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TISSUE ENGINEERING IN DENTISTRY.

Dental Science

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ABSTRACT

The development of tissue engineering and regeneration constitutes a new platform for translational medical research. Tissue engineering is a rapidly developing field, which combines the disciplines of materials science and biotechnology aiming to develop tissue constructs that can be implanted into the human body. It is a major component of the regenerative medicine by combining the principles of transplantation, materials science and bioengineering to restore a diseased or a damaged tissue to normal function. Tissue engineering has a considerable effect on dental practice, repair and replacement of mineralized tissues, the promotion of oral wound healing, correction of craniofacial abnormalities , integration of biocompatible prosthetic implant materials with the oral tissues, the regeneration of dental hard and soft tissues and the use of gene transfer adjunctively .

KEYWORDS

Tissue engineering, Stem cell, Regeneration, Gene therapy

INTRODUCTION

Tissue-engineering has emerged as a new and ambitious approach that combines knowledge from material chemistry with cell biology and medicine . 1 The recognition that body parts may regenerate was first made in 330 BC by Aristotle , when he observed that a lizard could grow back the lost tip of its tail . Since then , study of regeneration has come to find its applications in regenerative medicine and dentistry . Hermann (1952) was the first to carry out regenerative endodontic procedure, when he applied calcium hydroxide in vital pulp amputation. Nygaard Ostby in 1961 evaluated a revascularization method for re-establishing a pulp-dentin complex in permanent teeth with pulpal necrosis. Subsequent regenerative dental procedures included guided tissue or guided bone regeneration procedures and distraction osteogenesis (Block et al,1995) the application of platelet rich plasma for bone augmentation (Kassolis et al , 2000) , recombinant human bone morphogenic protein for bone augmentation (Fjuimura et al , 1995) , Nakahara in 2006 proposed two potenetial methods for whole tooth regeneration , the first approach incorporates principles of tissue engineering , utilizing the inherent potential of stem cells to renew themselves and differentiate into different cell lineages when seeded onto appropriate scaffolds containing a combination of growth factors . The second approach involoves replicating the natural developmental processes of embryonic tooth formation , achieved by transplanting artificial tooth germs into the bodies of appropriate animal hosts . 2 Three components required for engineering a bone are : (1) scaffolds, (2) cells and (3) cell signaling molecules, scaffold provides a physico-chemical and biological three-dimensional microenvironment for cell growth and differentiation , promoting cell adhesion , and migration , serves as a carrier for morphogen in protein therapy and for cell in cell therapy. It should be effective for transport of nutrients, oxygen and waste. Scaffolds include both natural and synthetic materials. Natural materials are collagen, alginate, agarose, chitosan, and glycosaminoglycans. Synthetic materials include hydroxyapatite/ tricalcium phosphate, and polymers like polylactic acid, polyglycolic acid, and polycaprolactone. Synthetic polymers are found to be more conductive and show less contraction as compared to collagen. 3 Stem cells are clonogenic cells capable of spontaneous division and distinction from various cell lines, they are classified into two groups - embryonic and adult cells. Adult stem cells are responsible for restoration and reconstruction of different tissues . 4

The dental pulp contains a population of stem cells , called dental pulp stem cells, they synthesize and secrete dentin matrix like the odontoblast cells they replace. They possess putative immune-suppressive activity, an advantage in cases of allogenic stem cell transplantation. Mesenchymal progenitors have been isolated from the pulp of human deciduous incisors , these cells named Stem cells from Human Exfoliated Deciduous teeth exhibit a high plasticity since they can differentiate into neurons, adipocytes, osteoblasts and odontoblasts. Stem cells from the apical papilla are a population of multipotent stem cells isolated from the root apical papilla of human teeth . 2

The regeneration of periodontium was the first tissue - engineering technology in dentistry , invented by Nyman and colleagues in 1982 . This procedure , termed guided tissue regeneration , involves inserting a barrier membrane under the periodontal tissue flap to prevent the in growth of gingival epithelium and connective tissue , while creating a space on the root surface for progenitor cells from the periodontal ligament including cementoblasts , fibroblasts , and osteoblasts to migrate in and form new periodontal structures including cementum , periodontal ligament , and alveolar bone . 5

The dental follicle has been considered a multipotent tissue , based on its ability to generate cementum , bone and periodontal ligament from the ectomesenchyme -derived fibrous tissue . Morphogens are the signaling molecules that regulate stem cells to form desirable cell type . They can be used to control stem cell activity , by increasing the rate of proliferation , inducing differentiation of the cells into another tissue type , or stimulating stem cells to synthesize and secrete mineralized matrix . A variety of growth factors have successfully been used for dentin-pulp complex regeneration. Once released , these growth factors may play key roles in signaling many of the events of tertiary dentinogenesis , a response of pulp-dentin repair . 2

The reconstruction of bone defects in the maxillofacial region is required due to extensive bone loss as the result of trauma , inflammation , and surgical treatment of tumors . Engineered bone tissue provide numerous benefits for the patient , it eliminates donor site morbidity encountered in the case of autogenous bone grafting techniques , and the absence of immune rejection which can occur when using allografts . Bone tissue engineering implies the use of adequate, biodegradable scaffolds for cell seeding , suitable cells with osteogenic potential and osteogenesis-inducing factors . 6

Biomaterials , which can be either synthetic , natural and pure or composite materials play an important role in dental tissue engineering to interface with surgical procedures and cell biology , include injectable biomaterials which can serve as stem cell carriers and supramolecular hydrogels , as well as in situ gelling hydrogels . Hydrogels can replace bone transplantation in the clinic in future to repair periodontal bone defects and periodontically accelerated osteogenic orthodontics . The combination of bioactive glass nanoparticles in these thermosensitive hydrogels can enhance the osteoconductivity of biomaterial . The use of growth factors and injectable biomaterial scaffolds has accelerated clinical translation and enhanced dental tissue engineering . 7

Bioreactors , devices are designed to attain optimal conditions to grow cells in vitro to be utilized in tissue engineering . The design of a bioreactor primarily depends on the type of tissue that is being constructed . Its function is to provide a suitable , reproducible and easily controlled cell culture environment , in terms of temperature , mimicking physiological conditions . The bioreactor tries to : achieve adequate , uniform three-dimensional proliferation of mesenchymal stem cells on a biodegradable substrate and matrix synthesis . Bioreactors for bone engineering applications are classified into rotating wall vessels , spinner flasks , perfusion (direct and indirect) bioreactors , Compression Bioreactors and Combined Systems . 6

Gene therapy is used as a means of delivering genes for growth factors , morphogens , transcription factors , extracellular matrix molecules locally to somatic cells of individuals with a resulting therapeutic effect. The gene can stimulate or induce a natural biological process by expressing a molecules involved in regenerative response for the tissue of interest . Both an in vivo and an ex vivo approach can be used for gene therapy . In the in vivo approach , the gene is delivered systemically into the bloodstream or locally to target tissues by injection or inhalation . The ex vivo approach involves genetic manipulation of cells in vitro , which are subsequently transplanted to the regeneration site .

Viral or nonviral vectors are used to enable the cellular uptake and expression of genes . The viruses can replicate genes of interest together with their own genome through the use of the host cell genetic machinery. Nonviral delivery systems of plasmids , peptides , cationic liposomes , DNA-ligand complex , gene gun , electroporation , and sonoporation have been developed to address safety concerns such as immunogenicity and insertional mutagenesis . Risks of gene therapy mainly arise from the vector system rather than the gene expressed . Clinical application still awaits the development of vectors that are safe , affordable , efficient , simple for application , and that have ability to express the required level of transgene for the sufficient long term . 8

New technologies in tissue engineering such as microfabrication , self-assembled biomimetic peptides , and 3-dimensional (3D) printing have developed . 3D organ printing involves 3 sequential steps : (1) preprocessing or development of blueprints for organs , (2) processing or actual organ printing , and (3) postprocessing or organ conditioning and accelerated organ maturation . The 3D cell printers can print single cells or cell aggregates onto the previously printed successive layers of thermosensitive gels in a layer-by-layer fashion. These sequential layers are assembled to create the 3D organ . 5

Additive manufacturing has been applied for scaffold developing. This method was firstly introduced by Herver Voelcker in 1970 to describe the algorithms for the purposes of 3D solid modeling . It has been widely used in industry because of its accuracy of shaping . It has advantage in fabrication of patient - specific scaffolds with multiple materials . Electrospinning uses electrostatic principle to manufacture the nanofibers required for tissue engineering applications. The nanofibers prepared by electrospinning have large specific surface area and high porosity in three-dimensional structure, which makes electrospinning nanofiber membranes have a wide application value in many fields . 9

Nanomaterials were used in dentistry for the first time in 2002 with the inclusion of nanofillers in composite resins for dental reconstruction , with tissue engineering have become integrated in dentistry with the introduction of nanotechnologies in the constitution of scaffold matrices , the use of growth factors and stem cells , and with the biomodulation techniques for dental tissue reconstruction . 10

Nanomaterials with predefined geometries , surface characteristics , and mechanical strength are used to control various biological processes . By controlling the mechanical stiffness of a matrix , cell–matrix interactions such as cellular morphology , cell adhesion , cell spreading , migration , and differentiation can be controlled . These mechanically stiff and bioactive nanocomposite hydrogels can be used as an injectable matrix for orthopedic and dental applications , a range of nanoparticles is used to provide bioactive properties to enhance biological properties . Possible combination of these approaches that involves nanoparticles as scaffolds with stem cells and growth factors involving signaling molecules will direct forward in a potential regenerative approach as a future vision for tooth biomedical engineering . 11

CONCLUSION

One of the most challenging aspects of establishing regenerative therapy is to determine the optimization and integration of different component procedures to generate an outcome of regenerated complex Comprehensive research programs and clinical applications are required for the possible future regenerative procedures development Studies need more investigation regarding in vitro and in vivo experiments to highlight their potentialities in this promising field .

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