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XI

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On behalf of the Committee, I am honored to welcome you all to 11th Scientific Forum and Dental Exhibition 2015 (FORIL XI 2015) organized by Faculty of Dentistry Trisakti University in Balai Kartini Exhibition and Convention Centre.

Since 1984, FORIL has made an excellence portion in updating science, skills and technology in dentistry. These scientific seminars and workshops will suffice the need of all dentists, scientist, students and other disciplines.

The proceeding book of FORIL XI 2015 contains of 75 papers, contributed from speakers of short lectures and poster presentations from dentists as well as students. These papers will cover various fields of new advances in dentistry and become a platform to update the dental knowledge and technology.

We hope this book will be worthwhile for the development of Indonesian dentists’ professionalism.

Best regards,

Rahmi Amtha, drg. MDS, Ph.D. Sp.PM

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Best regards,

Rahmi Amtha, drg. MDS, Ph.D, Sp.PM

Chairperson FORIL XI 2015
A Review of Tissue Engineering in Periodontal Regeneration
(A Literature Review)

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ABSTRACT

**Background:** Periodontitis is an inflammatory disease of the supporting tissues of the teeth resulting in progressive destruction of periodontal ligament and alveolar bone with pocket formation, recession or both that leading to tooth loss. The art and knowledge about regeneration in periodontal develop rapidly, not just in bone regeneration but also how to achieve tissue regeneration. **Objectives:** To determine definition, key areas, biomaterial for tissue engineering in periodontal regeneration. **Discussion:** Tissue engineering is one of the issues how the science of cell biology, developmental biology and also biomaterial could replace the tissue. The four key areas of future tissue engineering in periodontal regeneration are cells, scaffolds, signaling molecules, and blood supply. The use of growth factors, stem cell and biomaterials are discussed to achieve tissue engineering. **Conclusion:** The concept of tissue engineering in periodontal regeneration is to be promising. This review is aimed to explain and give a new perspective about future approaches of periodontal regeneration.

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

INTRODUCTION

**Background**

Periodontitis is one of inflammatory disease that have a high rank in Indonesia, from Indonesia Dental Health Profile (2000) 88.67% people live in the city had a gum disease.1 Based on SKRT (2011) 57% people in Indonesia had a gum disease.2 Based on WHO World Oral Health Report (2003) Periodontitis is an expensive treatment.3 Periodontitis is defined as an inflammatory disease of supporting tissues of the tooth caused by the microorganism, that result in destruction of the tooth attachment apparatus. Untreated periodontitis result in attachment loss and lead to tooth loss. The first important in treating periodontitis is eliminating the primary cause of inflammation is bacterial plaque along with other predisposition factor. After periodontal defect occurred, periodontal regeneration is one of the choices for periodontal treatment.6

A major goal in the treatment of periodontal defects is the simultaneous regeneration of cementum, periodontal ligament and alveolar bone structures in the face of the microbial assault and altered host immune response.7 Periodontal regeneration aims to restore these lost tissues to their original form and function by recapitulating the crucial wound healing events associated with periodontal development.8 Tissue engineering is a contemporary area of science based on the principles of cell biology, developmental biology and biomaterials science to develop new procedures and biomaterials to re-
place lost or damaged tissues. Conventional open flap debridement falls short of regenerating tissues destroyed by the disease, and current regenerative procedures offer a limited potential towards attaining complete periodontal regeneration. Recent advances periodontal treatment focuses on alveolar bone structure with guided tissue regeneration and growth factors, but no result in periodontal liga-

ment and cementum. Hence, stem cell prove to be a promising as well as an effective novel approach in the regeneration of the periodontal tissue.

This review will discussed a development of tissue engineering in periodontal regeneration from guided tissue engineering, growth factors until stem cell as a periodontal regeneration treatment based on key areas of future tissue engineering.

LITERATURE STUDY

1. Anatomy of Periodontium and Process of Periodontal defect

The periodontium consist of the investing and supporting tissues of the tooth are gingiva, peri-
odontal ligament, cementum and alveolar bone. It has been divided into two parts, first is the gingiva, the main function of which is protecting the underlying tissues, and the attachment apparatus, composed of the periodontal ligament, cementum, and alveolar bone.

![Figure 1. Anatomy of Periodontium](image)

Untreated periodontitis will lead us to peri-
odontal defect, and destroy alveolar bone, ligament periodontal and cementum. Alveolar bone consist of bone basis, compact bone and trabecular bone, in structure and morphology very unique because unstable and dependent to tooth. Periodontal ligament consist of different cell including synthetic cell (oseteoblast, fibroblast and cementoblast), resorptive cell (osteoclast, fibroblast, dan sementoclast), epithelial cell (epithelia of Malassez and endothelial cell) and connective tissue (mass cell, macrophage etc). Therefore, periodontal ligament functional as attachment from tooth to alveolar bone, support the tooth movement, nutrition and sensorial, formation aspects for synthesis and resorption of alveolar bone, cementum and protein. Function of cementum are anchorage to alveolar bone, occlusal interrelationship, fix root fracture, protect root canal, close necrotic pulp, protect dentine tubules.

2. Periodontal wound healing and regeneration

Wound healing is the process by which an in-
jured tissue repairs itself. This consists of three in-
terdependent, sequential phases that overlap with each other: inflammation, granulation tissue for-
amination and remodeling of the newly formed tissue. Wound healing first is comprising the rigid nonv-
cular mineralized tooth surface and second, the con-
nective tissue and epithelium of the gingival flap. Blood clot formation immediate after periodontal surgery, and has two function protect the denuded tissue, and serves as a provisional matrix for cell migration.

Clot formation followed by an early stage of in-
flammation. Within minutes, a fibrin clot attached to the root surface is developed. Within hours, one may observe the early phase of inflammation as inflam-
matory cells, predominantly neutrophils and mono-
cytes, accumulate on the root surface, and within 3 days the late phase of inflammation dominates the healing picture as macrophages migrate into the wound followed by the formation of granulation tis-

ue. At 7 days, a connective tissue attachment may be seen at the root surface; however, areas of the
Figure 2. Four Key Areas in Tissue Engineering in Periodontal Regeneration

Kornman & Robertson classified factors that may influence the successful management of periodontal osseous defects. Their classification includes bacterial contamination, innate wound-healing potential, local site characteristic and surgical procedure and technique. 15

4. Concept of Tissue Engineering

Tissue engineering is a contemporary area of science based on the principles of cell biology, developmental biology and biomaterials science to develop new procedures and biomaterials to replace lost or damaged tissues. Four key areas of future tissue engineering consist of cells, scaffolds, signaling molecules, and blood supply. 16 Based on Hsing and Mooney (2006) tissue engineering strategies often seek to recapitulate natural tissue formation processes, and appropriate cell populations, scaffold and inductive factors are selected to facilitate the repair and regeneration of the bone. 17

Scaffolds act as a delivery vehicle for cell transplantation and as a three-dimensional template for tissue regeneration, but also provide specific cues to regulate bone formation. Candidate biomaterials for scaffolds must meet several criteria are biologi-
cally compatible to minimize adverse inflammatory response; the mechanical, chemical and biological properties of the scaffold should be suitable for the specific application; scaffold characteristics (porosity, topography and material compositions, dictate certain of these features; scaffolds utilized for bone tissue engineering may be osteoconductive, osteo-inductive or both.17

The primary cell types involved in bone formation, osteoblasts and osteoprogenitor cells are important components of the bone-repair process and have been incorporated into various scaffolds to enhance bone repair. In order to obtain autologous or allogeneic cells for bone regeneration, osteoblasts and osteoprogenitors must be obtained from the patient or a donor. Isolation of sufficient numbers of primary human osteoblasts is difficult as it requires the sacrifice of healthy bone tissue.17

Signaling molecules that instruct the cells to form the desired tissue type including growth factors, differentiation factors and adhesion molecules.18

DISCUSSION
1. Periodontal Regeneration and the Need of Tissue Engineering
Guided Tissue Regeneration

For a long time guided tissue regeneration is a new hope for periodontal regeneration and still being a “gold standard” in periodontal surgery treatment for periodontal regeneration. The use of barrier membrane are effective as a space maintenances and hold a bone graft materials until wound healing achieve; a GTR design for tissue integration, cell occlusivity, clinical manageability, space provision, biocompatibility, membrane stability and membrane resorption.

From these studies it was reported that only cells of the periodontal ligament possessed regenerative capacity, and that exclusion of gingival tissues from the woundsite allowed periodontal ligament cells to re-populate the site, making regeneration biologically possible. Histological analysis of guided tissue regeneration healing shows that new connec-
tive tissue attachment to the root surface forms with minor contributions from new cementum and bone which, by definition, is not true regeneration.19

2. Growth Factors and Stem Cell as a Tissue Engineering

Strategies for bone tissue engineering

Tissue-engineering strategies often seek to recapitulate natural tissue-formation processes, and appropriate cell populations, scaffolds and inductive factors are selected to facilitate the repair and regeneration of bone. Tissue engineering aims to produce tissues that are both structurally and functionally identical to the original tissues that are replacing, and strategies for growing bone therapeutically are emerging based on the knowledge of the physiological role of different signaling molecules in the bone-forming process.

Growth Factors

Growth factors are soluble proteins that act as signaling agents for cells and influence critical functions such as cell division, matrix synthesis, and tissue differentiation, by receptor – ligand binding. It has important role for bone formation and bone repair, can be found in bone, cementum, and healing tissues.14

The target of growth factors are interact with cells of the osteoblast lineage and play role in the local regulation of bone formation. From mesenchymal stem cells into osteoprogenitor cells, then pre-osteoblast until osteoblast.14

Stem cell

The strategy of periodontal tissue regeneration therapies has been to control inflammation and stimulate stem progenitors to regenerate new periodontal tissues. Recent advances in stem cell biology and regenerative medicine have presented opportunities for tissue engineering as well as gene-based approaches in periodontal therapy.

Stem cells are the foundation cells for every organ and tissue in the body, including the periodontium. They have two defining characteristics: the ability for indefinite self-renewal to give rise to
more stem cells, and the ability to differentiate into a variety of specialized daughter cells to perform specific functions.  

There are two main types of stem cells — embryonic stem cells and adult stem cells — which are classified according to their origin and differentiation potential. Human embryonic stem cells, derived from the inner cell mass of blastocysts, are pluripotent stem cells capable of differentiating into cells of all three germ layers of the adult body.  

Adult stem cells are thought to function in long-term tissue maintenance and/or repair by replacing cells that are either injured or lost. They are generally multipotent stem cells that can form a limited number of cell types corresponding with their tissues of origin, although some studies have suggested that they are more versatile and can develop into many other cell types than previously expected. The most common source of adult stem cells is the bone marrow, which contains hematopoietic stem cells and bone marrow stromal cells or mesenchymal stromal/stem cells.  

Mesenchymal stem cells were initially identified in rodent marrow as colony-forming unit fibroblasts capable of forming bone, cartilage and fat, as well as reconstituting the hematopoietic microenvironment. Mesenchymal stem cells can effectively regenerate destroyed periodontal tissue. Those derived from bone marrow or adipose tissue have been used in experimental animal models. They have been shown to form cementum, periodontal ligament and alveolar bone in vivo after implantation into periodontal defects in beagle dogs. Mesenchymal stem cells have also been identified in adipose tissue. As adipose tissue requires less-invasive methods and is abundant, it is very appealing as a source of cells for regenerative periodontal therapy.  

**REFERENCES**


