SHORT COMMUNICATION

Natural and synthetic hydrogels for periodontal tissue regeneration

Dr. Marco Laurenti[1]
Dr. Mohamed-Nur Abdallah[2]

[1]MSc, PhD, Postdoctoral Fellow,
[2]BDS, MSc, PhD,
Faculty of Dentistry, McGill University, Montreal, Quebec, Canada

Corresponding Author
Dr. Marco Laurenti
Email: marco.laurenti@mail.mcgill.ca

Access this Article Online

Quick Response Code	www.idjsr.com
	Use the QR Code scanner to access this article online in our database
	Article Code: IDJSR SE 0161

Over the past few decades, there has been a great interest in periodontal regeneration therapy to restore the tissues destroyed by periodontal diseases, which are probably one of the most common bacterial infections in humans and the leading cause of tooth loss in adults. Periodontal diseases involve a set of inflammatory processes that are progressively destroying the tooth-supporting tissues (gingiva, periodontal ligament (PDL), alveolar bone and root cementum). Untreated periodontitis may cause irreversible destruction to these tissues leading to increased tooth mobility and subsequent tooth loss[1].

Currently, there is still no ideal therapeutic method to cure periodontitis or to optimally regenerate periodontal tissues in a predictable manner. Conventional mechanical or anti-infective periodontal therapies eliminate the inflammatory processes, and hinders or halts the diseases resulting generally in tissue repair without any notable signs of regeneration. Therefore, various regenerative approaches have been proposed and evaluated to restore the lost tooth-supporting tissues. These approaches included a wide range of surgical procedures and the use of various bone grafts, occlusal barrier membranes, purified protein mixtures, growth factors. Some of these approaches have achieved some success in regenerating the damaged periodontal tissues in certain ideal clinical cases; however, the outcomes are still very variable and unpredictable. Even with bone grafts, which are considered the current gold-standard material for bone regeneration, have reported failure rates up to 30% in maxillofacial and craniofacial surgeries, in addition to their drawbacks such as limited availability and donor-site morbidity. It is evident that a considerable research activity is required to improve the current periodontal therapies and to develop novel treatments to reach the ultimate goal of periodontal therapy, which is the predictable reconstruction of the lost periodontal tissues.

Periodontal tissue possess the capacity to regenerate itself and substantial efforts in the tissue engineering field have been done to understand this ability in order to overcome the current limitations of therapeutic and regenerative procedures [3]. Tissue engineering is a multidisciplinary field that aims to guide body regeneration by specifically controlling the biological environment or developing biological substitutes to restore tissue functions. The damage to any tissue or organ results in the destruction and loss of extracellular matrix (ECM) with the absence of functional cells. For this reason, it is of paramount importance to restore the structure, properties, and functions of the native natural tissue. The general approach to restore the initial tissue condition is to use a three-dimensional (3D) scaffold which has the function to temporary supports the cell growth and new tissue development. The 3D scaffold may be designed as purely structural support providing with biological moieties incorporated into the scaffold to guide cell and tissue growth. Regeneration of dental/craniofacial tissues may be successfully achieved from the inimitable blend of human cells seeded biomaterial scaffolds with/without growth factors[4]. The combination of stem-cells, biomaterials, and physio-biochemical factors is the basis and major contribution of tissue engineering to regenerative medicine. In this approach, the biomaterial is critical to the regeneration of tissue since it serves as a three dimensional artificial ECM or scaffold to provide structural organization and support for the proliferation and differentiation of cells to create a neo-tissue. It is the interaction of the cells' with the artificial ECM that is pivotal in re-creating and maintaining the functional and 3D structural integrity of the tissue [4a, 4c]. These scaffolds should be biocompatible facilitating cell attachment and proliferation, and biodegradable so that they do not require any surgical procedure for removal[5]. Hydrogels are highly hydrated polymeric biomaterials composed of hydrophilic polymeric network, either of synthetic or natural origin, and used as 3D scaffolds for periodontal tissue engineering applications[6]. Hydrogels are biodegradable, can be tailored to confer mechanical and structural properties similar to many ECM tissues, processed under mild conditions required to encapsulate biological moieties, and delivered in a minimally invasive manner[7].

Natural biomaterials have been extensively used in the development of matrix-based regenerative therapies that aim to accelerate clinical application due to their excellent biocompatibility, biodegradability, affinity for biomolecules and wound healing activity[8]. Materials such as collagen, hyaluronic acid, alginate and chitosan scaffolds have been used in periodontal regenerative research for more than two decades. The natural origin of these materials allows the design and engineering of biomaterial systems that function at the molecular level, often minimizing chronic inflammation. They can also be easily chemically and physically modified to form desired structures. The use of natural polymers in the form of hydrogels allows for the incorporation of biological agents by promoting cross-linking when the growth factor is dispersed in the polymer solution. Because natural polymers are often soluble in water, the creation of hydrogels may occur under mild fabrication conditions that are relatively harmless to the bioactivity of the growth factors. Normally, these hydrogels are degraded by enzymes and/or acid hydrolysis at a rate depending on the degree of crosslinking or the molecular weight [8].

Collagen is one of the most used biomaterials due to its excellent biocompatibility, weak antigenicity, biodegradability, and safety. Collagen hydrogel fits well with injectable cell delivery and highly porous cross-linked scaffolds provide good mechanical stability. For these reasons, collagen hydrogels have been used as support for in vitro growth of many types of tissues and to deliver different kinds of growth factors. Following the clinical use of collagen carriers delivering bone morphogenetic proteins for tibial shaft fractures [9], spine fusions and long-bone nonunions [10], collagen is currently being evaluated for widespread clinical periodontal regeneration. For example, there are commercially available collagen composite scaffolds such as Formagraft™ and OssiMend™ for periodontal regeneration currently used in animal studiesand clinical trials[11]. Chitosan is biodegradable natural polymer and it has been used as a cell vehicle material due to its ability to be molded into various geometries (e.g. porous structures). In addition, chitosan has minimal foreign body reaction and high affinity for in vivo macromolecules[12]. However, chitosan is not strongly supportive of tissue regeneration as demonstrated by its effect on the width of keratinized gingiva in dogs[13]. The addition of hydroxyapatite to chitosan hydrogels produced a 3D scaffold in which the pore sizes and interconnectivity were preserved, resulting in a suitable 3D environment to support cellular structure, proliferation and mineralization[14].

Synthetic polymers have been widely used for scaffolding applications because of their ability to provide controllable and reproducible structural properties, biocompatibility, and tailored biodegradation rates[15]. Scaffolds made of synthetic polymers can be produced by a variety of fabrication techniques, and they can be manufactured into preformed sizes and shapes according to clinical requirements. There are several synthetic polymers approved by the US Food and Drug Administration such as poly(glycolic acid) (PGA), poly(L-lactic acid) (PLA), their copolymers poly(lactic-co-glycolic acid) (PLGA), and poly(caprolactone) (PCL). Solid scaffolds are typically porous matrices fabricated by techniques such as solvent casting, gas foaming, particulate leaching, and electrospinning[5,15]. Other degradable polymers have also been explored and tested for periodontal tissue regeneration including poly(ethylene glycol) (PEG)[16], polylactide and polyglycolide[17]. Amorphous poly(D,L-Lactic acid) (PDLLA) used in combination with bioactive glasses ensure the creation of a macroporous structure within the bioceramic materials showing promising properties for periodontal tissue regeneration[5]. Synthetic polymers can be also used in combination with natural biomaterials. For example, the rapid degradation of fibrin, a biopolymer critical to hemostasis and wound healing, can be decelerated by modification with (PEG)[18].

Recently, nanocomposites based on polymers and nanosilica nanoparticles have been applied in periodontal tissue engineering. Silica nanoparticles are obtained by the sol–gel method and they can be incorporated into a polymeric matrix resulting in a nanocomposites with unique properties such as high mechanical resistance, chemical stability, and heat resistance[19]. Tubular nanocomposite scaffolds of poly(ethyl methacrylate-co-hydroxyethyl acrylate) [P(EMA-co-HEA)] were synthesized with different concentrations of silica nanoparticles by fiber-templating method in order to mimic the structure and functions of natural dentin[20]. These tubular structures were found to induce the precipitation of hydroxyapatite on their surface, and they can facilitate odontoblastic cell growth with the integration of host mineralized tissue. Hybrid P(EMA-co-HEA)/SiO_2nanocomposite matrix incubated in simulated body fluid for 14 days showed the best cellular distribution and neo-dentin like pattern. These constructs also showed enhanced mechanical properties to withstand functional stresses [20]. All these results indicate that the nanohybrid matrix scaffolds could be promising potential sources for dentin repair and regeneration.

Summary and Challenges

Periodontal regeneration remains a highly challenging task, since the existing therapeutic and regenerative approaches have not achieved a complete or predictable regeneration of the lost periodontal tissues in humans. The purpose of research into periodontal regeneration is to establish a new approach that overcomes the limitations of the current therapeutic and regeneration procedures. The synergistic approach of nanomedicine and tissue engineering is a promising field and has lead, so far, to a remarkable progress in the field of periodontal tissue regeneration. Several approaches utilizing collagen, chitosan, or nano-composites as hydrogels or rigid scaffolds have been found to promote and guide periodontal tissue regeneration. However, these studies are still limited to in vitro and in vivo studies which highlights the need of future investigation in this promising field.

Acknowledgment

The authors would like to acknowledge the Network of Oral and Bone Health Research, and the Faculty of Dentistry of McGill University for their financial support.

References

1. B. L. Pihlstrom, B. S. Michalowicz, N. W. Johnson, Lancet 2005, 366, 1809-1820.
2. H. F. Rios, Z. Lin, B. Oh, C. H. Park, W. V. Giannobile, J. Periodontol. 2011, 82, 1223-1237.
3. F. M. Chen, Y. Jin, Tissue Eng. Part. B-Re 2010, 16, 219-255.
4. aV. Rosa, A. Della Bona, B. N. Cavalcanti, J. E. Nor, Dent. Mater. 2012, 28, 341-348; bS. F. Yang, K. F. Leong, Z. H. Du, C. K. Chua, Tissue Eng. 2001, 7, 679-689; cS. F. Yang, K. F. Leong, Z. H. Du, C. K. Chua, Tissue Eng. 2002, 8, 1-11.
5. K. Rezwan, Q. Z. Chen, J. J. Blaker, A. R. Boccaccini, Biomaterials 2006, 27, 3413-3431.
6. aC. R. Nuttelman, S. M. Henry, K. S. Anseth, Biomaterials 2002, 23, 3617-3626; bB. Duan, X. Y. Yuan, Y. Zhu, Y. Y. Zhang, X. L. Li, Y. Zhang, K. D. Yao, Eur. Polym. J. 2006, 42, 2013-2022.
7. J. L. Drury, D. J. Mooney, Biomaterials 2003, 24, 4337-4351.
8. J. F. Mano, G. A. Silva, H. S. Azevedo, P. B. Malafaya, R. A. Sousa, S. S. Silva, L. F. Boesel, J. M. Oliveira, T. C. Santos, A. P. Marques, N. M. Neves, R. L. Reis, J. R. Soc. Interface 2007, 4, 999-1030.
9. R. Cancedda, P. Giannoni, M. Mastrogiacomo, Biomaterials 2007, 28, 4240-4250.
10. A. P. White, A. R. Vaccaro, J. A. Hall, P. G. Whang, B. C. Friel, M. D. McKee, Int. Orthop. 2007, 31, 735-741.
11. aF. Feng, K. Akiyama, Y. Liu, T. Yamaza, T. M. Wang, J. H. Chen, B. B. Wang, G. T. Huang, S. Wang, S. Shi, Oral. Dis. 2010, 16, 20-28; bT. G. Kim, U. M. Wikesjo, K. S. Cho, J. K. Chai, S. D. Pippig, M. Siedler, C. K. Kim, J. Clin. Periodontol. 2009, 36, 589-597.
12. I. Y. Kim, S. J. Seo, H. S. Moon, M. K. Yoo, I. Y. Park, B. C. Kim, C. S. Cho, Biotechnol. Adv. 2008, 26, 1-21.
13. G. Lotfi, M. A. Shokrgozar, R. Mofid, F. M. Abbas, F. Ghanavati, A. A. Bagheban, R. P. Shariati, J. Periodontol. 2011, 82, 1367-1375.
14. aA. C. Akman, R. S. Tigli, M. Gumusderelioglu, R. M. Nohutcu, J. Biomed. Mater. Res. A 2010, 92, 953-962; bY. Zhang, B. Shi, C. Li, Y. Wang, Y. Chen, W. Zhang, T. Luo, X. Cheng, J. Control Release 2009, 136, 172-178; cF. Liao, Y. Chen, Z. Li, Y. Wang, B. Shi, Z. Gong, X. Cheng, J. Mater. Sci. Mater. Med. 2010, 21, 489-496.
15. P. Gunatillake, R. Mayadunne, R. Adhikari, Biotechnol. Annu. Rev. 2006, 12, 301-347.
16. P. Valderrama, R. E. Jung, D. S. Thoma, A. A. Jones, D. L. Cochran, J. Periodontol. 2010, 81, 737-747.
17. G. Serino, W. Rao, G. Iezzi, A. Piattelli, Clin. Oral. Implan. Res. 2008, 19, 26-31.
18. J. M. Galler, A. C. Cavender, U. Koeklue, L. J. Suggs, G. Schmalz, R. N. D'Souza, Regen. Med. 2011, 6, 191-200.
19. aD. S. Achilias, D. N. Bikiaris, V. Karavelidis, G. P. Karayannidis, Eur. Polym. J. 2008, 44, 3096-3107; bM.Sadej-Bajerlain, H. Gojzewski, E. Andrzejewska, Polymer 2011, 52, 1495-1503; cS.Barus, M. Zanetti, M. Lazzari, L. Costa, Polymer 2009, 50, 2595-2600.
20. A. V. Lluch, A. C. Fernandez, G. G. Ferrer, M. M. Pradas, J. Biomed. Mater. Res. B 2009, 90b, 182-194.