ISSN Print: 2394-7489
ISSN Online: 2394-7497
IJADS 2015; 1(4): 71-74

www.oraljournal.com
Received: 11-07-2015
Accepted: 12-08-2015

Dr. Nayanjyoti Deka
Post graduate student,
Department of Periodontology,
Rajarajeswari Dental College
and Hospital Mysore road,
Bangalore, Karnataka 560074.

Correspondence
Dr. Nayanjyoti Deka
Post graduate student,
Department of Periodontology,
Rajarajeswari Dental College
and Hospital Mysore road,
Bangalore, Karnataka 560074.

Tissue engineering approach for periodontal regeneration

Nayanjyoti Deka

Abstract
Periodontal regeneration attributes to a complete recovery of the periodontal tissues in both height and function, that is, the formation of alveolar bone, a new connective attachment through collagen fibers functionally oriented on the newly formed cementum. Regeneration of the periodontal tissues is a complex phenomenon requiring interplay between various processes in a timely manner. Healing of the periodontal tissues is also rendered more complex because it must occur in an open system permanently contaminated and under a significant bacterial load. Added to this complexity are the occlusal forces on the tooth complex in the transverse and the axial planes which affect the stability of the healing wound.
Complete regeneration of periodontium still considered a difficult and often resulted in incomplete regeneration. Tissue engineering and other cell based therapies have emerged as an alternative approach for the regeneration of several tissues damaged by disease or trauma, including the periodontium. This article reviews the approach of periodontal regeneration using tissue engineering.

Keywords: tissue engineering, periodontal regeneration, stem cells, growth factors

1. Introduction
Tissue engineering is a novel and exciting field that aims to re-create functional, healthy tissues and organs in order to replace diseased, dying, or dead tissues [1]. It is an interdisciplinary field that applies principles and methods of engineering and the life sciences towards the development of biological substitutes that restore, maintain, and improve the function of damaged tissues and organs [2]. It was proposed by 1993 Langer *et al*. in 1993 as a possible technique for regenerating lost periodontal tissues [3] The goal of tissue engineering is to promote healing, and ideally, true regeneration of a tissue's structure and function, more predictably, more quickly, less invasively, and more qualitatively than allowed by previous passive techniques.
Thus tissue engineering approach to bone and periodontal regeneration combines three key elements to enhance regeneration (figure 1). These are conductive scaffolds/Extracellular matrix, stem/Progenitor cells and signaling molecule [4]

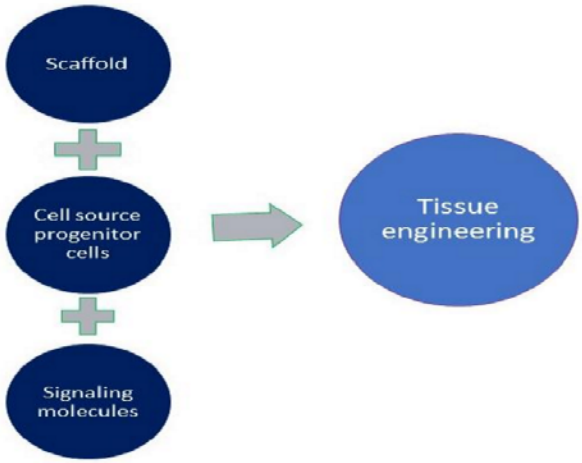

Fig 1: tissue engineering key elements

2. Scaffold

A scaffold serves as a physical support to the wound area and maintains and the shape of the defect. It serves as material for cellular adhesion, migration, proliferation. It also restrict and act as a barrier so that no unwanted cell can grow in wound area production of extracellular matrix and potentially serves as a delivery vehicle for growth factors. The scaffold may be resorbable and non resorbable and may be natural or synthetic. A variety of material has been used in scaffold of tissue engineering. Biomaterials used as scaffolds are described below.

2.1 Ceramics: Natural and synthetic HA (hydroxyapatite) and beta tricalcium phosphate (TCP) are osteoconductive, biocompatible, and do not stimulate immunological reaction. TCP is a naturally occurring material comprising of calcium and phosphorous and is used as a ceramic bone substitute.

2.2 Polymers: polymers include synthetic polyesters, such as polylactic acid, polyglycolic acid, natural polymers like collagen fibrin, albumin, hyaluronic acid, cellulose, chitosan, polyhydroxyalkanoates, alginate, agarose and polyamino acids etc.

2.3 Synthetic polyesters: PGA (polyglycolic acid) is a polymer of glycolic acid. PLA (polylactic acid) is the polymer of lactic acid. Copolymers of PGA have been used for many types of biomaterials, including sutures (vicryl). PLGA (polylacticcoglycolic acid) is a copolymer of PGA and PLA. Due to its biocompatibility, controlled structural and mechanical properties, tailored degradation rates, and its potential as growth factor delivery vehicles, it has been considered as the prime candidate for use in regenerative medicine and dentistry.

2.4 Natural polymers

2.4.1 Chitosan: It is a biodegradable natural carbohydrate biopolymer that has been shown to improve wound healing and improve bone formation. It is nontoxic and non-immunogenic, and have such structural characteristics that makes it possible to be used as a bone substitute and as a scaffold for cell attachment.

2.4.2 Collagen: Collagen can be process to make collagen foam, collagen fiber and collagen membrane which have favorable properties that can be used for scaffold of tissue engineering [5].

3. Cells source Progenitor cell for tissue engineering

Cell source is critical parameters for successful outcome of tissue engineering. Mainly it employs stem cells from various sources, which has capability give rise to required cells. Within the sphere of periodontal tissue engineering, mesenchymal derived cells have been applied for simultaneous regeneration of the attachment apparatus components.

3.1 Dental Pulp Stem Cells: In 2003, Shi and Gronthos isolated dental pulp stem cells through immunoselection [6]. Human pulp cells (odontoblasts) retain its ability to form functional odontoblast even when after fully developed complete tooth development. It has the ability to form reparative dentin when expose to deep caries and mild trauma or pulp capping. When third molar is extracted and it is cultured in suitable condition it Human dental pulp cells odontoblastlike cells that produce dentin [7].

3.2 Periodontal Ligament Stem Cells: Periodontal ligament stem cells (PDLSCs), which reside in the perivascular space of the periodontium, possess characteristics of mesenchymal stem cells and are a promising tool for periodontal regeneration [8] Principle of guided tissue regeneration is based on this principle that periodontal ligament cell have the potential to give rise to various cells [9] Multipotent progenitors from human PDL were shown to generate bone. These cells have also been shown to retain stem cell properties and tissue regeneration capacity even after recovery from solid-frozen human primary tissue (Shi 2005). These findings suggest that cryopreserved PDLSCs from extracted teeth could prove useful for clinically relevant therapeutic applications in the future [10]

3.3 Dental Follicle Stem Cells: The dental follicle has long been considered a multipotent tissue, based on its ability to generate cementum, bone and PDL from the ectomesenchyme derived fibrous tissue. Human dental follicle progenitor cells obtained from human third molars exhibit a characteristic ability to attach to tissue culture plastic. Dental follicle stem cells express side population stem cell markers and the demonstrated ability to differentiate into not only osteoblasts/cementoblasts but also adipocytes and neurons.

3.4 Dental Epithelial Stem Cells: Once enamel is formed and maturation stage is reached, oral ectoderm-derived ameloblasts are unable to proliferate or regenerate. However, continuously growing mouse incisors, and molars in some mammalian species, exhibit constantly replenishing populations of enamel organ tissue-derived stellate reticulum, stratum intermedium and surrounding outer enamel epithelial cells, providing a source of tissues to harvest for characterization of dental epithelial stem cells [11]. A specialized structure located at the apical region of the labial cervical loop in mouse incisors was characterized and named the 'apical bud' were suggested to act as stem cell containing compartments that could differentiate into ameloblasts through interaction with adjacent mesenchymal cells [12]

4. Signaling molecules in tissue engineering

Signaling molecules and growth factors are biological mediators that play critical roles regulation of wound healing by the stimulation of a series of events and cascades for tissue regeneration. The incorporation of growth factors and signaling molecule in tissue engineered scaffolds also facilitates sustained release of these molecules for longer periods of time. Various growth factors proteins, peptides, cytokines are stimulate events required for regeneration. Signaling molecules are proteins that may act locally or systemically to affect the growth and function of cells in various manners.

4.1 Insulin like growth factor 1: Insulin like growth factor 1 is found in substantial levels in platelets and is released during clotting along with the other growth factors. It is a potent chemotactic agent for vascular endothelial cells resulting in increased neovascularization. It promotes osteogenesis and cementogenesis. Matsuda *et al*. in 1992 demonstrated the mitogenic effects of insulin growth factor on periodontal ligament fibroblastic cells and concluded that a synergistic effect results from using a combination of platelet derived growth factor and insulin like growth factor 1.

4.2 Transforming growth factor β: TGFβ is found in highest concentration in bone and platelets. TGF-β is a strong promoter of extracellular matrix production. It selectively stimulates periodontal ligament fibroblast proliferative activity. It stimulates type I collagen, fibronectin and osteocalcin biosynthesis, as well as bone matrix deposition and chemotaxis of osteoblast. On the other hand, TGF-β decreases synthesis of metalloproteinases and plasminogen activator, and also increases the synthesis of tissue inhibitor of metalloproteinases and plasminogen activator inhibitor, thus resulting in the decrease of connective tissue destruction. It may act as bone coupling factor linking bone resorption to bone formation [4]

4.3 Growth differentiation factor-5: Growth differentiation factor-5 is a member of the transforming growth factor-beta superfamily. It plays critical roles in tendon, skeletal, and ligament morphogenesis In vitro studies have shown that recombinant human growth ⁄ differentiation factor-5 inhibits alkaline phosphatase activity in human periodontal ligament cells. When delivered in a suitable carrier, recombinant human growth factors might allow regeneration of all periodontal tissues without the complications of ankylosis and root resorption [4].

4.4 Periodontal ligament derived growth factor: Nishimura *et al*. in 1995 isolated a novel polypeptide factor from human periodontal cells periodontal ligament derived growth factor called PDLCTX. This peptide is highly specific autocrine chemotactic agent for human periodontal ligament cells, which is 1000 fold more potent than many known growth factors (IGF, PDGF, TGF). In addition, PDLCTX has no chemotactic effect on gingival fibroblast or epithelial cells thereby promising its utility for biological therapeutic regime needed for cell specific periodontal regeneration [13].

4.5 Platelet-derived growth factor: Ross *et al*. in 1974 and Kohler and Lipton in 1974 described that the material released from platelets is the principal source of mitogenic activity present in serum, and it is one of the principal growth factors related to wound healing by growth of many cells. In vitro studies have demonstrated that platelet-derived growth factor enhances the proliferation and mitogenic activity of periodontal ligament-derived. It enhance bone and cementum formation. Lynch and co-workers demonstrated that that platelet-derived growth factor-BB alone could significantly stimulate formation of new cementum and inserting collagenous fibers. Table 1 showing In brief various actions of growth factors.

4.6 Fibroblast growth factor: Fibroblast growth factor is the member of heparin binding growth factor family. There are 7 forms of fibroblast growth factor. Besides its name its activity exists beyond that of fibroblast and includes a wide variety of cell types such as smooth muscles, endothelial cells, chondrocytes and osteoblasts. It has a profound effect on periodontal soft tissue and bone healing as it is mitogenic for fibroblasts, chondrocytes, osteoblasts, smooth muscle. FGF also stimulates, DNA synthesis, angiogenesis, and cell replication.

4.7 Bone morphogenetic proteins: BMPs are bone growth factors synthesized and secreted by osteoblasts and incorporated into the organic matrix during bone formation. They are released during osteoclastic resorption and induce differentiation of mesenchymal cells into osteoblasts, stimulating osteogenesis in the remodeling and healing processes. Presently, 20 structurally related BMPs belonging to the TGF-β superfamily have so far been recognized, and two of them, the BMPs 2 and 7, distinguish for their osteoinductive property, emerging as an alternative for filling of bone defects. However, the difficulty for their clinical use is that, because they are rapidly diffusible in biological media, to achieve maximum efficacy without the need for excessively high doses they should be associated with a carrier system that allows its continuous release in a rate compatible to that of new bone formation. In addition to undergoing controlled biodegradation, other essential requirements for a potential carrier are biocompatibility, reduced immunogenicity and no toxicity; ideally they should be osteoconductive, have mechanical stability and adequate porosity to allow infiltration of cells and support vascular ingrowth, and be sterile and user-friendly [14]

Table 1: growth factors and their actions

Insulin-like growth factor-1	Cell migration, proliferation, differentiation and matrix synthesis
Transforming growth factor- beta 1	Proliferation of cementoblasts and periodontal ligament fibroblasts
Growth differentiation factor-5	Plays critical roles in tendon, skeletal, and ligament morphogenesis inhibits alkaline phosphatase activity in human periodontal ligament cells,
Periodontal ligament derived growth factor	Highly specific autocrine chemotactic agent for human periodontal ligament cells, which is 1000 fold more potent than many known growth factors (IGF, PDGF, TGF)
Platelet-derived growth factor	Migration, proliferation and non-collagenous matrix synthesis of mesenchymal
Fibroblast growth factor-2	Proliferation and attachment of endothelial cells and periodontal ligament cells
Bone morphogenetic	Protein Proliferation, differentiation of osteoblasts and differentiation of periodontal ligament cells into osteoblasts
Fibroblast growth factor-2	Proliferation and attachment of endothelial cells and periodontal ligament cells

5. Conclusion

The regeneration of the periodontium is known to be challenging to the clinicians. Thus, the development of new therapies tissue engineered scaffolds opened a new era of the periodontal regeneration. In the near future along with conventional therapy these newer approaches will be useful for regenerating lost tissues and may become key in regenerating oral function disrupted by periodontal disease. The regeneration of the periodontium is known to be challenging to the clinicians. Thus, the development of new therapies based on cells and/or tissue engineered scaffolds opened a new era of the periodontal regeneration.

6. References

1. Kaigler D, Mooney D. Tissue Engineering's Impact on Dentistry. Journal of Dental Education. 2001; 65(5):456-62.
2. Yen AH, Yelick PC. Dental Tissue Regeneration – A Mini-Review. Gerontology 2011; 57:85-94.
3. Requicha JF, Viegas CA, Munoz F, Reis RL, Gomes ME. Periodontal Tissue Engineering Strategies Based on Nonoral Stem Cells. The anatomical record 2014; 297:6-15.
4. Dabra S, Chhina K, Soni N, Bhatnagar R. Tissue

engineering in periodontal regeneration: A brief review. Dent Res (Isfahan) 2012; 9(6):671-80.
5. Pandit N, Malik R, Philips D. Tissue engineering: A new vista in periodontal regeneration. J Indian Soc Periodontol. 2011; 15(4):328-337.
6. Bansal R, Jain A. Current overview on dental stem cells applications in regenerative dentistry. J Nat Sci Biol Med. 2015; 6(1):29-34.
7. Brar GS, Toor RS. Dental stem cells: dentinogenic, osteogenic, and neurogenic differentiation and its clinical cell based therapies. Indian J Dent Res. 2012; 23(3):393-7.
8. Zhu W, Liang M. Periodontal Ligament Stem Cells: Current Status, Concerns, and Future Prospects. Stem Cell Int 2015; 2015:972313.
9. Nosrat A, Ryul Kim J, Verma P, Chand S, Tissue P. engineering considerations in dental pulp regeneration. Iran Endod J. 2014; 9(1):30-9.
10. Tatullo M, Marrelli M, Paduano F. The Regenerative Medicine in Oral and Maxillofacial Surgery: The Most Important Innovations in the Clinical Application of Mesenchymal Stem Cells. Int. J Med Sci. 2015; 12(1):72-77.
11. Asatrian G, Pham D, Hardy WR, James AW, Peault B. Stem cell technology for bone regeneration: current status and potential applications. Stem Cell Cloning 2015; 8:39-48.
12. Saito MT. Silverio KG, Casati MZ, Sallum EA, Nociti FH. Jr. Tooth derived stem cells: Update and perspectives. World j stem cells 2015; 7(2):399-407.
13. Sood S, Gupta S, Mahendra A. Gene therapy with growth factors for periodontal tissue engineering–A review. Med Oral Patol Oral Cir Bucal 2012; 17(2):301-10.
14. Peres JA, Lamano T. Strategies for stimulation of new bone formation: a critical review. Braz Dent J. 2011; 22(6):443-8.