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Mesenchymal Stem Cells in Orofacial Region – A Review.

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ABSTRACT

Stem cells are multipotent cells with continual self-renewal property. Mesenchymal stem cells are a group of stem cells derived from the hematopoietic stem cells of the bone marrow. The MSC in the dental origin is from the dental papilla, apical papilla, dental dollicle and periodontal ligament stem cells. The most important are the stem cells from the dental pulp tissue and those obtained from the deciduous tooth. MSC play a vital role as an immunomodulator and the differentiation is usually commited and restricted unlike other stem cells. Being derived from the ectmesenchyme they also have neural crest properties. The present review discusses the mesenchymal stem cells and its role in the oral region.

Keywords: Mesenchyme, stem cells, apical stem cells, dental papilla, follicle

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INTRODUCTION

The role of stem cells has gained importance in the recent years and has become an important field in understanding tissue regeneration and in therapeutics. Stem cells are undifferentiated cells which have a capacity to divide and replicate continuously [1,2].They are specialized cells which under appropriate biochemical signaling can be transformed into desirable cells with a unique self-renewal property. This property often used in repair and regeneration of various damaged tissues and organs [3].Out of the different types of stem cells known, mesenchymal stem cells belong to the category of adult stem cells, obtained most abundantly from bone marrow cells. They are multipotent cells which has the ability to differentiate into various lineages including the osteogenic, chondrogenic, and adipogenic types. They can also differentiate into other types like myogenic, neurogenic and tenogenic type [4,5].

Historical aspects of MSC's:

The identification of MSC's dates back to 1970, when Friedenstein et al identified a population of bone marrow derived hematopoietic stem cells and few groups of plastic adherent stromal cells. These cells were initially referred to as stromal cells and later werereretermed as Mesenchymal stem cells capable of forming single cell colonies [6]. These cells were later expanded in culture to produce round cells resembling fibroblastoid cells under the name Colony forming unit – fibroblast. In 1980's, the differentiation of a MSC into its lineages: osteoblasts, chondrocytes, and adipocytes were demonstrated [6,7]. Caplan later demonstrated that the turnover of bone and cartilage turnover was mediated by MSC's [8]. Later in 1990's, the possibility of a MSC to differentiate into myogenic phenotype and its expansion to various colonies with multilineagepotenetial was also demonstrated [9]. In late 1990's, Kopen et al described the transdifferentiation of MSC into ectoderm derived tissue [10]. As we entered the 21st century, MSC gained more importance and the transdifferentiate into endoderm-derived cells was also demonstrated [11]. The role of MSC in therapeutic applications and in immunomodulatory therapy was suggested by its ability to suppress T lymphocyte proliferation [12]

Types of Stem Cells

The various types of stem cells include the embryonic stem cells, adult stem cells and pluripotent stem cells. The adult stem cells includes the hemoatopoietic and the mesenchymal stem cells [13]. The various stem cells that are used in oral and maxillofacial region are predominantly from the bone marrow (Hematopoietic and mesenchymal) stem cells and from the adipose tissue. The bone marrow derived stem cells are abundant and been an important source of stem cell isolation [14]. The adipose tissue derived stem cells are pluripotent cells which exhibit a multilineage differentiation [15].

Mesenchymal Stem cells in the Orofacial region:

The mesenchymal stem cells derived from the dental region are abundant and the first type of stem cells that was isolated from dental region was the human pulp tissue and it was termed as post-natal dental pulp stem cells(DPSC) [16]. The other population of stem

cells in the orol region includes the stem cells extracted from deciduous teeth(SHED) [17] and the periodontal ligament stem cells(PDLSC) [18]. Stem cells can also be isolated from the apical papilla(SCAP) [19] and the dental follicle progenitor cells(DFPSC) [20]

MSC from Dental sites:

Dental tissues are specialized tissues and unlike a bony tissue which undergoes continous remodeling, dental tissue stem cells does not undergo this process. This makes the differentiation potency more restricted and committed as compared to the BMMSC. The interactions of the ectomesenchyme with the neural crest in the initial stages of development make them possess characteristics akin to those of neural crest cells [20].

Dental Pulp Stem Cells(DPSC):

There are cells which can differentiate into odontoblasts under appropriate signals and thereby contribute to the process of reparative dentinogenesis in case of dental injury [21]. The odontoblastic lineages are characterized by presence of polarized cell bodies with odontoblastic process extending into the dentinal tubule [22].

Apart from the dentinogenic potential possessed by them, a subpopulation also exhibit adipogenic and neurogenic differentiation resulting in a adipocyte or neuron like morphology with respective marker. osteogenic, chondrogenic and myogenic differentiation have also been demonstrated in vitro [23]. Invivo experiments involve the exposure of DPSC with calcium hydroxide, calcium phosphate which are used as pulp-capping agents by dentists. Since tooth repair is natural process, it suggests that dental pulp consists of mesenchymal stem cells. It has been demonstrated that a vascularized pulp like tissue with DSPP expressing odontoblast like cells are synthesized over time [24].

Stem Cells From Exfoliated Deciduous Teeth(SHED):

Mesenchymal cells can be isolated from deciduous teeth sockets predomintly the incisors. These cells are called SHED (Stem cells from human exfoliated deciduous teeth). They have high plasticity and are known to differentiate into neurons adipocytes, odontoblasts and osteoblasts. They induce formation of bone or dentin but fail to produce pulp-dentin complex [25].A striking feature to be noticed is that SHED induces recipient murine cells to differentiate into osteogenic lineages, though it is not a property attributed to DPSCs. This suggests that deciduous teeth had dual roles in guiding the eruption of permanent teeth and in inducing bone formation during the eruption of permanent teeth [25].

Periodontal Ligament Stem Cells(PDSC):

Periodontal ligament is specialized tissue locate between cementumor alveolar bone. Its property of continuous regeneration is because it contains mesenchymal progenitors such as STRO-1 Positive cells which are responsible for its plasticity, which helps them to form osteogenic, adipogenic, and chondrogenic phenotypes in- vitro. Therefore it proves they have cells which can regenerate tissues such as cementum, alveolar bone [26].

Stem Cells from Apical Part of Papilla (SCAP):

These are cells from the apical part of dental papilla, which have the potential to differentiate into odontoblasts and therefore have more proliferative rate and greater potential in tooth formation. They are easily accessible as isolated from third molars [27].

Stem Cells From Dental Follicle (DFSC):

They are obtained from dental follicle of third molars.They express stem cell markers such as NOTCH 1, STRO-1 and NESTIN. They are known to differentiate into cementoblasts in vitro and to form cementum in-vivo. Immortalizeddental follicle cells have proven to be capable to re-create periodontal ligament after in-vivo implantation [27].

Scope of stem cells in dentistry:

Various researches demonstrate the potential role of stem cells in root formation. The APMSC play a role in root formation. The pulpal stem cells aid in healing and regeneration by biological based materials to encourage physiological development and formation of root end. While it was previously called revascularization, currently the process is the physiological tissue formation and regeneration initiated by stem cells[28]. Stem cells also play a role in replantation and transplantation and in tissue engineering and regeneration resulting in the formation of tissue similar to native pulp[28].

Mesenchymal Stem cells as an alternative to guided bone regeneration:

The placements of implants in a socket devoid of alveolar bone is usually a challenge for an implanologist. The insufficiency is replaced by augmentation such as. Guided bone regeneration (GBR) which aims at regenerating bone, via the use of barrier membranes, in areas with alveolar ridge deficiencies, thus allowing implant placement in an appropriate angulations. An important aspect that plays a role in the overall regeneration of the bone augmentation procedure is the recruitment of osteoprogenitor and mesenchymal stem cells from the surrounding wound environment into the osseous defect [29]. Progenitor cells, such as mesenchymal stem cells, have in the gingival connective tissues have been identified recently and named gingival mesenchymal stem cells (GMSCs) [30]. These progenitors exhibit self-renewal, clonogenicity and multipotent differentiation properties. They also have an osteogenic potential which is capable of bone regeneration. GMSC inhibits the lymphocyte proliferation and inflammatory cytokines and suppress the inflammatory response. It also promotes the recruitment of regulatory T-cells and anti-inflammatory cytokines providing an environment for osseous integration [31].

Mesenchymal stem cell Niche:

The concept of stem cell niche as a special microenvironment to retain the stemness was proposed in 1978 [32]. The niche is a three dimensional fixed compartment, which participates in regulation of stem cell proliferation, control the fate of stem cell progeny, and in prevention of the stem cells from exhaustion[33]. The major site of MSC niche is the bone marrow in which a complex interaction between cellular and noncellular components

occurs. Hematopoietic stem cells reside in two different areas: endosteal niche which maintains HSC quiescence over the long term and perivascular niches which regulates the HSC proliferation and mediate circulation. The DPSC niche in human dental pulp was are localized in perivascular and perineural sheath regions and showed positivity for STRO-1, CD146, and pericyte-associated antigen. They are located as small clusters of cells in the extravascular region. The dental stem cells and the bone marrow MSC's secure at least a niche in the perivascular region [34].

Immunomodulation of Mesenchymal Stem cells:

There are two perspectives which are important in immune regulation by mesenchymal stem cells. The first one is the immunosuppressive effects of allogenic mesenchymal stem cell and the second is the effect of in cytokines on the MSC activity [35].The potential mechanisms underlying this immunosuppression of the xenografts and allografts are the capacity of MSCs to down-modulate immune reactions which are executed by T cells, dendritic cells, NKcells , and B-cells. MSCs thus have a potential role in enhancing the engulfment of tissue cells for prophylactic prevention and in the treatment of GVH disease and autoimmune disease to prevent rejection and promote transplanttolerenace and increase the survival rate. SCAP and PDLSCs have also demonstrated immunosuppressive properties [36,37].

CONCLUSION

Therefore based on the above data's collected and studies conducted it can very well be said that stem cells especially mesenchymal stem cells isolated from various sources such as dental tissues have been proved to be of great potential in the field of dentistry. Despite challenges of isolating, expanding and defining stem cell population, mesenchymal stem cells hold tremendous promise for tissue regeneration at a clinically useful level. There are dramatic examples of potential use of stem cells in regenerative medicine but immense work has to be done to characterized graft versus host stem cell immune interactions and to identify mechanisms enabling the delivery or homing of stem cells to the site of interest in the times to come.

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