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PERIODONTAL TISSUE ENGINEERING – A DREAM OR REALITY

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ABSTRACT

Regeneration of lost tissue has always been the preferred expected treatment outcome. Regeneration of lost periodontal tissues is always a taunting task for periodontists despite having plenty of surgical options. Tissue Engineering is one such solution to this problem. The 3 components of Tissue engineering viz. signaling molecules, cells and scaffolds together can make complete regeneration of lost tissue possible. In this review we also focus on methods available to bioengineer periodontal tissues and latest advancements in tissue engineering.

KEYWORDS: Regeneration of lost tissue has always been the preferred expected.

INTRODUCTION

Imagine a day when people with liver failure can be cured with implanted "neo-organs" made of liver cells and plastic fibers, when insulin-dependent diabetics will not have to take frequent insulin injections because they have semi-synthetic replacement pancreases, when kidney dialysis machines are obsolete because anyone with damaged kidneys can be outfitted with new ones grown from their very own cells. Sounds like science fiction? But day might not be as far away as we think.

The gold standard to replace an individual's lost or damaged tissue is the same natural healthy tissue. This standard has led to the concept of tissue engineering or regenerating new tissue from pre-existing tissue.[1]

Regeneration of periodontal tissues so that their original form, architecture and function are restored has been an elusive but laudable goal. In order to fully appreciate what is involved, the ''cross-talk'' among the components of the periodontium (cellular and matrix), together with the inherent regenerative capacity of this tissue, need to be considered.[2]

Current strategies used for treatment of lost Periodontal tissues include the utilization of autogenous grafts, allografts, and synthetic materials (alloplasts). One of the major shortcomings with autografts, as well as allografts, is the fact that humans do not have significant stores of excess tissue for transplantation.[3] With allografts, there always exists the possibility of eliciting an immunologic response due to genetic differences, as well as inducing transmissible diseases.[4]

Hence, the field of tissue engineering has developed over the past decade to recreate functional, healthy tissues and organs in order to replace diseased, dying, or dead tissues.

Dental Tissue Engineering

The complete regeneration of the lost tissue by tissue engineering involves triad of signaling molecules, cells and Scaffolds which form the base regeneration. These key elements are:

1. The morphogenetic signaling families like BMPs, FGFs.
2. The progenitor/stem cells which includes cells derived from marrow, dental pulp and PDL-derived cells.
3. The extracellular matrix scaffold which consists of collagens, fibronectin and proteoglycans, including hyaluronic acid. Synthetic foams, fibers, gels and membranes can be incorporated with biomimetic biomaterials.

Strategies to Engineer Tissues

Currently, strategies employed to engineer tissue can be categorized into three major classes, namely Conductive, Inductive and Cell transplantation.

Conductive approaches utilize biomaterials in a passive manner to facilitate the growth or regenerative capacity of existing tissue. Example includes use of barrier membranes for regeneration of lost periodontal tissues.[5] Induction involves activating cells in close proximity to the defect site with specific biological signals. The origins of this mechanism are rooted in the discovery of bone morphogenetic proteins (BMPs). Uristfirst showed that new bone could be formed at nonmineralizing, or ectopic, sites after implantation of powdered bone (bone demineralized and ground into fine particles).[6] One limitation of inductive approaches is that the inductive factors for a particular tissue may not known. In this situation the third tissue engineering approach, cell transplantation, becomes very attractive.[7] Cell transplantation approach involves direct transplantation of cells grown in the laboratory. The clinician is required to biopsy a small sample of tissue containing the cells of interest. Principles of cell biology are required to multiply cells million-folds in the laboratory and maintain their function. Meanwhile, the bioengineer manufactures the tissue, in bioreactors, and the material onto which the cells will be placed for transplantation. Finally, the clinician is required to transplant the engineered tissue.[8]

Achieving Periodontal Regeneration

The regeneration of the periodontal tissues is dependent on four basic components.

1) The appropriate signals,
2) Cells,
1. Blood supply and
2. Scaffold need to target the tissue defect.

Each of these elements plays a fundamental role on the healing process in a simultaneous and temporal timeframe and is interconnected into the generation of new tissues. Cells provide the machinery for new tissue growth and differentiation. Growth factors or morphogens modulate the cellular activity and provide stimuli to cells to differentiate and produce matrix toward the developing tissue. New vascular networks promoted by angiogenic signals provide the nutritional base for tissue growth and homeostasis. Finally, scaffolds guide and create a template structure three-dimensionally to facilitate the above processes critical for tissue regeneration.[9]

A limiting factor in the achievement of periodontal regeneration is the presence of microbial pathogens that contaminate periodontal wounds and reside on tooth surfaces as plaque-associated biofilms. Appropriate strategies in controlling infection at the reparative wound site are required to optimize periodontal regeneration.[10]

Growth Factors

Several bioactive molecules have demonstrated strong effects in promoting periodontal wound repair in preclinical and clinical studies. These bioactive molecules include PDGF, IGF-I, FGF-2 , TGF-1, BMP-2, -4, -7 and -12, and enamel matrix derivative (EMD) that have shown positive results in stimulating periodontal regeneration. In addition, PDGF, BMP-2, and BMP-7 have been shown to promote periimplant bone regeneration. BMPs initiate both cementum and periodontal ligament regeneration. Naturally-sourced BMPs and particularly recombinant human osteogenic protein-1 (hOP-1 or BMP-7) appear particularly effective in initiating cementogenesis. Recently, a comparative study in periodontal defects found that rhBMP-2 in association with collagen sponges promoted superior bone regeneration than rhBMP-12. Cementum formation is similar for both BMPs, however, only the rhBMP-12 treatment induces to functionally oriented PDL bridging newly formed bone and new cementum.[11]

Cells

Periodontal regeneration relies on independent but linked processes viz. osteogenesis, cementogenesis, and connective tissue formation.

The cellular constitution of the gingival connective tissue and alveolar bone include: fibroblasts, macrophages, mast cells, osteoblasts and osteoblast precursor cells, cementoblasts and cementoblast precursor cells, osteoclasts and odontoclasts, assorted inflammatory cells, and cells that make up vascular channels and nerves. Inflammatory cells include polymorphonuclear leucocytes, lymphocytes, and plasma cells.[12] The connective tissue also contains undifferentiated ectomesenchymal cells that serve as a replacement source for more differentiated cells, primarily fibroblasts.

The PDL contains fibroblasts, macrophages, undifferentiated ectomesenchymal cells, cementoblasts and cementoclasts, osteoblasts and osteoclasts, cell rests of Malassez and vascular and neural elements that are capable of generating and maintaining three distinct tissues, PDL, and the mineralized tissues: cementum and alveolar bone.[12,13] As specific cell lineages retain the potential of regeneration, stimulatory and selective approaches have been attempted to re-engineer lost periodontal supporting tissues.[9]

Guided Tissue Regeneration and Cell Re-Population

Guided tissue regeneration (GTR) could be driven by excluding or restricting the re-population of periodontal defects by epithelial and gingival connective cells. Thus, providing space and favorable niche to maximize PDL cells, cementoblasts, and osteoblasts to migrate selectively, proliferate and differentiate within the periodontal defects help in promoting the reconstruction of the supporting tissue and attachment.[14] Current used materials include polylactic acid, polyglycolic acid, polyglactin, and both soluble and non-soluble collagen barriers.

Gene Therapy for Periodontal Engineering

High concentrations of growth factors are required to promote tissue regeneration. Therefore, supplemental local growth factor production via gene transfer could be superior to bolus delivery methods.[15] Gene therapy consists of the insertion of genes into an individual's cells either directly or indirectly with a matrix to promote a specific biological effect.[9]

Nanotechnology

The potential of nanotechnology is limited only by our imagination. Our present capacity to create polymer scaffolds for cell seeding, growth, factor delivery & tissue engineering purposes is well recognized. In future these processes may well be manipulated via nanodevices implanted to sites of tissue damage.

Future Perspectives

A major challenge that has been overlooked has been the modulation of the exuberant host response to microbial contamination that plagues the periodontal wound environment. For improvements in the outcomes in periodontal regenerative medicine, scientists will need to examine dual delivery of host modifiers or anti-infective agents to optimize the results of therapy. Multidisciplinary approaches combining engineering, dentistry, medicine, and infectious disease specialists in repairing the complex periodontal wound environment.[9]

CONCLUSION

Many advances have been made over the past decade in the reconstruction of complex periodontal and alveolar bone wounds. The advent of viable tissue engineering will have an effect on therapeutic options available to oral health specialists. Lot of research is going on in the field of medical tissue engineering and dentistry is not untouched. Periodontology in particular has lot of scope when we consider regeneration of lost tissue and in dentistry it is still considered to be the least predictable by conventional therapy. This too widens the scope in the field of Periodontology which is still in its infancy.

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