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Dental Stem Cells-An Overview

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Abstract

Teeth are the natural, non-invasive source of stem cells. Dental stem cells are easy, convenient and affordable to collect and has a varying range of potential therapeutic applications. Tissue engineering is the main field in the regenerative medicine and dentistry. The mesenchymal dental stem cells have high proliferation and capacity to differentiate into odontoblasts, cementoblasts, osteoblasts and other cells. The objective of this review journal is to discuss the history of stem cells, different types of stem cells, their isolation approaches, collection and preservation of dental stem cells and their applications.

Keywords: Dental stem cells, Regeneration, Reconstructive dentistry, Multi-lineage differentiation, Dental pulp stem cells(DPSCs)

Introduction

Stem cells are undifferentiated cells that can divide and give rise to identical undifferentiated cells. Under specific conditions, they tend to discriminate into different cells that comprise the human body(18). The stem cells can be divided into 2 groups 1) The embryonic stem cells and 2) The adult stem cells. The adult stem cells are located in bone marrow, skin, adipose tissue, and dental pulp among the human tissues(1-4,18). The basic stem cell knowledge is well established in artificial skin therapies whereas investigation is still ongoing for conditions like Diabetes

Mellitus and atherosclerosis(5-7). Stem cells can be separated from oral tissues like Craniofacial bone, PDL, Dental Follicle, Dental Pulp, Tooth Germ, Periosteum, Apical Papilla, and Mucosa Gingival(8,9). The main three parameters that are being centered on Dental tissue Engineering are 1) The type of cell that should be used, 2) The scaffolds, where the cells should be seeded, and 3) The growth factor/ molecular signals that should be applied(18). The dental stem cells have mesenchymal stem cells(MSCs))- alike qualities that have the capacity for self-renewal multi-lineage discrimination potential. Among oral tissue-derived stem cells, Human dental pulp stem cells(hDPSCs) are being studied extensively because of their easy accessibility and lower invasive harvesting. These cells tend to form dentin-like tissue and differentiate into osteoblast-like cells which in turn form bone in vitro. By giving some specific stimuli, DPSCs differentiate into several cell types which include neurons, adipocytes, and chondrocytes(8). This journal focuses on the different stem cells, identification, isolation, prevention, and storage of stem cells.

Origin Of Stem Cells

Stem cells are known to be" progenitor or precursor" cells which are defined as clonogenic cells that can

perform both self-renewal and multi-lineage differentiation(10,16). German biologist Hackel was the first to term" stem cell" in 1868(11,16) and it was coined by Wilson(12,16). The existence of hematopoietic stem cells was given by Alexander Makismov in Berlin(13,16).

Replacing Regenerating human cells, tissues organs for therapeutic applications is the goal of regenerative medicine(14,16). The conception of this in the medical field is advanced after the discovery of stem cells and it has also set up usages in dentistry after dental stem cell identification(16). In 2000 Gronthos et al discovered and isolated odontogenic progenitor population in adult dental pulp giving an advancement in dental history(15,16). The cells are known to be dental pulp stem cells(DPSCs). After this discovery, numerous experimenters reported different dental stem cells which will be dealt with below.

Stem Cells Of Dental Tissues

Dental pulp stem cells [DPSCs]:

Dental pulp stem cells are the first human stem cells, that are isolated from adult human pulp by enzymatic digestion of impacted third molar(32). They show analogous characteristics to BM stem cells. A comparison of both shows analogous gene expression for more than 4000 genes(33). Odontoblastic differentiation potential is an important point of DPSC. Treatment with TGF beta 1 or in combination with FGF 2 causes the differentiation of DPSC into odontoblast(34). In recent studies, it has been shown that DPSC can also differentiate into carcinoma cells(35). Immature dental pulp stem cells(IDPSC) is a sub-population DPSC. They show engraftment in different tissues after transplantation in immunocompromised individuals(36).

Stem cells from human- exfoliated deciduous teeth [SHEDs]:

SHED has been linked as a population of clonogenic, largely proliferative postnatal stem cells that can differentiate into osteogenic and odontogenic cells(37). In vivo, transplanted SHED can induce bone formation, induce dentin, and survive in the mouse brain along with neural markers(38). When cultivated in a neurogenic medium SHED don't grow as individual cells.

SHED has immunomodulatory characteristics. They inhibit T helper 17 cells and reduce their number of peripheral blood(39).

Periodontal Ligament Stem Cells[Pdlscs]:

PDLSC is isolated from cryopreserved periodontal ligament(40). It shows analogous characteristics between DPSC and BMSC. These are multi-potent and can separate into osteogenic, adipogenic, neurogenic, and chondrogenic cells in vitro(41). PDLSCs new therapeutic agents in reconstructive dentistry(42).

Dental Follicle Progenitor Stem Cells[Dfpscs]:

The Dental Follicle which covers the tooth has a role in the formation of cementum, PDL, and alveolar bone. They were separated from the follicles of 3rd molars(18,23). Later they were modified into osteoblasts, adipocytes, and nerve-like cells in vitro(18,24-26), they could also form cementum in vivo(18,27). Implanting DFPSCs in the mice leads to the formation of new PDL after 4 weeks of implantation(18,28). This led to the formation of PDL and also led to the development of regenerative therapies and reconstructive treatments. There are three morphologically different populations of DFPSC in human dental sacs: HDF1, HDF2, and HDF3(29,30). DFPSCs express markers like CD90, CD59, CD29 and CD13. It does not express hematopoietic stem cell markers(22,31).

Stem Cells From Apical Papilla[Scaps]:

They are separated from the upper dental papilla, the precursor of dental pulp from the 3rd molars and teeth with open apices. These stem cells differentiated into osteoblasts and odontoblasts both in vitro and in vivo(18-20). SCAPs are more efficient than the DPSCs. SCAPs and PDLSCs with HA/TGT [Hydroxyapatite/tricalcium phosphate] were transported to the mice leading to the formation of dentin and cementum/sharpey's fibers respectively(18,21). Thus SCAPs have a role in regenerative endodontic therapy[Revascularization]. Cell surface antigens for mesenchymal stem cells like CD146, CD90, CD44, CD24 and STRO-1 are expressed(22).

Identification Of Dental Pulp Stem Cells

Four generally used stem cell identification ways(16,17) are,

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1. Fluorescent antibody cell sorting By using specific antibody labels to stain the cells and using a flow cytometer stem cells can be identified and isolated from a mixed cell population.
2. Immuno magnetic bead selection
3. Immuno histochemical staining
4. Physiological and histological criteria which include phenotype, proliferation, chemotaxis, mineralizing activity, and isolation.

Isolation Of Dental Pulp Stem Cells

Various ways of separating stem cells from dental pulp are(16),

1. Size sieved isolation :

A 3 collagenase Type 1 solution is used for the enzymatic digestion of whole dental pulp tissue which is done for 1 hr. at 37 degrees Celsius. By filtering and seeding, cells with peripheries around 3 and 20µm are attained for the culturing and modification process. By this, most of the small-sized cells with a high chance of stem cells can be isolated.

2. Stem cell colony civilization :

Single-cell suspension cells are prepared by enzymatic digestion of the DPT which is helpful in the conformation of colonies containing 50 or many cells which are then amplified.

3. Magnetic-activated cell sorting(MACs) :

The immune magnetic method is used for the separation of stem cells based on the type of surface antigens they contain(CD271, CD34, CD45, STRO-1 & and C- KIT). This isolation procedure is simple, affordable, and can handle a large number of cells but the purity of stem cells is low.

4. Fluorescence-activated cell sorting(FACs) :

The technique of isolation is based on cell size and luminescence from cell suspension which is accessible and effective. Downsides include high-end equipment, largely skilled workers, reduced viability of FACs-sorted cells, and isn't useful to recover large quantities of cells.

Collection, Isolation, And Prevention Of Stem Cells

Collection:

Freshly extracted tooth is most frequently collected and is transferred into a vial containing hypotonic phosphate buffered saline solution. Vial is sealed and placed into thermette. Thermette along with insulated transport vessel maintains the sample in hypothermic state which is essential for transportation. This procedure is known as sustentation(43).

Isolation:

A basic approach to segregating MSCs in tissue samples involves the enzymatic digestion of tissues followed by the growth of isolated cells(44).

The identification of MSCs involves a series of in vitro tests

1. colony forming assays(used to confirm clonogenicity)
2. phenotypic assay(estimate cell morphology or shape)

In vitro functional assay tests putative MSCs for multi-potency by verifying that differentiated cells demonstrate the applicable phenotypic characters(45).

In vivo, functional assays are used to confirm that stem cells implanted into a new environment integrate with adjacent cells, survive, and function as differentiated cells(46).

Tooth Stem Cell Banking

The approach used for storage are

I) Cryopreservation :

This the process of preventing by cooling the stem cells to sub-zero temperature. Cells harvested near end of log phase are best. Liquid nitrogen at<-150 ° c is used(47).

II) Magnetic freezing :

It's known as cell alive system that works on the principle of a weak magnetic field to water or cell tissue which will lower the freezing point of that body up to 6- 7 °c(48).

DSCs have various clinical benefits in the field of regenerative medicine, the preservation of DSCs for medical use established the concept of" tooth bank"(49). Bio Eden has multinational laboratories in UK and Thailand with global expansion plans. In Japan, the first tooth bank was established in Hiroshima university and it was named as" Three

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brackets" in 2005. The Norwegian tooth bank setup in 2008 is collecting exfoliated primary teeth from children in Norway. Stemade introduced the concept of dental stem cells banking in India recently by launching its operations in Mumbai and Delhi(50).

THERAPEUTIC POTENTIALS OF Dscs:

Angiogenesis And Vasculogenesis:

Vasculogenesis is used to treat ischemic heart disease which is still being in process in regenerative medicine. SP cells rich in stem cell activity(8,51,52) is found in human PDL cells and porcine dental pulp tissues(8,53). These cells have the property of vasculogenesis. They separated SP cells which have CD31 and CD146 genes. DPSCs cells are maintained at there stem cell niche by EphB/ephrin-B molecule. After an injury, the DPSC moves to the dentin surface which is guided by EphB/ephrin-B interactions. The results thus show the role of EphB/ephrin-B molecule in dental pulp regeneration(8,54).

Liver Disease:

Liver cirrhosis, an irreversible fibrotic changes occurring in liver can lead to impaired liver function, portal hypertension and finally to hepatocellular carcinoma. Liver transplantation is the only treatment. For both the pediatric and adults who suffer from liver function has a MSC-based therapy which have SHED as the main cell source(8,55). Choe et al. explained that melatonin enhance hepatic differentiation of hDPSC by modulating p38, ERK, BMP and NF-jB pathways(8,56). The result thus show grafted hDPSC and melatonin as a combined therapy could treat liver cirrhosis.

Therapeutic Applications In Dentistry:

DSCs are used in repair of damaged dentin, pulp resvascularization and regeneration. The DSCs combined with novel scaffolding materials help us to reach the goal of engineering oral tissues. Whole tooth regeneration, a present dental regenerative research which is under progress would decrease the difficulties with the current dental treatments like prosthesis, implants, and tooth transplantation(8,57).

Regenerative Endodontic Therapy:

The current dental treatment of infected pulp is done by removing necrotic pulp and replacing the root canal with bio inert cements to obturate the root canals. The drawback is that it could not restore the lost pulp and the vitality of tooth is completely lost. DPSC is used to regenerate healthy pulp which is simple and very effective treatment. DPSC have shown a pulp like tissue both ex vivo and in vivo(8,58-62).

Dentin Regeneration:

Pulp-dentin complex gets regenerated by the formation of tertiary dentin, reactionary dentin and reparative dentin. DPSCs with clonogenic ability, high reproductive activity and multi-lineage differentiation potential is important for tertiary dentinogenesis(8,15,63-65). The DPSCs first differentiate into odontoblast later forms tertiary dentin at the damaged sites(66). Regeneration of dentin is done by two different approaches(67,68). The first one where a device is used as a filling material into the deep cavity of tooth. They used few growth factors or molecules to form reparative dentin. The second one put scaffold with odontoblast-like cells on open pulp to grow over it(69-71).

Conclusion

Stem cell examination has expanded at an exponential rate, though its therapeutic uses progress at a slower phase. It has a promising future in tissue revitalization and the management of disease. It allows the form of defective tissues or functions through the transplantation of autologous cells. The DSCs can undergo self- renewal and have multipotent differentiation ability, but don't have the ethical issues associated with other sources(8).

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