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SMART SCAFFOLDS IN REGENERATIVE ENDODONTICS

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ABSTRACT
A majority of the world's population suffers from the debilitating effects of dental caries. Progressive caries causes loss of dental hard tissues that are difficult to repair. Root canal therapy, fixed dental prosthesis and, existing restorative materials are known to be the only options available to retain the decaying tooth. With regenerative endodontics, it has now become possible to regain the lost vitality of the tooth and regenerate the dental hard tissues with their cellular functions. Advances in the field of tissue engineering has enabled clinicians to have predictable results while doing dentofacial surgeries or regenerative root canal therapy that will adjourn failures resulting from poor wound healing.

KEYWORDS: Smart scaffolds, Regenerative endodontics, Root canal therapy.

INTRODUCTION
Regenerative endodontics is an upcoming branch of tissue engineering focused to heal damaged and inflamed pulp tissues. The American Association of Endodontists' Glossary of Endodontic Terms (2012) defines regenerative endodontics as "biologically based procedures designed to physiologically replace damaged tooth structures, including dentin and root structures, as well as cells of the pulp-dentin complex.[1] The cells necessary to accomplish regenerative endodontics are dental pulp stem cells (DPSCs) from human exfoliated deciduous teeth and human periodontal ligament stem cells (PLSCs).[2-4] To create a practical regenerative endodontic therapy, these stem cells must be organized into a three-dimensional structure using tissue-engineering scaffold materials to create a "tissue construct".
Scaffolds are the biomaterials that act as carriers for specific cell-type and support tissue regeneration. An ideal scaffold facilitates cell growth, differentiation, and organization at the desired site. The porosity of the scaffold should allow cell placement, resulting in an effective transport of nutrients and waste.[5,6]

Classification of Scaffolds
Scaffolds can be classified as follows.

- Based on the degradability of matrices
  - Biodegradable scaffolds
  - Permanent or biostable scaffolds
- Based on form
  - Solid blocks
  - Sheets
  - Porous sponges
  - Hydrogels (injectable scaffolds)
- Based on the presence or absence of cells
  - Cell-free scaffolds
  - Scaffolds seeded with stem cells
- Based on origin
  - Biological or natural scaffolds
  - Artificial or Synthetic scaffolds

Scaffolds that have been most commonly used for regenerative procedures are natural scaffolds, such as collagen, chitosan, silk, fibrin, and synthetic scaffolds, such as polyglycolide and polyglycerol sebacate. Blood clot, platelet-rich plasma (PRP) as well as platelet rich fibrin PRF have been effectively tried as a natural scaffold in regenerative endodontics.

PRP is an autologous first-generation platelet concentrate. It is a rich source of different growth factors such as platelet-derived growth factor (PDGF), transforming growth factor (TGF-β), insulin-like growth factor (IGF), vascular endothelial growth factor (VEGF), epidermal growth factor, and epithelial cell growth factor (ECGF). These are released via the degranulation of α-granules and stimulate bone and soft-tissue healing when placed at the site of inflammation.[7] PRF is a secondgeneration platelet concentrate. The procedure consists of drawing blood which is collected into a test tube without an anticoagulant and is centrifuged instantaneously. A tabletop centrifuge can be used for 10 min at 3000 rpm or 12 min at 2700 rpm. PRF has proved to be an ideal source of viable cells for pulp-dentin complex regeneration. It has been shown that it prevents the early invasion of undesired cells, thereby acting as a viable barrier between the desired and undesired cells.[8]

One of the difficulties of developing new treatments for regenerative endodontics is that the biomaterials to be used as scaffolds for tissue regeneration need to have similar biochemical properties to that of the extracellular matrix (ECM) of the dental tissues.[9] The ECM derived proteins and glycosaminoglycans are ideal materials for scaffolds, however they are difficult to process and combine with other biomaterials. The smart tissue scaffolds being developed can overcome these limitations to sustain the release of proliferative cells longer than the traditional scaffolds.[10]

Smart Scaffolds

Smart (or intelligent) biomaterials and constructs refer to those that: (i) possess inductive or activating/ stimulating effects on cells and tissues by engineering the material's responsiveness to internal or external stimuli, such as pH, temperature, ionic strength and magnetism, to promote damaged tissue repair and regeneration; or (ii) have intelligently tailored individual properties and controlled functions to actively participate in tissue regeneration in a valuable way.[11]

Smart dental resins that respond to pH to protect tooth structures

A group of smart materials that can respond to pH changes in the oral cavity is a desirable feature of restorative resins. The basic mechanism of caries is demineralization due to attack by acid produced by bacteria and thus the demineralization-remineralization cycle needs to be balanced for antagonizing this effect. Newly developed Dental composites were found to exhibit significant calcium ion release at a cariogenic pH of 4 and limited ion release at pH 7. These ions inhibit the carious process and protects the tooth during acid attack.[11]

Shape-memory smart scaffolds

Another class of smart scaffolds has a shape-memory capability. Shape-memory polymers (SMPs) can return from a deformed shape to their original shape by an external stimulus, such as temperature change,[12] an electric or magnetic field, and light. BMP2-loaded shape-memory porous nanocomposite scaffold (SMP scaffold) that consists of chemically crosslinked poly(ε-caprolactone) and hydroxyapatite (HA) nanoparticles was fabricated for the repair of bone defects.[13]

Immune-sensitive smart scaffolds

Injectable microspheres were synthesized by integrating heparin-modified gelatin nanofibers which were rather ECM-like. The nanofibrous heparin-modified gelatin microspheres (NHG-MS) could spatiotemporally deliver the anti-inflammatory cytokine IL4 to polarize the proinflammatory M1 macrophages into an anti-inflammatory M2 phenotype, thus facilitating osteogenic differentiation and bone formation. This design mimicked the natural extracellular matrix derived protein structure since heparin can naturally bind with IL4, thus protecting it from degradation.[14]

Polymeric microspheres

These are being developed as drug delivery devices. They can be used to deliver growth factors for the differentiation of dental pulp stem cells because of being derived from ECM.[14]

Multifunctional recombinant polymer scaffolds

A new biomimetic scaffold made of elastin like recombinant polymeric electrospun microfibres has been developed. The new design has introduced rigidity to the scaffold along with an antimicrobial peptide. This research has provided us with a technique to modify the scaffold for additional functionality concerning pulpal tissues.[15]

CONCLUSION

Scaffold-based tissue engineering has been the forebearer of efficient cell delivery strategies for regenerative procedures in Endodontic therapy by being able to produce effective and stable three-dimensional (3D) tissue analogues. Future research in these concepts to develop scaffold free techniques is required to obtain a more biocompatible, inductive and structurally stable construct.

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