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Application of Stem Cells in Dentistry

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Abstract

Stem cells are called non-differentiated cells in the human body that have the ability to differentiate into specialized cells with a new specialized function. Dental tissues have been investigated for many years as a potential source for stem cell isolation. Important criteria for dental tissue stem cells are: healthy pulp, intact blood flow, absence of infection, deep caries and other pathologies. The best source of stem cells are the teeth of young, healthy patients, whose stem cells have the greatest ability of proliferation, but stem cells from permanent teeth of middle-aged people can also be used in the same way. This is a great advantage in terms of the length of life and almost safe use in future regenerative therapy, especially when it is known that the best stem cells for therapy are their own, because in this way the risk of neuro-compatibility and tissue rejection is minimized. The stem cells of dental pulp have opened new perspectives in the therapeutic use of these cells not only in the regeneration of dentine, tissue of periodonium and bone-joint tissue of the craniofacial region, but also in the treatment of neuro-trauma, autoimmune diseases, myocardial infarction, muscular dystrophy and connective tissue damage.

Keywords: Stem cells; Dental tissue; Regenerative dentistry

Introduction

Stem cells are called non-differentiated cells in the human body that have the ability to differentiate into specialized cells with a new specialized function [1]. They can differentiate into different types of cell types in the body. Because of their unlimited ability, stem cells play a role in the repair and repair of damaged cells and tissues, can compensate other cells in the body and regenerate damaged tissue. After the stem cell is divided, each newly born cell has the potential to remain stem cell or convert to a new type of differentiated cell [2].

The term stem cells first appeared in scientific literature as early as 1868 in the work of German biologist Ernest Haeckel. Haeckel used the term "stem cells" to describe a progenitor single-celled organism, which he assumed was the precursor of all multi-celled organisms [3]. In the mid-20th century, there was an increased interest in stem cell research. One of the greatest achievements in stem cell research is the work on specific gene modification by embryonic stem cells for which in 2007 Mario R, Capecchi, Martin J, Evans and Oliver Smithies were awarded the Nobel Prize for Medicine [4].

Research conducted on stem cells recently attracted a lot of interest in the therapeutic potential of these cells. Modern research is considering the role of these cells in the fight against severe degenerative diseases, the main characteristic of which is the progressive loss of cells and tissues [5].

Stem cells have attracted special attention from scientists after discovering their presence in much more tissue than previously thought. Today there is evidence of the presence of stem cells in the heart muscle and brain, locations that until recently were not known to exist [6].

Stem cells are classified in relation to their function on: normal and cancerous stem cells, based on the source of isolation to: embryonic, fetal, stem cell from the umbilical cord blood and adult stem cells. The existence of adult stem cells to date has been proven in peripheral blood, bone marrow, hair follicle, digestive tract epithelium, skeletal and cardiac muscle, lungs, retina, fat tissue, liver, pancreas, periostyum and tooth [7-10].

Dental tissues have been studied for many years as a potential source for stem cell isolation [11]. Important criteria for dental tissue stem cells are: healthy pulp, intact blood flow, absence of infection, deep caries and other pathologies. The best source of stem cells are the teeth of young, healthy patients, whose stem cells have the greatest ability of proliferation, but stem cells from permanent teeth of middle-aged people can also be used in the same way. This is a great advantage in terms of the length of life and almost safe use in future regenerative therapy, especially when it

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is known that the best stem cells for therapy are their own, because in this way the risk of neuro-compatibility and tissue rejection is reduced to a minimum [11,12].

5 different populations in postnatal dental tissues were isolated:

1. Stem Cells of the Dental Pulp (DPSCs)
2. Stem Cells of Primary Tooth (SHEDs)
3. Stem Cells of Apical Papilles (SCAPs)
4. Stem Cells of Periodontal Ligament (PDLSCs)
5. Precursor Cells of Dental Follicle (DFPCs) [13]

Stem cells of the dental pulp

Dental pulp cells are localized in the perivascular region of the pulp. They are highly proliferative; clonogenic, multipotent, and exhibit a high degree of plasticity [14]. Experimental studies have shown that the pulp contains cell populations containing osteogenic markers that correspond to osteogenic differentiation inducers. Dental pulp cells are located mainly in the pulpy-rich cell area in perivascular and perineural areas [15]. They can be differentiated into different cell lines such as: adipocytes, osteocytes, hondrocytes, and myocytes *in vitro*, including *in vivo* studies that show differentiation pulmonary stem cell cells in odontoblaste [16]. Stem cells of dental pulp show an elevated immunosuppressive activity compared to adult mesenchymal stem cells of the bone marrow [17].

DPSCs have pronounced bone markers such as: bone sialoprotein, alkaline phosphatase, osteocalcin, osteonectin, and Collagen Type I and III. During their breeding in substrates with the addition of hydroxyapatite, bone and cement tissue forms [18]. Laino et al. have shown that DPSCs can be differentiated into functional osteoblasts *in vitro* and produce extracellular and mineralized matrix [19]. DPSCs have all the traits needed for successful therapeutic use: 1) are easily available for insulation; 2) multipotential; 3) show interaction with biomaterials that are used as matrices induce the proliferation of these cells; 4) are long-lasting [20].

Stem cells of primary teeth

Primary teeth represent a rich source of stem cells. It is a heterogeneous cell population that has a clonogenic capacity. Compared to DPSCs, they grow and proliferate significantly faster and have a greater number of divisions [21]. SHEDs can be differentiated *in vitro* into osteogenic, odontogenic, myogenic, and chondrogenic lines. *In vivo* exhibit osteoinductive capacity [22].

Stem cells of apical papilles

Stem cells can also be isolated from the apical soft tissue papilla that surrounds the top of the root of the permanent teeth in development. Apical papilla is a precursor of radicular pulp.

These cells show the possibility of differentiation in the cells of estrogenic, odontogenic, adipogenic and neurogenic lines. Compared to DPSCs and SCAPs, there are less pronounced markers such as dentine sialoprotein, phosphoglycoprotein extracellular matrix, transforming the growth factor [23]. They also have the ability to differentiate into the pulpodentine complex during transplantation into an immunodeficiency mouse [24]. SCAPs have a greater ability to regenerate dentine than DPSCs [25].

Stem cells of parodontal ligament

This cell population is found in a human healthy periodontal ligament. They are localized in the coronary and apical parts of the root furcation. PDLSCs have the ability to differentiate into cells similar to cement oblasts, osteoblasts, adipocytes, chondrocytes, and fibroblasts [26]. Recent studies have shown that transplantation of these cells into periodontal defects leads to the attachment of the periodontal ligament to the surface of the teeth and the regeneration of the lost alveolar bone tissue [27].

Precursor cells of dental follicle

These cells are located in a dental follicle, an ectomesenhimal structure that surrounds the enamel organ and dental tissue of the tooth during development, prior to emergence. *In vitro*, after adequate induction, DFPCs show osteogenic, odontogenic, and cementogenic differentiation [28]. *In vivo* implantation of DFPCs in the immunodeficient mouse, the result is the formation of fibrous and rigid tissue rich in osteocalcin, bone sialoprotein, and Collagen Type I [29].

The challenge and the promotion of osteogenesis in order to compensate physiologically and pathologically lost bone tissue is a major challenge in modern dentistry. Although bone tissue has the ability to repair and regenerate, bone loss after periapical infections, periodontal illness or trauma can lead to tooth loss if adequate treatment is not applied. In order to avoid auto transplantation of bones from distant parts of the body, modern dentistry is resorting to the application of various alloplastic materials, allografts and xenografts. However, all these materials have their limited application and disadvantages. Allogens and xenogenic grafts have similar biochemical characteristics as bone, but a major disadvantage is the inability to initiate osteogenesis [30].

The stem cells of dental pulp have opened new perspectives in the therapeutic use of these cells not only in the regeneration of dentine, tissue of periodonium and bone-joint tissue of the craniofacial region, but also in the treatment of neuro-trauma, autoimmune diseases, myocardial infarction, muscular dystrophy and connective tissue damage.

However, in addition to the low availability of stem cells, the great problem is the very low quantity and discretionary quality of the transmitted cell lines. The amount of stem cell cells that possess the necessary cell markers and abilities is very limited. More experimental research is needed on the use of signaling molecules and specially designed carriers to target the behavior of stem cells as well as their correct differentiation into the desired tissue. Their development will lead to new solutions to many clinical problems that pose a challenge even in today's modern dentistry.

Conclusion

Development in stem cell research is progressing very rapidly. Stem cells will make great progress in the treatment of dental caries, periodontal disease, oral mucosal regeneration, dental pulp, salivary glands in patients with xerostomia and other craniofacial structures. In the future, dental practices can become "stem cell banks" for patients who would later have had the need to replace alveolar bone, teeth or some other oral tissue.

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