



Translational dentistry: stem cell and tissue engineering in regenerative dentistry

Flores-Preciado Julio Cesar¹, Castillo-Córdova Jacqueline², Bustamante-Pico Luis Alejandro², López-Berny Manuel².

¹Associate Professor, Mexicali School of Dentistry, Autonomous University of Baja California, Mexico

³Student, Dental Surgeon, Mexicali School of Dentistry, Autonomous University of Baja California, Mexico

Corresponding Author: Flores-Preciado Julio Cesar

Submitted: 05-09-2022

Accepted: 13-09-2022

ABSTRACT: Currently there is great interest in the therapeutic application of stem cells for tissue regeneration, this being a topic of global scientific interest. Current reports on mesenchymal stem cells indicate that it is possible to isolate several cells from different adult tissues, including bone marrow, neural tissue, muscle, skin, retina, cornea, among others. Regarding the use of mesenchymal stem cells from the oral cavity, it is reported that, from them, both those that have their origin in the dental pulp and those present in the periodontal ligament, in the apical papilla, the dental sac and other regions mucous membranes of the oral cavity, the formation of structures belonging to the dentin-pulp and periodontal complexes is possible. Likewise, their ability to stimulate new bone formation is reported, so they have a possible application in craniofacial bone regeneration.

One of the main advantages offered by the isolation of mesenchymal stem cells from the oral cavity over other means of obtaining, is the accessibility and easy handling of the samples, as well as the minimally invasive and painless techniques, compared to those obtained from bone marrow.

Due to their multipotential nature, families of mesenchymal stem cells from the oral cavity are a rich source of cell complexes that, by means of specific activation and induction techniques, have the capacity to differentiate into other cell complexes, which at a given moment can be used in therapies of regeneration associated with tissue engineering and regenerative medicine.

KEYWORDS: Mesenchymal stem cells, tissue engineering, regenerative medicine, bone defects, translational dentistry.

I. INTRODUCTION

A stem cell is a forming cell, undifferentiated, with the ability to self-renew (that is, produce other cells in a tissue), through cell

division; being able to carry out a specific cell differentiation by following an autonomous or induced differentiation pathway or guide, and, therefore, being able to form cells of one or more tissues; mature, functional, specific, and differentiated.

[1] It is possible to classify this cell group into two main ranges:

A. According to the origin or means of obtaining:

Embryonic stem cells (ESC): Embryonic Stem Cells). They derive from the inner cell mass of the embryo at the blastocyst stage (7-14 days of embryonic development). They can generate the three embryonic tissues: endoderm, mesoderm, and ectoderm.

Specific adult stem cells or organ. They derive from the mitotic division of embryonic stem cells, found in adult organs or tissues, and can generate specific cells for a tissue or organ. In this cell group, we can find the stem cells of the umbilical cord, the hematopoietic stem cells, and the undifferentiated mesenchymal stem cells, where those that have an origin from a tissue or structure of the dental cavity or oral cavity stand out.

B. According to its ability to differentiate:

Totipotent stem cells. They are those cells with the ability to grow and form a complete organism, both in embryonic and extra-embryonic components.

Pluripotent stem cells. To this group belong all those cells capable of producing cell groups corresponding to tissues in embryonic development and in mature structures.

Multipotential cell groups. They are those capable of only differentiating into a limited number of cells. An example is the bone marrow, which can differentiate into blood cells (red blood cells, white blood cells and platelets).

Unipotently cell groups. Cells with the ability to form only one cell type belong to this group.



II. METHODS

The objective of this study was to identify the relationship between the principles of tissue engineering and its applications in translational dentistry, intensely in the use of mesenchymal stem cells from the oral cavity. To find this relationship, an evidence-based search was carried out in databases (PubMed, Google Scholar), as well as postgraduate theses that are part of the institutional repository.

III. DEVELOPMENT

Mesenchymal stem cells of the oral cavity

[2] It corresponds to a family of cells derived from the mesenchymal lineage (MSC) that also have a capacity for self-renewal and differentiation to multiline. Stem cells derived from dental tissue are isolated from specialized tissues with powerful abilities to differentiate into odontogenic cells, so their interest derives in applications in regenerative therapy in translational dentistry.

[3] Dental stem cells (DSCs) constitute an exclusive population of self-renewing cells with potential utility in generating a biological replacement for human teeth. DSCs are organized into two types:

Epithelial cells, which contribute to the formation of dental epithelial structures and include the outer epithelium, stellate reticulum, stratum intermedium, and inner epithelium.

Mesenchymal cells, which contribute to the formation of mesenchymal structures such as the dental papilla, dental sac, dental follicle, and specific tissues such as the dentin-pulp complex, cementum, periodontal ligament, and alveolar bone.

Dental tissues of mesenchymal origin exhibit self-renewing properties due to the presence of stem cells even in adult stages. To date, 5 basic families derived from a dental structure or portion have been adopted either during odontogenesis and in adult stages, dental pulp stem cells (DPSCs), stem cells from exfoliated deciduous teeth (SHEDs), periodontal ligament stem cells (PDLs), stem cells of the dental papilla (SCAPs), and dental follicle stem cells (DFSCs).

IV. TISSUE ENGINEERING

[4] Tissue engineering is an interdisciplinary domain that uses the principles and techniques of life sciences and engineering with the aim of developing materials capable of rehabilitating, improving, or replacing non-functional or severely affected tissues. Its general

principle associates a three-dimensional matrix with autologous or allogeneic cells and growth factors. This strategy implies knowledge of the regulatory mechanisms that precede the embryonic development of tissues and organs to be repaired or created.

[5] Tissue engineering bases its scientific foundations through the synergy of three fundamental components (Fig. 1):

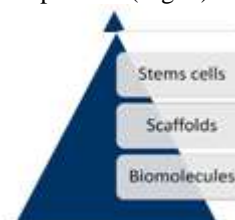


Fig. 1. Tissue engineering triad

Cells, that participate in the construction of a new tissue must have reproductive capacity, that is, cells in the cell cycle that have not yet entered the process of terminal differentiation; they are therefore cells capable of giving rise to other cells, such is the case of the mesenchymal stem cells of the oral cavity.

Scaffolds, among the characteristics of the materials, is that of being biocompatible or biologically acceptable.

Biomolecules, they are inducers or growth factors, the cell responds to the extracellular microenvironment by detecting chemical signals or physical stimuli that trigger their appropriate response by activating different molecular and biological mechanisms that lead to division, migration, differentiation, maintenance of the phenotype or apoptosis.

Applications of tissue engineering in regenerative therapy

Bone engineering

[6] Bone defects secondary to injury, disease, or congenital disorders represent a major health problem. Current strategies that are aimed at replacing bone defects include the use of autologous grafts, heterologous grafts, and synthetic biomaterials. Although these grafts restore tissue stability and function, there are still limitations. Bone bioengineering uses conductive and inductive strategies for the regeneration of small bone defects. Guided tissue regeneration (GTR) after periodontal surgery represents a conductive approach in bone regeneration. Bone morphogenic proteins (BMPs), related proteins, and the genes that code for these proteins allow inductive strategies to be used in situations where GTR is not sufficient. Its use associated with stem cells in the placement of surgical implants has



recently been proposed, demonstrating bone neoformation.

Cartilage engineering

Cartilage destruction is common in many diseases and after trauma. The design of biopolymers with mechanical and degradation properties has allowed bioengineering to develop cartilage tissues in animal models with defined sizes and shapes that could potentially be used in craniofacial reconstruction.

A new class of biomaterials called ECM (extracellular matrix) is now commercially available, designed in the form of prosthetic templates that mobilize the body's own cells and induce them to rebuild tissue, gradually replacing the prosthesis. This tissue bioengineering project aims to change the artificial replacement of organs for their natural regeneration. This technology can be applied in many ways for medical and dental problems (periodontal tissues, bone and TMJ tissue).

Dentin and dental pulp engineering

The production of dentin and dental pulp have been developed in animal model and in vitro study using tissue engineering strategies. One of the strategies is to induce the formation of new cells from the dental pulp using BMPs. Pulp tissue engineering may also be possible using cultured fibroblasts and the use of synthetic polymeric matrices. The dental pulp contains mesenchymal stem cells, which can proliferate and differentiate into dentin-forming odontoblasts. Damaged odontoblasts can be replaced by new populations of odontoblasts derived from pulpal stem cells.

Craniofacial bone defects

[7] Tissue engineering combined with the use of stem cells and gene therapy offers a biological, chemical, and physical tool to solve clinical problems involving periodontal disease, caries, tumours, trauma and craniofacial anomalies.

Craniofacial anomalies are frequent and recurring in dental care, mainly in surgery, periodontics, and prosthetics. The strategies used by bioengineering to create new tissues and organs are based on the combination of biomaterials with bioactive molecules that induce tissue formation by stimulating the proliferation of the stem cells used. This action can be performed through various procedures, such as:

Conductive strategies, through the passive use of materials such as cell membranes or frameworks,

Inductive strategies, by placing cells or bone morphogenic protein factors (BMPs), which are activated at the site of the defect, inducing tissue formation, and

Cell transplant strategies, through direct transplantation of cultured and differentiated cells in the laboratory and subsequent placement in inducing scaffolds, which act as growth supports and generate tissue to later implant in the patient.

[8] In regenerative therapy, tissue engineering is oriented towards the development of materials capable of facilitating the repair, regeneration, or replacement of damaged tissue. When a tissue is repaired or regenerated, the natural process must be improved, which constantly produces alterations and structural and functional limitations. From the first investigations at the end of the 20th century to the present, tissue engineering, initially as a multidisciplinary basic science that combined knowledge from different areas, later became a science based on technical and technological evidence applied to the development of research, to finally become a translational discipline that projects and links the knowledge generated in basic research with applied or clinical research, thus developing a new branch of knowledge generation, translational medicine [9,10]

[11] In dental sciences, the area of biomaterials has experienced a high research development focused on the production of inductive or bioactive dental materials from a restorative point of view, of innovation and with reports of success cases, but limited to basic tissues associated with tooth structure. Because the components associated with the oral cavity are part of the organic environment and whose tissues undergo measures of maintenance of balance or homeostasis like the rest of the tissues, it is possible to associate the capacities and potentials of repair and regeneration with a limited approach as well. than the rest of the tissues.

Therefore, it is also possible to establish the development of dentistry as a science which, not more than twenty years ago, was transformed from an evidence-based discipline, which was based on the application of theoretical knowledge and techniques applied to dentistry. clinic in compliance with the expectations of patient care, so that today, with advances in research and multidisciplinary association, a new area of opportunity is being developed, translational dentistry that, although it continues to respond to the commitment of clinical application, transfers the needs of patient care, to the development of basic and experimental clinical research, to finally



apply the knowledge and discoveries generated during preclinical trials, in the development of projects and studies of substantiated clinical application.

V. CONCLUSION

The current trend in terms of therapeutics is aimed at the comprehensive solution of conditions or illnesses that affect and impair the patient's quality of life, since treatments for aggressive diseases are very radical and postoperative results are delayed, sometimes painful and with low expectations of full recovery. Tissue engineering has established a very important synergy with biomedical areas, giving them new applied tools for comprehensive therapeutics. The new trend in the field of tissue engineering is the use of cell complexes and biomaterials focused on regenerative therapeutic use.

Dentistry as a basic and clinical science must establish an approach associated more with regenerative therapy than with corrective therapy, since research provides tools and knowledge of interest, but above all it allows clinical needs to migrate to research in translational dentistry.

REFERENCES

- [1]. Flores-Preciado J. Culture, isolation, and identification of dental pulp stem cells from permanent teeth. Postgraduate thesis, UABC repository, 2013.
- [2]. Huang GT-J, Gronthos S, Shir S. Mesenchymal stem cells derived from dental tissues vs. those from other sources: their biology and role in regenerative medicine. *Journal of dental research*, 2009, 88(9):792-806.
- [3]. Sell S. *Stem cells handbook*. Springer Science & Business Media, 2013.
- [4]. Pérez-Saldamando J. Evaluation of cell viability in a jarosite scaffold for applications in pulp coatings. Postgraduate thesis, UABC repository, 2022.
- [5]. Mhanna R, Hasan A. Introduction to tissue engineering. *Tissue engineering for artificial organs: regenerative medicine, smart diagnostics, and personalized medicine*. Wiley-VCH. 2017, 1:1-34.
- [6]. Castells-Sala C, et al. Current applications of tissue engineering in biomedicine. *Journal of Biochips & Tissue Chips*, 2013, 2:1-14.
- [7]. Agalli A. Craniofacial bone tissue engineering: Current approaches and potential therapy. *Cells*, 2021,10(11):1-32.
- [8]. Bonferoni M, et al. Biomaterials for soft tissue repair and regeneration: a focus on Italian research in the field. *Pharmaceutics*, 2021, 13(9):13-41.
- [9]. Mao A, Mooney D. Regenerative medicine: current therapies and future directions. *Proceedings of the National Academy of Sciences*, 2015, 112(47): 14452-14459.
- [10]. Howard D, et al. Tissue engineering: strategies, stem cells and scaffolds. *Journal of anatomy*, 2008, 213(1):66-72.
- [11]. Bakopoulou A, et al. Dental tissue engineering research and translational approaches towards clinical application. *Oral Healthcare and Technologies: Breakthroughs in Research and Practice*. IGI Global, 2017. 186-220.