### CELL DELIVERY SYSTEMS FOR PERIODONTAL REGENERATION.



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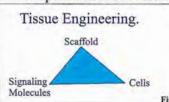
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The management of periodontal defects has been an ongoing challenge in clinical periodontics. This is mainly a result of the fact that the tissues which comprise the periodontium, the periodontal ligament, and the cementum and alveolar bone, represent three unique tissues in their own right. Thus, reconstruction of the periodontium is not just a simple matter of regenerating one tissue but involves at least three quite diverse and unique tissues.

Currently, clinical and scientific research is focusing on a number of approaches for periodontal regeneration. Of these, the following have been studied in detail: Alloplastic materials, which are generally synthetic filler materials; autografts, which represent tissue grafted from one site to another in the same individual; allografts of tissue between individuals of the same species but with different genetic composition; xenografts, which consist of grafted mapterials between different species.

In another approach to induce periodontal regeneration, polypeptide growth factors have been locally applied to the root surface in order to facilitate the cascade of wound-healing events that lead to the formation of new cementum and connective tissue. Yet another approach, known as guided-tissue regeneration, has been developed to achieve periodontal regeneration. It now seems likely that a combination of several techniques may offer the best chance of a beneficial outcome. Through a combination of transplanted biomaterials containing appropriately selected and primed cells, together with an appropriate mix of regulatory factors and extracellular matrix components to allow growth and specialization of the cells, new therapies are emerging of significant clinical potential.<sup>[1]</sup>

Tissue engineering is defined as the reconstruction of living tissues to be used for the replacement of damaged or lost tissue/organs of living organisms and is founded on the principles of cell biology, developmental biology and biomaterials science. [2-3] A clear distinction should be made between tissue engineering, which is the implantation of in vitro-seeded cells and matrices, and guidedtissue regeneration, which involves the use of acellular matrices that are spontaneously repopulated by the host after implantation. Successful tissue engineering requires an interplay among three components (Fig. 1):



The implanted and cultured cells that will create the new tissue; a biomaterial to act as a scaffold or matrix to hold the cells; and biological signalingmolecules that instruct the cells to form the desired tissue type. This review will focus mainly on the use of scaffold materials used to transplant cells as a means of delivering either cells or proteins to a defect site.

## Types of cell-delivery devices and scaffolds

Most cell-seeding scaffolds are fabricated from two classes of biomaterials, derived from either synthetic or natural products. In addition, they may be constructed from either resorbable or nonresorbable materials (Table 1).

# Nonresorbable materials 1. Expanded polytetrafluoroethylene (ePTFE, GoretexTM).

Membranes made from expanded polytetrafluoroethylene have traditionally been used as guided-tissue barrier membranes. However, it is possible that these membranes could also be used to nurture specific cells that are expanded ex vivo and then delivered to a defect site. In the same context, almost any guided-tissue regeneration membrane could be used in such a manner, utilizing either nonresorbable or resorbable materials.

Table 1. Examples of cell-delivery devices and Scaffolds in periodontics. Non resorable Expanded polytetrafluoroethylene (ePTFE) Ceramic Titanium mesh Resorable Alpha-hydroxyacids Polyglycolic acid Poly(I-lactic acid) Copolymers of poly(lactic-co-glycolic acid) no acid-based polymers Collagen-like protiens Elastin-like protiens Natural products Hyaluronan Gelatin Alginate Synthetic hydrogels Poly (ethylene glycol) Poly (ethylene oxide) Matrix extracts Matrigel

## 2. Porous ceramic scaffolds

In general, many of these materials have been developed and investigated with regard to bone tissue engineering. Hydroxyapetite is an example of a material with good mechanical properties but, owing to its porosity, poor strength. Another problem with porous hydroxyapetite is the lack of interconnectivity of the pores, making neovascularization of any implant almost impossible. Biodegradable porous ceramic materials have also been developed and investigated. Of these, the most popular material possessing high biocompatibility and biodegradability is beta-tricalcium phosphate.

## 3. Titanium mesh

Another nonresorbable scaffold that has received considerable attention in recent years is titanium mesh. [4] This material has good mechanical properties regarding stiffness and elasticity and is relatively easy to handle during surgical placement. The lack of bioresorbabilty of this material can be beneficial for the management of large osseous defects whereby the mesh retains sufficient rigidity to avoid collapse, which would be expected of teflon membranes or biodegradable scaffolds.

## Resorbable materials

## 1.Alpha-hydroxy acids

The alpha-hydroxy acid polymers include polyglycolic acid, poly(L-lactic acid) and copolymers of poly(lactic-co-glycolic acid). Their ester bonds are rather susceptible to hydrolysis and thus degrade by nonenzymatic means. Accordingly, these natural breakdown products are removed from the site of implantation by normal tissue respiratory routes and do not generally elicit a foreign body response.

## 2. Alginate

An alternative to alginate gels as a cell carrier is the incorporation of cells into beads of alginate. <sup>[5]</sup> The technique is based on entrapment of individual cells and tissues into an alginate droplet that is transformed into a rigid bead by gelation in a divalent cation-rich solution. The cells are surrounded by a nondegradable, selectively permeable barrier, which isolates the transplanted cells from host tissue and larger molecular weight solutes.

## 3. Amino acid polymers

These scaffolds can be synthesized using fermentation and gene transfer technology to produce molecules that resemble natural amino acid-containing matrix molecules, such as collagens, and elastin. While these materials have the advantage of being able to interact well with cells, issues of biosafety (immunogenicity), largescale production and purification from unwanted contaminants remain a problem.<sup>[6]</sup>

## Scaffolds derived from natural products:

## 1. Hyaluronate

It plays significant role during organogenesis, cell migration and development in general. Modifications to hyaluronan include esterification and cross-linking to provide some structure and rigidity to the gel for cell-seeding purposes. These biopolymers are immunologically inert and completely biodegradable and support the growth of fibroblasts, chondrocytes and mesenchymal stem cells.<sup>[7]</sup>

### 2. Chitosan,

A biopolymer that is biodegradable in mammals has been used quite extensively as a tissue-engineering scaffold. While chitosan can support cell attachment for celldelivery purposes, it is not strongly supportive of cell growth. Accordingly, chitosan needs to be either modified chemically or conjugated with other molecules or peptides to enhance its biocompatibility for cell attachment.

Collagen scaffolds have been investigated as a cell delivery device for many years. Collagen is regarded as one of the most useful biomaterials owing to its excellent biocompatibility and safety associated with its biological characteristics, such as biodegradability and weak antigenicity.

## 3.Synthetic hydrogels

Synthetic hydrogels, such as poly(ethylene glycol) and poly(ethylene oxide), are also showing considerable promise for use as a 3D scaffold for cell delivery. By varying the initial cross-linking density, the degradation profiles of the gel can be controlled. Poly (ethylene oxide) is currently approved by the U.S. Food and Drug Administration for several applications in medicine and, together with polyglycolic acid, is one of the most common synthetic materials used for tissue engineering. One of the most common synthetic materials used for tissue engineering.

## 4. Extracellular matrix scaffolds

Extracellular matrix extracts or derivatives have been developed as commercial products for cell delivery. In particular, many skin and extracellular matrix substitutes, such as MatrigelTM (BD Biosciences, San Jose, CA), DermagraftTM (Advanced Tissue Sciences Inc, La Jolla, CA), have been developed to allow the incorporation of ex vivo-expanded cells. Consequently, they are unlikely to be routinely used as cell delivery devices in the longer term.

#### **New directions:**

The field of tissue-engineering constructs and scaffolds is expanding at a very rapid rate. It would, within the confines of this review, be impossible to detail all of the most recent developments. However, there are two particular new directions in which the authors are specifically interested that involve the coculture of cells and nanotechnology. In attempts to deliver cells to a complex environment, such as the periodontium, it is possible that delivery of cells of multiple phenotypes may be required.

#### Conclusion:

The study of scaffold materials for use in tissue engineering should lead to improved predictability of this new technology based on cell and molecular biology. In the future it will become increasingly important to consider the concepts of scaffolds that are not only space making and exclusionary, but also biocompatible and able to elicit appropriate gene expression by the cells for which it is providing the carrier capacity.

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Paper accepted for presentation at 7th International Orthodontic Conference: Sydney Australia. Topic: Grading System, Class I extraction Vs non extraction cases in South Indian

Population.



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II Prize for Poster Presentation in 10th FODI & IES PG Convention At Shillong.