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Full Length Review Article

TISSUE ENGINEERING FOR DENTINAL- PULP COMPLEX REGENERATION

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ABSTRACT

Tissue engineering is the employment of biologic therapeutic strategies aimed to the replacement, repair, maintenance, and/or enhancement of tissue function that applies the principles of engineering and life science. The key ingredients for tissue engineering are stem cells, morphogen or growth factor that regulate their differentiation, and scaffold that constitute the microenvironment for their growth. Recently, there has been increasing interest in applying the concept of tissue engineering to regenerate dentinal pulp complex. The ultimate goal of a regenerative pulp treatment strategy is to reconstitute normal tissue continuum at the pulp dentin border.

INTRODUCTION

Tissue engineering is an multidisciplinary field that appilies the principles engineering and life sciences toward the development of biological substitutes that restore, maintain, or improve tissue function (Bansal *et al*., 2011). The modern development of tissue engineering started in the late 1980s when synthetic biodegradable materials were introduced as scaffolds for cell expansion (Prashanth and Shantha, 2014). Tissue engineering is the field of the functional restoration of tissue structure and the physiology for impaired or damaged tissue because of cancer, disease, and trauma. With tissue engineering techniques, it may be possible to repair damaged tissue or even create replacement organ. Tissue engineering can help in the regeneration of enamel and dentin to restore the lost tooth structure in future (Anilkumar and Geetha, 2010). The representation of three different tissue engineering approaches: conductive and inductive approaches and cell transplantation. Tissue engineering is generally considered to consist of three key elements stem cell/progenitor cells, scaffold/ extracellular matrix, and morphogen (Anilkumar and Geetha, 2010 and Saber, 2009).

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Stem cell

The most promising cell sources for tissue engineering are the stem cell. Stem cell is an undifferentiated cell, which has the potential to proliferate and generate progenitor cells that can differentiate into specialized cells throughout post natal life. Stem cell are considered to be the most valuable cells for regenerative medicine (Zhang and Pamela, 2010 and Saber, 2009).

A classic stem cell should process two properties namely self renewal and potency (Mouli *et al*., 2012).

1. Self renewal is the capacity of the cell to undergo numerous cycles of cell division maintaining the undifferentiated state.
2. Potency means the differentiation capacity of the stem cell.

Stem cells can be classified according to the growth stage into: (Zhang and Pamela, 2010 and Mouli *et al*., 2012)

1. Embryonic Stem Cells (ES cells)

ES cells are stem cells derived from the inner cell mass of an early, preimplantation stage embryo known as a blastocyst. ES cells are prluripotent cells, which means that they can give rise to all differentiated cell types derived from all three germ layers.

2. Postnatal or Adult Stem Cells (AS cells)

AS cells are the self renewable progenitor cells residing within most differentiated tissue and organ, can found in almost all kinds of tissues. As cells are through to migrated to the area of injury and differentiate into specific cell types to facilitate repair of the damage tissue.

3. Induced Pluripotent Stem Cell (IPS)

IPS is an evolving concept in which 3-4 gene found in the stem cells are transfected into the donor cells using appropriate vector.

Stem cells are often categorized by their source: (Marawar *et al*., 2012 and Bansal *et al*., 2011)

1. Autologous stem cells

Cells are obtained from the same individual in whom they will be implanted

2. Allogenic stem cells

Cells originated from a donor of the same species

3. Xenogenic stem cells

Cells that are those isolated from individuals of another species

Types of stem cells: (Das *et al*., 2013)

Stem Cell Type	Cell Plasticity	Source of Stem Cell
Totipotent	Each cell can develop in to a new individual	Cells from early (1-3 days) embryos
Pluripotent	Cells can form any (over 200) cell types	Some cell of blastocyst (5-14 days)
Multipotent	Cells differentiated, but can form a number of other tissue	Fetal tissue, cord blood and post natal stem cell including dental pulp stem cell

The oral and maxillofacial region can be treated with stem cells from the following source: (Mouli *et al*., 2012)

1. **Bone marrow**

Is composed of both heatopoietic stem cells and mesenchymal stem cells, the majority of oro-maxillofacial oral structures are formed from mesenchymal cells.

2. **Adipose tissue**

Adipose tissue contain a group of pluripotent mesenchymal stem cells that exibit multilineage differentiation. Advantages of adipose tissue are that it is easily accessible and abundant in many individuals.

3. **Stem cells from oral and maxillofacial region.**

This stem cells predominantly contain mesenchymal stem cells.

Scaffolds

Scaffolds use to provide a physicochemical and biological three-dimensional microenvirontment for cells to attach and growth or tissue construct for cell growth and differentiation, promoting cell adhesion and migration, therefore mimicking the in vivo condition (Saber, 2009 and Huang, 2009). Scaffold should be effective for transport of nutrients, oxygen, and waste. It should be gradually degraded and replaced by regenerative tissue, retaining the feature of the final tissue structure.

Two types of scaffolds: (Das *et al*., 2013 and Nakashima *et al*., 2006)

1. Biological or natural, eg: Collagen, Glycosaminoglycan
2. Artificial or synthetic, eg: Polylacticacid (PLA), Polyglycolicacid (PGA), Polyethyleneglycol (PEG), and polylacticco glycolic acid (PLGA)

Biomaterial scaffolds are likely indispensible for tooth regeneration. Ideal scaffold for tooth regeneration should allow functionality of multiple cell types including odontoblas, cementoblast, pulp fibroblast, vascular cell, and/or neural ending, and potentially ameloblast. Ideal scaffold for tooth regeneration must be clinically viable, should be biocompatible, non toxic and may need to undergo biologically safe degradation. Either native or synthetic polymers, or a hybrid, are valid choice as scaffolding materials for tooth regeneration. For dental pulp regeneration, the ideal scaffold should also support vascularizaion and innervations of pulp tissue. (Yildirim, 2011)

Growth factor/ Signaling molecules

Growth factor are proteins that bind to receptors on the cell surface and induce cellular proliferation or differentiation. Many growth factor are quite versatile, stimulating cellular division in numerous cell types, while others are more cell specific (Das *et al*., 2013 and Zhang and Pamela, 2010). Growth factor are extracellularly secreted signals governing morphogenesis or organogenesis. They regulate the division or specialization of stem cells to the desirable cell type and mediated key cellular event in tissue regeneration including cell proliferation, chemotaxis, differentiation, and matrix synthesis (Saber, 2009). A variety of growth factors have successfully been used for dentin-pulp complex regeneration, including Transforming Growth Factors (TGFs), Bone Morphogenic Proteins (BMPs), Platelet Derived Growth Factor (PDGF), Insulin Like Growth Factor (IGF), Fibroblast Growth Factors (FGFs). (Zhang and Pamela, 2010)

Dentinal Pulp Complex Regeneration

A tooth is a major organ and consists of multiple tissues. The hard tissues of tooth include the enamel, dentin, and cementum. The only vascularized tissue of the tooth is dental pulp that is encased in the mineralized dentin. (Yildirim, 2011) Caries, pulpitis, and apical periodontitis increase health care cost and attendant loss of economic productivity. They ultimately result in premature tooth loss and therefore diminishing the quality of life. (Nakashima *et al*., 2006)

Hard tissue is difficult to repair especially dental structures, when the tooth is damage but still reparable, regeneration of parts of the tooth structure can prevent or delay the lost of the whole tooth. The vitality of dentin-pulp complex is fundamental to the life of tooth and is a priority for targeting clinical management strategies (Huang, 2009 and Chandki *et al*., 2012). The pulp is an organ known to have tremendous reparative/regenerative abilities to form dentin in response to any injury. Pulp healing is complex and dependent on the extent of injury, among many other factors. Many of molecular and cellular processes involved in these healing events recapitulate developmental processes (Nakashima *et al*., 2006 and Simon *et al*., 2011). When the pulp is diagnosed with irreversible pulpitis, no treatment can reverse the situation, regardless of the amount of remaining normal pulp tissue. With the advent of modern tissue engineering concept and the discovery of dental stem cells, regeneration of pulp and dentin has been tested (Huang, 2009). Tissue engineering is the science of design and manufacture of new tissues to replace lost parts because of diseases including cancer and trauma. Regeneration of the pulp inside the damage tooth can be the basic clinical application of stem therapy in dentistry (Nakashima *et al*., 2006 and Mouli *et al*., 2012). For the regeneration of the entire tooth or tooth elements, we are ingrained to believe that stem cells or other cells must be transplanted. When tissue engineering was initiated as an interdisciplinary approach to heal tissue defect, three key elements were proposed: cells, scaffold, and signaling factor (Yildirim, 2011).

Steps involved in regeneration of tooth are: (Mouli *et al*., 2012)

1. Harvesting and expansion of adult stem cells
2. Seeding the stem cells into scaffold which provides optimized environment
3. Cells are instructed with targeted soluble molecular signals spatially
4. Confirming the gene expression profile of the cells for next stage in odontogenesis

During wound healing process after the exposure of pulp, the pulp cells and the undifferentiated mesenchymal cell that have de-differentiated from pulp cells, endothelial cells, and pericyts, migrate to the expose site from the deeper region of the pulp and replace degenerated odontoblasts (Nakashima *et al*., 2006). Growth factor play role in signaling many events in pulp dentine regeneration. Two important families of growth factor that a vital role are Transforming Growth Factor (TGF) and Bone Morphogenic Protein (BMP) (Bansal *et al*., 2011).
TGF β1 and TGF β3 are important in cellular signaling for odontoblas differentiation and stimulation of dentin matrix secretion. These growth factor are secreted by odontoblast and are deposited within the dentin matrix, where they remain protected in an active form through interaction with other components of the dentin matrix (Bansal *et al*., 2011). TGF β1 is well established in odontoblast differentiation during primary development and in tertiary dentinogenesis. TGF β1 is involved in injury signaling and tooth healing reaction. BMPs induce higher quantity and more homogenous reparatory dentin. Some growth factors like BMP-2, BMP-4, BMP-7 have been shown to direct pulp progenitor/stem cell differentiation into odontoblasts and result in dentin formation making the BMP family the most likely candidate as growth factor (Zhang and Pamela, 2010 and Simon *et al*., 2011). Regeneration of any tissue back to its original condition, to enhace regeneration, blood clot has been used as a rich source of growth factor to help tissue repair. Regeneration of dentin relies on having vital pulp and regenerated pulp tissue should be functionally component, example capable of forming dentin to repair lost structure (Huang, 2009). The associated broad spectrum of responses in pulp includes neural and vascular regeneration. Dental pulp is richly innervated, pulpal nerves play a key role in regulation of blood flow, dentinal blood flow, and pressure. The increasing interest in tissue engineering of tooth must take into account neuro-pulpal interactions and nerve regeneration. The vascular system in the dental pulp plays a role in nutrition and oxygen supply and as a conduit for removal metabolic waste. The critical importance of vasculature in tissue repair and regeneration is well known. Vascular endothelial growth factor (VEGF) is an excellent regulator of angiogenesis and is known to increase vascular permeability (Nakashima *et al*., 2006). The goal of modern restorative dentistry is to functionally and cosmetically restore the tooth structure and the greatest potential for this engineered tissue is in the treatment of tooth decay (Anilkumar and Geetha, 2010).

REFERENCES

Anilkumar, K. and Geetha, S. 2010. *Tissue Engineering-Future Concepts in Endodontics-A Short Review.*Journal of Clinical and Diagnostic Research. 4, pp. 3282-3286.

Bansal, M. and Rajesh, B. 2011. *Regenerative Endodontics: A State of the Art*. Indian Journal of Dental Research. 22(1), pp. 122-131. Available online at http://imsear.hellis.org/bitstream/123456789/139964/1/ijdr2011v22n1p122.pdf

Chandki, R., M. Kala, Priyank, B. and Ruchi, B. 2012. *From Stem to Roots: Tissue Engineering in Endodontics.* J Clin Exp Dent. 4(1), pp. 66-71. Available online at http://www.medicinaoral.com/odo/volumenes/v4i1/jcedv4i1p66.pdf

Das, U. K., Aditya, M. and Nabanita, B. 2013. *Crossing Horizon in regeneration.* International Journal of Pharmaceutical Science Invention. 2 (6), pp. 1-8. Available online at http://www.ijpsi.org/Papers/Vol2%286%29/Version-1/A02610108.pdf

Huang, T. J. G. 2009. *Pulp and Dentin Tissue Engineering and Regeneration: Current Progress*. Regen Med. 4(5), pp. 1-18.

Marawar, P. P., Mani, A., Sachdev, S., Sodhi, N. K, and Anju, A. 2012. *Stem Cell in Dentistry: An Overview.* Pravara Med Rev. 4 (2), pp. 11-15. Available online at http://www.pravara.com/pmr/pmr-4-2-4.pdf

Mouli, P. E. C., Manoj, K., B. Shenthil, S. Parthiban, R. Priya, and R. Subha, 2012. *Journal of Pharmaceutical Science and Research.* 4(7), pp. 1872-1876. Available online at http://www.jomfp.in/article.asp?issn=097329X;year=2012;volume=16;issue=1;spage=58;epage=63;aulast=Sunil

Nakashima, M., Koichiro, I. and Li Zheng, 2006. *Gene Therapy for Dentin Regeneration with Bone Morphogenetic Proteins*. 6(5), pp. 551-560. Available online at http://www.endotreatment.gr/media/files/REGENERATIVE-ENDODONTICS/PIIS-6.pdf

Prashanth, K. K. and Shantha, M. H. 2014. *Regenerative Endodontics: An Update.* Journal of International Academic Research for Multidiciplinary. 2(4), pp. 650-658.

Saber, S. E. 2009. *Tissue Engineering in Endodontics.* Journal of Oral Science. 51(4), pp. 495-507. Available online at http://files.cultivoscelulares.webnode.es/200000132-1dd901ed30/Tissue%20engineering%20in%20endodontics.pdf

Simon, S. R. J., Berdal, A., Cooper, P. R., Lumley, P. J., Tomson, P. L. and Smith, A. J. 2011. *Dentin Pulp Complex Regeneration: from Lab to Clinic.* Adv dent Res. 23 (3), pp. 340-345. Available online at http://www.endoexperience.com/documents/DentinPulpComplexRegeneration-fromLabtoClinic2011.pdf.

Yildirim, S., Susan, Y. F., Keith, K., Hong, Z., Chang, H. L., Ang, L. *et al*. 2011. *Tooth Regeneration: A Revolution in Stomatology and Evolution in Regenerative Medicine.* Int J Oral Sci. 3, pp. 107-116. Available online at http://www.nature.com/ijos/journal/v3/n3/pdf/ijos201116a.pdf

Zhang, W. and Pamela, C. Y. 2010. *Vital Pulp Therapy-Current Progress of Dental Pulp Regeneration and Revascularization.* International Journal of Dentistry. 10, pp. 1-9. Available online at http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2861196/pdf/IJD2010-856087.pdf

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