SEVEN publicações acadêmicas

Stem cells of dental origin and their applications: A literature review

Crossref doi
https://doi.org/10.56238/globalhealthprespesc-066

Alan Ferreira de Moraes
Graduating in Dentistry
Federal University of Paraná (UFPR), Curitiba - PR
E-mail: alan.ferreira@ufpr.br

Ivo Hartmann
Advisor
Master in Cell Biology
Federal University of Paraná (UFPR), Curitiba - PR
E-mail: Ivo.hartmann@ufpr.br

ABSTRACT
Stem cells are undifferentiated cells with the capacity for self-regeneration and formation of functional cells of tissues and organs. Current studies in biotechnology aim to understand and control the differentiation of these cells for scientific applications. Several types of stem cells are derived from dental tissues, including dental pontal stem cells (DPSCs), stem cells isolated from the pulp of exfoliated deciduous teeth (SHED), periodontal ligament stem cells (PDLSCs), apical papilla stem cells (SCAPs) and dental follicle cells (DFCs). These cells have potential for different applications in dentistry and tissue regeneration. Studies have investigated their properties and differentiation capacity for clinical and therapeutic use. The present review aims to evaluate what is known about these cells, as well as the possible clinical applications in regenerative therapies in current dentistry.

Keywords: Dental Stem Cells, Tissue regeneration, Regenerative Dentistry.

1 INTRODUCTION

Stem cells are populations of undifferentiated cells characterized by the great capacity for self-regeneration and duplication, in addition to the potential to originate different types of functional cells that constitute tissues and organs of the organism(1). Several current studies in the areas of biotechnology seek to understand and control these differentiation processes for use by science(2).

These cells are categorized according to their differentiation potential, being classified into totipotent, pluripotent, multipotent, oligopotent and unipotent. In addition, these cells are also classified according to their origin, divided into embryological stem cells, adult tissue stem cells, resident tissue stem cells, and induced pluripotent stem cells (1).

Mesenchymal stem cells are human somatic stem cells, have attracted attention due to their potential for practical use. Mesenchymal stem cells have low immunogenicity, accumulate at the site of tissue injury, and secrete growth factors, cytokines, and bioactive substances. For these reasons, they have attracted attention due to their potential for therapeutic use(3). Several types of stem cells have been found in dental and periodontal tissues, evidencing the possibility of extraction and use of these cells in dentistry.(4)(5).

Therefore, the objective of this work is the evaluation of the main stem cells of dental origin, as well as the possible clinical applications focused on dentistry due to their high therapeutic potential of tissue regeneration and their other uses in bioengineering.

2 METHODOLOGY

For the development of this literature review, the database was used *PubMed* and *Scielo*, to find articles that addressed the topic related to stem cells of dental origin and their applications in dentistry, using the following descriptors: dental stem cells, tissue regeneration, in Portuguese and English languages. We selected papers with publication date from the year 2003 to the present date (2023) that presented information relevant to this review.

3 LITERATURE REVIEW

3.1 STEM CELLS OF DENTAL ORIGIN

There are numerous types of stem cells originating from dental tissues, such as dental tip stem cells (DPSCs), stem cells isolated from the pulp of exfoliated primary teeth (SHED), periodontal ligament stem cells (PDLSCs), apical papilla stem cells (SCAPs), and dental follicle cells (DFCs)[4][5].

3.1.1 Dental pulp stem cells

In some studies, mesenchymal stem cells were isolated and obtained from the dental pulp of deciduous teeth, first premolars and third molars extracted, these being called Dental Pulp Stem Cells. DPSCs have the ability to differentiate into odontoblast-like cells and produce mineralized tissue both in *vivo* and *in vitro*. In addition, these cells can differentiate into bone, muscle, endothelial, chondrocytes and adipocytes[3][7]. Also, the production of dentin-like structures with pulp tissue inside and one and a lining of odontoblastic cells after DPSCs transplantation in immunocompromised rats have been observed in studies[5].

3.1.2 Stem cells from the pulp of exfoliated primary teeth

Multipotent stem cells were found in exfoliated human deciduous teeth (SHED), which have characteristics such as high proliferation rate, clonogenic and differentiation capacities for different tissues, such as bone tissue, nerve cells, adipocytes and odontoblast([5][3]. In comparison, the SHEDs demonstrated a higher proliferation rate in relation to the DPSCs, but they have difficulties in forming a complex similar to the complete dentin-pulp in vivo[3][6].

3.1.3 Periodontal ligament stem cells

Mesenchymal stem cells were found in the periodontal ligament, with the capacity to differentiate into mesenchymal, ectodermal and endodermal strains *in vitro*, which suggest the multipotency of these cells[(8).]

The PDLSCs, under certain experimental culture conditions, differentiated into cementoblast-like cells, adipocytes, and collagen-forming cells. These cells demonstrated the ability to generate structures similar to cementum and periodontal ligament, and contributed to the repair of periodontal tissue[(9).]

3.1.4 Apical papilla stem cells

The apical papilla is described as a connective tissue positioned at the root apex of teeth that are still developing[(10),] which becomes present from at least two-thirds of the root has already been formed, being well visualized histologically above the epithelial diaphragm. Although the apical papilla is a continuation of the dental pulp, in cases of pulp necrosis, the papilla fights the process of necrosis of the pulp and tends to survive due to its access to the apical collateral circulation[(11)].

Another type of mesenchymal stem cells were isolated from the apical papilla of permanent teeth with incomplete development. SCAPs have the ability to differentiate into several different cell lines, being odontoblasts, osteoblasts, nerve cells, adipocytes, chondrocytes and hepatocytes, demonstrating a high therapeutic potential in the large area of health[(12)].

3.1.5 Dental follicle cells

The dental follicle is an embryonic connective tissue, derived from the neural crest cells, that surrounds the enamel organ along with the developing dental germ papilla. In addition to the function of forming the periodontium tissues (alveolar bone, periodontal ligament and cementum), the follicle plays an important role in coordinating tooth eruption by regulating the resorption and formation of the alveolar bone, thus evidencing its crucial role in dental development[(13)(14).]

DFCs are characterized as pluripotent stem cells, precursors of periodontal tissue, and can differentiate into cells of the alveolar bone, periodontal ligament and cementum *in vivo*. In addition, they also have the ability to differentiate into adipocytes, chondrocytes and nerve cells *in vitro*. More recent studies have also shown the ability to differentiate into cardiomyocytes and saliva-producing glandular cells[(14).]

3.2 APPLICATIONS OF DENTAL STEM CELLS IN CLINICAL DENTISTRY

3.2.1 Regeneration of dental tissues

Currently, the treatment for caries diseases, for example, is characterized mainly by the removal of carious tissue and its replacement by a synthetic material for the restoration of dental form and function(15). In some studies, it has already been possible to use a solution of different growth factors to form an odontogenic environment, capable of inducing the differentiation of DPSCs into functional odontoblasts for the formation of a regular dentin-pulp complex(16).

Still, other studies have shown the use of mesenchymal stem cells with the use of certain growth factors and also biomaterials for the formation of the dental organ, which was later successfully transplanted into an immunocompromised host with the necessary blood supply. In all studies, the formation of enamel and dentin was evidenced(6).

In a certain research, a three-dimensional culture method of for the growth of teeth in the jaw of the rat was used. Thus, epithelial and mesenchymal cells were seeded sequentially in a drop of collagen gel and then implanted in the dental cavity of adult rats. With this technique, the dental germ produced formed a tooth with all dental structures, such as odontoblasts, ameloblasts, dental pulp, blood vessels, crown, root and even periodontal tissues, such as the periodontal ligament and alveolar bone(17).

In the case of pulp damage, usually irreversible, there is the possibility of Endodontic Regeneration Therapy (ERT), which consists of replacing inflamed or necrotic pulp tissue through tissue regeneration in cases of endodontic treatments. In RET, there is the transplantation of stem cells of dental origin (DPSCs, SCAPs, SHEDs and PDLSCs) combined with growth factors and biomaterials within the root canal, resulting in the formation of the dentin-pulp complex resulting from the differentiation of these stem cells into odontoblasts. The ideal pulp regeneration process should not only form the same structure as the natural dental pulp, but also restore its function, with the formation of blood vessels and innervations(18)(19).

3.2.2 Regeneration of periodontal tissues

Traditionally characterized as infectious inflammatory diseases resulting from the interaction of the oral biofilm and the inflammatory and immune response of the host to combat microorganisms. However, this response can be harmful to periodontal tissues, causing a progressive loss of tissue at the site of injury(20).

The unique anatomy and composition of periodontal tissues results in a complex regeneration process. Current treatment techniques focus on the control of the microbiota at the site, reduction of inflammation and removal of injured tissues for the regeneration of periodontal tissues with the formation of a long junctional epithelium binding tissue, which does not provide a strong connection between the dental root and the adjacent gingival connective tissue[20][21].

With this, several processes related to tissue regeneration have been studied, one of them being tissue engineering based on the use of stem cells that with certain conditions, differentiate into cells of periodontal tissues, thus restoring their function. Stem cells from the periodontal ligament PDLSCs gain more visibility, given their ability to differentiate into cementoblasts and osteoblasts[21]. In addition, studies have shown that stem cells from the periodontal ligament can be inserted into sites of periodontal defects without adverse immunological or inflammatory consequences[22].

Stem cells derived from the dental follicle (DFCs) were able to form periodontal tissue with occasional blood vessels, and are also considered for the treatment of periodontitis and reconstruction of the insertion period[23].

3 CONCLUSION

Based on the articles studied, it is clear the range of options for obtaining and using dental stem cells, playing an essential role in regenerative dentistry. Therefore, it is necessary to continue the rigorous research on the subject so that more and more therapeutic possibilities for injuries in the field are discovered. In addition, the importance of the dentist in obtaining and processing the cells from dental elements extracted in procedures is notorious, so that there is no biological waste of these cells with enormous potential. Cell Processing Centers must continue to fulfill their important role of cultivating, processing, storing and delivering stem cells under conditions where they are capable of being used in properly regulated advanced therapies.

REFERENCES

KOLIOS, G.; MOODLEY, Y. Introduction to Stem Cells and Regenerative Medicine. Respiration, v. 85, n. 1, p. 3–10, 2013.

MCKEE, C.; CHAUDHRY, G. R. Advances and challenges in stem cell culture. Colloids and Surfaces B: Biointerfaces, v. 159, p. 62–77, nov. 2017.

NITO, C. et al. Dental-Pulp Stem Cells as a Therapeutic Strategy for Ischemic Stroke. Biomedicines, v. 10, n. 4, p. 737, 22 mar. 2022.

HU, L.; LIU, Y.; WANG, S. Stem cell-based tooth and periodontal regeneration. Oral Diseases, v. 24, n. 5, p. 696–705, 24 jul. 2017.

ZHAI, Q. et al. Dental stem cell and dental tissue regeneration. Frontiers of Medicine, v. 13, n. 2, p. 152–159, 4 jul. 2018.

PENG, L.; YE, L.; ZHOU, X. Mesenchymal Stem Cells and Tooth Engineering. International Journal of Oral Science, v. 1, n. 1, p. 6–12, mar. 2009.

ZHANG, W. et al. In vivo evaluation of human dental pulp stem cells differentiated towards multiple lineages. Journal of Tissue Engineering and Regenerative Medicine, v. 2, n. 2-3, p. 117–125, 2008.

TOMOKIYO, A.; WADA, N.; MAEDA, H. Periodontal Ligament Stem Cells: Regenerative Potency in Periodontium. Stem Cells and Development, v. 28, n. 15, p. 974–985, ago. 2019.

SEO, B.-M. et al. Investigation of multipotent postnatal stem cells from human periodontal ligament. The Lancet, v. 364, n. 9429, p. 149–155, jul. 2004.

MAGDA et al. Importância das células-tronco da papila apical nos procedimentos de revascularização pulpar. Mostra de Extensão, Ciência e Tecnologia da Unisc, v. 0, n. 1, p. 234, 2020.

NADA, O. A.; EL BACKLY, R. M. Stem Cells From the Apical Papilla (SCAP) as a Tool for Endogenous Tissue Regeneration. Frontiers in Bioengineering and Biotechnology, v. 6, 24 jul. 2018.

KANG, J. et al. Stem Cells from the Apical Papilla: A Promising Source for Stem Cell-Based Therapy. BioMed Research International, v. 2019, p. 1–8, 29 jan. 2019.

BI, R. et al. Function of Dental Follicle Progenitor/Stem Cells and Their Potential in Regenerative Medicine: From Mechanisms to Applications. Biomolecules, v. 11, n. 7, p. 997, 7 jul. 2021.

ZHANG, J. et al. Dental Follicle Stem Cells: Tissue Engineering and Immunomodulation. Stem Cells and Development, v. 28, n. 15, p. 986–994, ago. 2019.

BUSATO, ALS. Dentística: Filosofia, Conceitos e Prática Clínica. 1.ed. São Paulo: Artes Médicas, 2006.

YU, J. et al. Differentiation of Dental Pulp Stem Cells into Regular-Shaped Dentin-Pulp Complex Induced by Tooth Germ Cell Conditioned Medium. Tissue Engineering, v. 12, n. 11, p. 3097–3105, nov. 2006.

AKIHIKO KOMINE et al. Tooth regeneration from newly established cell lines from a molar tooth germ epithelium. Biochemical and Biophysical Research Communications, v. 355, n. 3, p. 758–763, 13 abr. 2007.

WEI, Y. et al. Neural Regeneration in Regenerative Endodontic Treatment: An Overview and Current Trends. International Journal of Molecular Sciences, v. 23, n. 24, p. 15492, 7 dez. 2022.

XIE, Z. et al. Functional Dental Pulp Regeneration: Basic Research and Clinical Translation. International Journal of Molecular Sciences, v. 22, n. 16, p. 8991, 20 ago. 2021.

OPPERMANN, RV. Periodontia Laboratorial e Clínica. 1 .ed. São Paulo: Artes Médicas, 2013.

HAN, J. et al. Stem cells, tissue engineering and periodontal regeneration. Australian Dental Journal, v. 59, p. 117–130, 23 set. 2013.

LIU, J. et al. Periodontal Bone-Ligament-Cementum Regeneration via Scaffolds and Stem Cells. Cells, v. 8, n. 6, p. 537, 4 jun. 2019.

MORSCZECK, C.; REICHERT, T. E. Dental stem cells in tooth regeneration and repair in the future. Expert Opinion on Biological Therapy, v. 18, n. 2, p. 187–196, 15 nov. 2017.