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RESEARCH ARTICLE

POTENTIAL USE OF STEM CELLS IN IMPROVING ORAL HEALTH RELATED QUALITY OF LIFE

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ABSTRACT

Stem cells are the body's master cells that regenerate the body's many cells, tissues, and organs. They have a great potential in enhancing future dental and medical practice with significant improvement in the quality of life of patients. In dentistry and its related branches, it is of great interest to restore periodontal defects, lost teeth or craniofacial bone defects using stem cell-mediated therapy. The dental stem cell biology might provide meaningful insights into the development of dental tissues and cellular differentiation processes.

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INTRODUCTION

Stem cells are basic cells which can be compared to a mass of clay which is wet. Like the clay which as long as it is wet can be molded to any shape, the stem cells as long as they retain their 'stemness' can become any type of cell in the body of any organ (http://www.ncrm.org/stemcell.htm. Accessed). Stem cells are the body's "master" cells that regenerate the body's many cells, tissues, and organs. Most cells in your body can only make new cells of the same type – blood cells make blood cells, skin cells make more skins cells and so on (http://www.store-a-tooth.com/index.php). Stem cells are unique not only because they can turn into many different types of cells – a stem cell might create blood, kidney, heart, or bone for example – but also because they can divide many more times than other cells[3]. So stem cells have a great potential in enhancing future dental and medical practice with significant improvement in the quality of life of patients. This could turn out to be an effective system level approach in reducing disease burden in communities and increasing the lifespan of population. The morbidity and mortality rate of the population could be significantly improved along with improved cost effectiveness in health care.

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Stem cell Biology

Stem cells are specialized cells with the unique potential of self-renewal and cell specification following stimulation with appropriate Biochemical/Biophysical cues. Initially uncommitted, following specific signals, these cells have the capacity to differentiate into lineage-committed cells. Three broad categories exist to classify these cells: 1. Following, fertilization of an egg, the zygote replicates numerous times, ultimately giving rise to the 216 different cell types, which comprise the human body. The first three divisions of the zygote, however, yield 8 cells, each of which is capable of developing into a human being. These cells are referred to as totipotent stem cells. 2. As the cells continue to divide from the 8 cell stage, the number of stem cells yielded increases, however, their capacity to Trans-differentiate into different cell types becomes more limited. Five days post-fertilization, the Blastocyst forms. The outer cell layer generates the placenta and the inner cell mass of approximately 50 cells creates the embryo. These latter cells are designated pluripotent embryonic stem, or ES cells. Although each is capable of generating most embryonic cell types, they are not capable, individually, of creating a human being. 3. As the embryo continues to develop, the cells become more and more specialized and commit to specific cell types. In order for this differentiation to occur, as the embryo develops, genes necessary for earlier stages of development "switch off", until only those required for a specific tissue function/phenotype remain active. However, a small number of only partially differentiated stem cells persist in some adult tissues, and are referred to as multipotent stem cells. These are capable of forming a limited number of specialized cell types, and generally function locally to replace fully differentiated cells lost through depletion or damage. (Christian Morsczeck *et al*., 2008; Stewart, 2004; Bluteau *et al*., 2008) Despite current hurdles, potential clinical applications for stem cell technologies include: the production of cardiomyocytes to replace damaged heart tissue, the manufacture of insulin-producing pancreatic cells for patients with diabetes and the generation of neurones for the treatment of patients with Parkinson's disease, tooth engineering. Indeed, the use of bone marrow transplants for patients with leukaemia, is an example of stem cell therapy already in practice. Although ES cells may initially appear the more versatile when required for the regeneration or repair of specific tissues, these cells can only be used in the form of allografts unless therapeutic cloning techniques are used to generate autologous ES cells. (Stewart, 2004) Furthermore, recent studies have highlighted the potential of ES cells to become cancerous with age, adding additional complexity to these cells. Post-natal stem cells may not develop this problem, and can be used for autologous transplants. Progress is being made in the potential use of these adult cells, particularly for the treatment of muscle and connective tissue diseases and damage. (Draper *et al*., 2004)

Dental stem cells

Complex human tissues harbor stem cells and/or precursor cells, which are responsible for tissue development or repair. Recently, dental tissues such as periodontal ligament (PDL), dental papilla or dental follicle have been identified as easily accessible sources of undifferentiated cells. The dental stem cell biology might provide meaningful insights into the development of dental tissues and cellular differentiation processes. Dental stem cells could also be feasible tools for dental tissue engineering. Constructing complex structures like a periodontium, which provides the functional connection between a tooth or an implant and the surrounding jaw, could effectively improve modern dentistry. (Christian Morsczeck *et al*., 2008; Stewart, 2004)

Stem cells in Tooth Bioengineering

As tooth formation results from epithelial-mesenchymal interactions, two different populations of stem cells have to be considered: epithelial stem cells (EpSC), which will give rise to ameloblasts, and mesenchymal stem cells (MSC) that will form the odontoblasts, cementoblasts, osteoblasts and fibroblasts of the periodontal ligament. Thus, tooth engineering using stem cells is based on their isolation, association and culture as recombinants *in vitro* or *ex vivo* conditions to assess firstly tooth morphogenesis and secondly cell differentiation into tooth specific cells that will form dentin, enamel, cementum and alveolar bone. (Bluteau *et al*., 2008; Duailibi *et al*., 2006) The various stem cells which can be used in tooth bioengineering are Stem Cells from Human Exfoliated Deciduous Teeth (SHED), Adult Dental Pulp Stem Cells (DPSC), Stem cells from the Apical Part of papilla (SCAP), Epithelial stem cells from developing molars, Epithelium - originated dental stem cells, Stem cells from the Dental Follicle (DFSC), Periodontal ligament stem cells (PDLSC), Bone marrow derived mesenchymal stem cells (BMSC). (Christian Morsczeck *et al*., 2008; Bluteau *et al*., 2008)

Association of epithelial and mesenchymal stem cells

Since teeth are formed from two different tissues, building a tooth logically requires the association/cooperation of odontogenic mesenchymal and epithelial cells. The recombination of dissociated dental epithelial and mesenchymal tissues leads to tooth formation both *in vitro*and *in vivo.* (Amar *et al*., 1989) Numerous attempts have been made in order to form teeth *in vivo* with very promising results. Single cell suspensions obtained from rat, pig or mice tooth germs have been seeded onto the surface of selected biomaterials (e.g. collagen-coated polyglycolic acid, calcium phosphate material, collagen sponges) and successfully re-implanted into the omentum of immunocompromised animals. All these reports describe the presence of both dentin and enamel. This indicates that the recombined cells could re-organize themselves and form individual layers and, furthermore, that they can differentiate properly into odontoblasts and ameloblasts. (Duailibi *et al*., 2004; Young *et al*., 2002)

Future Implications

Dentin matrix components (DMC) may promote cell proliferation and differentiation, and ultimately contribute to dentin regeneration. (Salehi *et al*., 2016) Stem cells derived from periodontal ligament tissues are a promising therapy for the regeneration of lost/damaged periodontal tissue [12] Stem cells could restore damaged tissue or organs. In dentistry and reconstructive facial surgery, it is of great interest to restore lost teeth or craniofacial bone defects using stem cell-mediated therapy (Park *et al*., 2016) Dental mesenchymal stem cells can be easily isolated and potentially used to promote pulp and periodontal regeneration. Stem cells and induced pluripotent cells could be potentially used for regeneration of entire teeth for partially edentulous or completely edentulous individuals (Jimenez-Rojo *et al*., 2015) Dental mesenchymal stem cells could be to promote pulp regeneration and their similarities with bone marrow stromal cells suggest applications in musculoskeletal regenerative medicine too (Jimenez-Rojo *et al*., 2015).

Conclusion

The science of regenerative medicine in which stem cells are the major tools for repairing the damages to organs is in evolving/early stage of development and there have been many misunderstandings and hype. Dental stem cells are also one of the important sources of stem cells which can be used for treating various disorders and for tissue engineering. However, the engineering of tooth substitutes is hard to scale up, costly, time-consuming and incompatible with the treatment of extensive tooth loss. Scientific knowledge is not enough and the main challenge in stem-cell therapy is to find a compromise between the benefits to the patients, regulatory agencies, increased stem cell requirements, costs, coverage by health insurance and the role of pharmaceutical companies.

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