cell tissue which will lower the freezing point of that body by up to 6-7°C. CAS system is a lot cheaper than cryogenics and more reliable [24,25].

Criteria of Tooth Eligibility for Stem Cells from Human Exfoliated Deciduous Teeth Banking

Primary incisors and canines with no pathology and at least one third of root left can be used for SHED banking. Primary molar roots are not recommended for sampling as they take longer time to resorb, which may result in an obliterated pulp chamber that contains no pulp, and thus, no stem cells. Deciduous molars are removed early for orthodontic reasons, it may present an opportunity to use these teeth for stem cell banking [1-5,26].

Tooth Stem Cell Banking

BioEden (Austin, Texas, USA), has international laboratories in UK and Thailand with global expansion plans. Stem cell banking companies like Store A- Tooth and Stem Save are also expanding their horizon internationally. Stemade introduced the thought of dental stem cells banking in India recently by launching its operations in Mumbai and Delhi [27,28].

Dental Applications of Stem Cells

Stem cells from dental sources have set up applications in treatment of various diseases and defects which involves craniofacial regeneration, dentin regeneration, periodontal regeneration, cementum regeneration, pulp regeneration, cleft lip and palate, salivary gland regeneration, Tmj reconstruction, whole tooth regeneration, cancer therapy, cancer models for biology of cancer, oral mucosa

models for studying oral biology , cell and organ models for studying molecular physiology behind processes like tooth eruption, forensic dental profiling, correlation and collection of ante-mortem and postmortem data.

The Use of Stem Cells in Osseous Regeneration

Adult MSCs in the gingival connective tissues have osteogenic potential and are ability of bone regeneration in mandibular defects [29]. GMSCs also suppress the inflammatory response by decrease lymphocyte proliferation and inflammatory cytokines and by promoting the recruitment of regulatory T-cells and anti- inflammatory cytokines. Thus, GMSCs potentially promote the "right" environment for osseous regeneration [17,18,19,30]. Neurosurgery: According to the study by *Nosrat, et al*. [2001] In a vitro culture system of interactions between the dental pulp cells and trigeminal neurons. When DPC are co-cultured with trigeminal neurons, they help survival and a precise and elaborate neuritis outgrowth pattern from trigeminal neurons, whereas skin fibroblasts do not provide a similar support. Interestingly, grafting the dental pulp tissue into hemisected spinal cord increases the number of surviving motor neurons, indicating a functional bioactivity of the dental pulp- derived neurotropic factors in vivo by rescuing motor neurons [17,31,32,33].

Challenges of Stem Cell Therapy

A major difficulty with stem cell therapy is to identify the stem cells within a culture of real fabric. The cultures contain many different cells and are a challenge to identify specific cell types. When stem cells are identified and then isolated from tissues, appropriate solutions must be created to trigger these cells into the desired cell types. Finally, even though the cells may be identified, isolated and grown, there are supplementary issues like immune response and efficiency. A person's immune system can identify the transplanted cells as foreign bodies and that it can generate an immune reaction that results in refusal of the new cells [20,34].

Prospects of Dental Stem Cells in Medicine

Dental stem cells are used to be applied in medical faculty which includes heart therapies, regenerating brain tissue, for muscular dystrophy therapies and bone regeneration. SHED can be used to produce cartilage and adipose tissue [16-19].

Conclusion

Stem cell-based dental tissue regeneration is a new and exciting field that has the potential to change the way of today's dental practice. Like other powerful technologies, dental stem cell research poses challenges as well as risks. The oncogenic potential of these cells is still to be determined in long-term clinical studies. The major limitations are the difficulty to identify, isolate, purify and grow these cells consistently in labs [35-38]. Immune rejection is also one of the issues, which require a thorough consideration; nevertheless, use of autologous cells can overcome this. Researchers still need to grow blood and nerve supply of teeth to make them fully functional. Dental stem cell banking will be an easy way to store one "s own stem cells. Nevertheless, challenge for the dental professional in the anticipated era of stem cells and tissue engineering is imminent

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None.

Conflict of Interest

None.

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