Stem cells and their applications in Dentistry: a Literature Review

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ABSTRACT

Since stem cells were discovered, professionals in many different areas of healthcare have been using them as an important tool for fighting diseases, particularly diseases for which science has been unable to find cures. A stem cell is an undifferentiated unit with powerful self-renewal properties that is capable of organizing other cell types in the body. Many studies have shown the utility of embryonic or adult stem cells for forming teeth and for regeneration of bone and soft tissues. In view of the importance of the subject, this article provides a review of the literature on studies of stem cells and their potential applications in dentistry.

Keywords: Stem Cells, Dentistry, Regeneration.

Células-tronco e sua aplicabilidade na odontologia: uma Revisão de Literatura

RESUMO

Desde a descoberta da célula-tronco, diversos profissionais da área da saúde têm se utilizado dessa alternativa como importante meio para combater muitas doenças, principalmente aquelas cuja cura tem desafiado a ciência. Uma célula-tronco é uma unidade não especificada, com grande potencial de autorrenovação, capaz de organizar diferentes tipos celulares no organismo. Várias pesquisas apontam para a utilização de células-tronco embrionárias ou adultas na formação dental, regeneração tecidual e óssea. Baseado na importância deste tema, este estudo teve por objetivo fazer uma revisão da literatura sobre estudos e aplicabilidade dessas células na odontologia.

Palavras-chaves: Células-Tronco, Odontologia, Regeneração.

INTRODUCTION

Researchers and health professionals consider stem cells to be an important weapon in the fight against diseases, particularly those that have resisted the efforts of science for a long time, and they have become the subject of a great deal of recent research. The key to these cells' utility is their ability to differentiate into many different cell types depending on the stimulus received and they have been used in treatments for diseases such as cancer

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and neural degeneration, in rehabilitation of tetraplegic and paraplegic patients and even in dentistry (1). In parallel, many studies have shown the utility of embryonic or adult stem cells for forming teeth and for regeneration of bone and soft tissues (2-4).

Stem cells are nonspecific cells with powerful self-regeneration properties and they are capable of organizing other cell types in the body. Stem cells are defined as undifferentiated cells that have precursor properties, are capable of forming many different cell types and have the property of unlimited self-renewal (5).

Stem cells can divide into two cells identical to the original stem cell or into differentiated cell types, depending on their origin and differentiation potency. There are basically two types of stem cells: embryonic and somatic (or adult). Embryonic stem cells are derived from the inner cell mass of a blastocyst, which is an accumulation of primordial cells (4-5 days after fertilization). These cells are classified as totipotent and they can form any of the tissue types found in the adult body, in addition to having unlimited proliferation potential (6).

Adult stem cells are classified as pluripotent and are undifferentiated cells that remain quiescent in tissues until stimulated, when they can create cell types that are compatible with the tissue in which they reside. By definition, adult stem cells are capable of differentiation into at least two lineages and have the property of self-renewal. Their primary function is to maintain and repair the tissues in which they are found. Additionally, they can form specialized cell types from other tissues if they are transplanted (6).

Stem cells can be found in bone marrow and blood. Bone marrow appears to contain three stem cell populations: hematopoietic stem cells, stromal stem cells and endothelial precursor cells. Hematopoietic stem cells are cells isolated from blood and bone marrow that can differentiate into a variety of different specialized cells and suffer apoptosis (1).

Stromal cells are a mixed population that can create bone, cartilage and fat and also fibrous and connective tissues. Endothelial stem cells can form new blood vessels via three mechanisms: angiogenesis – capillaries originating from shoots off existing vessels; arteriogenesis – the appearance of vessels that were probably dormant, although some authors believe that neoformation is possible; and vasculogenesis – formation of new vessels or remodeling of existing ones (1).

The umbilical cord and placenta are rich sources of stem cells. Recent research has suggested that umbilical cord blood contains cells that are able to develop totipotent cells or even all three of the germ layers: endoderm, ectoderm and mesoderm (1).

Within dentistry, the hope is to regenerate both bone and dental tissues, including the periodontal ligament, dental pulp and enamel, so that new teeth could even be created, even in the presence of caries, pulpitis and periapical diseases, which are the primary causes of tooth loss (5).

It is clear from even this brief overview of stem cell types and their applications that research has shown great potential for applications in dentistry and that mesenchymal stem

cells are the most often mentioned. Given the importance of the subject, the objective of this paper is to present a review of the literature on stem cells in dentistry.

LITERATURE REVIEW

History

Stem cell treatments are considered to be among the principle scientific breakthroughs of the twentieth century and one of the greatest hopes for the future of medicine. In an era of medical innovations based on cell treatments, stem cells offer the chance to elucidate many of the human body's mysteries and to produce new treatments for hitherto incurable diseases (7).

According to Borojevic (8), regenerative medicine is a new medical specialty that aims to repair or substitute tissues that have been injured or suffered degeneration. Bioengineering utilizes biomaterials and stem cells from adjacent tissues to implant or promote an influx of cells with the objective of integrating a new structure into the injured tissue. Use of stem cells makes it possible to recreate tissues by generating them. These treatments have shown themselves ever more promising over the years since initial research demonstrated successful use of the new technology.

Tissue bioengineering is the branch of science that studies the functional and physiological reconstruction of tissue structures lost or damaged by diseases such as cancer or by traumas. There are three prerequisites for bioengineering: stem cells or progenitor cells, a matrix that acts as a scaffold and signaling proteins, known as growth factors, to stimulate cell differentiation (9).

Clinical use of embryonic stem cells is science's main hope of developing treatments for many neuromuscular diseases and other conditions for which no cure is currently known. In 1998, Dr. James Thomson of the University of Wisconsin extracted the first stem cells from an embryo rejected by a fertility clinic, and created the world's first embryonic stem cell lineage (10).

Studies with adult stem cells, known as mesenchymal cells, which can be extracted from bone marrow, are less recent. In 1968 the first bone marrow transplant was performed to treat leukemia, making it in effect the first ever transplant of adult stem cells. At the time it was believed that because these were hematopoietic stem cells, they would only have the ability to differentiate into blood cells. In 1988, the first ever transplant of stem cells from cord blood was performed in France, from a sister to her brother in order to cure Fanconi anemia and the results were positive (11).

Stem cells in dentistry

Tissue bioengineering is now the subject of much debate in many different dental specialties. There is an ever growing body of research into treatments for functional and

esthetic restoration (12). Stem cell treatments are one example of this and the possibility using adult cells sourced from patients' own bodies means that it can be expected that in the near future such treatments may become routine at dental practices (5).

The hope is that it will become possible to regenerate bone and dental tissues including the periodontal ligament, dental pulp and enamel, and that the creation of new teeth may also become feasible, even in the presence of caries, pulpitis and periapical diseases, which are the primary causes of tooth loss. In view of this possibility of achieving restoration with regenerative medicine, it can be considered that a new era of dentistry is beginning (5).

There are, for example, mesenchymal cells in the periodontal region that can differentiate into fibroblasts, osteoblasts or cementoblasts, all of which are responsible for repairing the periodontal ligament. These cells can therefore be used for periodontal regeneration procedures (5). Periodontitis is an inflammatory disease that manifests clinically as loss of periodontal supporting tissues, including the periodontal ligament, cementum and alveolar bone and is therefore a candidate for new treatments aiming for complete periodontal regeneration, using cell-based treatments. This objective is already the case in several situations, such as bone grafts, growth factors and membrane barriers used to reduce bone loss (13).

Mesenchymal stem cells have also emerged as a promising prospect for bone reconstructions. Clinical studies have reported positive results for periodontal defects, alveolar ridge defects, congenital alveolar clefts, extensive defects of the skull, maxillary sinus lifting and post-radiation mandibular atrophy (14).

Restoring alveolar ridge height is another particular concern for periodontists, because bone defects that emerge after tooth loss generally result in greater bone loss in both the horizontal and vertical planes, which limits the efficacy of dental implants and other prosthetic treatments (15).

Notwithstanding stem cell technology is already available for regenerative treatments using mesenchymal stem cells and is being introduced into clinical practice when there is a need to increase alveolar bone. Studies have also shown that the recent increase in demand for dental implants creates a pressing need to increase alveolar bone, the alveolar ridge and the maxillary sinus. The Academy of Osseointegration has declared that these new technologies based on stem cells can be used to improve implant success rates, as exemplified by use of osteogenic stem cells at osteotomy sites (15).

In the field of dental prostheses, the principal treatment method has always been materials-based reconstruction avoiding major surgical procedures, but technologies using stem cells have expanded clinical concepts with relation to regeneration. This more biological perspective has even allowed scientists to imagine developing teeth to substitute patients' missing teeth (15).

It is known that dental pulp has a powerful reparative capacity. The formation of a mineralized barrier in sites where pulp is exposed, after direct pulp capping, is a

classic example of the dental pulp's reparative properties. The discovery that high quality stem cells can be extracted from dental pulp, even from exfoliated deciduous teeth, has increased the range of regeneration options for the dentin–pulp complex in teeth with compromised root canals (6).

Although conventional restorative materials, such as amalgam, resins and glass ionomer cement, have proved effective for maintaining teeth in the oral cavity, they clearly offer limited durability and need substitution after a certain period of time. Additionally, a significant percentage of treated teeth suffer inflammation of pulp and necrosis, demanding further root canal treatment, prosthetic work or and/or tooth extraction. The primary objective of dental engineering of pulp tissues is to substitute the inflamed or necrotic pulp with healthy and functional tissue that is capable of forming new dentin, in addition to finding an alternative to conventional root canal treatment with the advantage that living teeth can be restored (16).

It is, however, perceptible that knowledge is being accumulated slowly in the field of regenerative medicine. In dentistry, dental tissue engineering strategies may be used in the future to treat caries, periodontitis, root canal disorders, alveolar damage and facial fractures and for dental implants and to increase the height of the alveolar bone (17).

FINAL COMMENTS

It can be concluded that studies into the use of stem cells are becoming more and more common in medicine. This is the start of a new phase in which the body itself is used to discover treatments for countless diseases for which only palliative treatments exist. A large proportion of research progress has been achieved using mesenchymal stem cells, which are easily extracted from patients' own bodies before treatment.

Dentistry has followed these developments in search of new treatments and has adopted these new options because the oral cavity is vulnerable to extensive tissue losses, including bone loss, periodontal damage and consequent tooth loss. Nevertheless, there is still a need for greater knowledge about stem cells, their niches and the molecular mechanisms of cell growth and differentiation so that these treatments can become routine in dental surgery.

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