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Tissue-engineered Ligament: Implant constructs for Tooth Replacement (Ligaplants)

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Abstract:

Periodontitis is the disease causing the destruction of the soft and hard tissues surrounding the tooth. If left untreated, periodontal destruction may progress and lead to mobility and ultimately loss of teeth. Replacement of the missing tooth with implant has gain a popularity among the population. But for a successful implant, factor such as sufficient bone (height and width) is very crucial. If a tooth was extracted, a certain period (3 months) of healing within the bone socket must be allowed prior placing an implant. With the development of ligaplants, bone with large defects may be overcome by ligaplants. The cultured PDL cells that surrounded the implants will act as supporting and anchorage in the place of normal PDL.

Keywords: Periodontal ligament, tissue engineering, tooth implant, temperature-responsive polymer

INTRODUCTION

The periodontal ligament is the soft connective tissue interposed between the roots of the tooth and the inner wall of the alveolar sockets[1]. Apart from its role in the tooth anchoring, the periodontal ligament(PDL) provides progenitor cells for alveolar bone formation and remodeling[2,3,4]; and it plays the role of the periosteum in the alveolar socket that faces the root of the tooth.

Periodontitis is characterized by the destruction of tissues, such as alveolar bone, cementum and the periodontal ligament which may be followed by tooth loss[5]. A possible approach to the replacement of tooth loss is tissue engineering of the PDL. As the PDL has been shown to possess a capacity for spontaneous regeneration, during which the biomechanical tissue strength is restored[6], and innervations is reestablished[7,8]. Regeneration of the PDL likely emanates from PDL progenitor cells[9] which can assemble new PDL-like structures in vivo[10]. Regeneration proceeds with a new layer of cementum, attached to original cementum of the tooth root, into which new transverse fibres are integrated[11]. Then, if a new cementum layer were to be laid down on the surface of the engineered-device, this would accommodate the integration of a properly attached PDL with the potential to stimulate the regeneration of adjacent alveolar bone[1].

Tissue-engineering has emerged as a new and ambitious approach that combines knowledge from material chemistry with cell biology and medicine. These strategies used biodegradable polymers to make scaffolds into the cells were inserted to produce tissues in the presence of growth factors[12]. The first generation of tissue engineering can be used for constructing cartilage[13,14] or bone[15]. The second generation of tissue engineering requires a new method of tissue reconstruction not based on scaffolds.[5]

LIGAPLANTS

The combination of PDL cells with implant biomaterial is known as Ligaplants (Figure 1). Recently, replace lost teeth without considering the PDL, implants of inert biomaterial are directly inserted into jawbones. Before these procedures, local bone defects and generally poor bone quality necessitate bone reconstruction[16]. Besides that, localized bone loss around the implant fixture represents a clinical challenge[17] especially in the cases of gingival recession where maybe due to modified tissue architecture, which requires further surgical interventions[18]. So, to overcome this problem, a implant system with tissue-inducing properties might be useful. Technically, implants with PDL maybe installed in the extraction socket of the missing tooth, thereby facilitating the surgical procedure. Natural implant anchoring might also be compatible with further growth and development of the alveolar bone housing, and it may allow tooth movements during orthodontic therapy. Conclusively, ligaplants have the capacity to induce the formation of the new bone, when placed in sites associated with large periodontal bone defects[5].

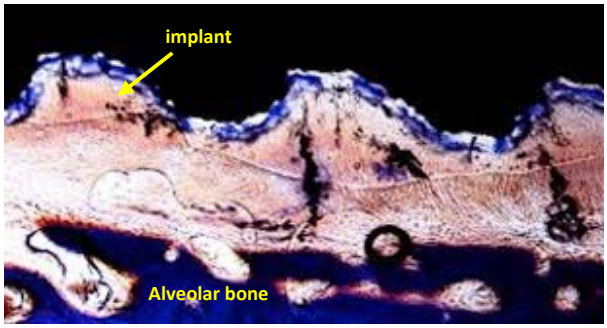

Figure 1: Ligaplants

MATERIALS AND METHODS OF OBTAINING LIGAPLANTS

Tooth transplantation with double PDL stimulation is one of the best examples of its healing capacity. Fourteen days before transplantation, the donor tooth is extracted and immediately replanted in its original alveolus. This deliberate trauma triggers a healing process within the PDL, which includes cell proliferation and differentiation. The in vivo cell culture reaches its peak of activity after 14 days, after which the transplantation of the tooth can be performed with millions of cells full activity attached to its root by new Sharpey's fibres.[5,19,20]

Using this model in its biological and clinical aspect, we now use it similar cell culture around an artificial root using tissue engineering techniques.

- Preparation of temperature-responsive culture dishes
  N-isopropylacylamide monomer in 2-propanaol solution was spread onto polystyrene culture dishes. Then the dishes were subjected to electron beam irradiation with an Area Beam Electron Processing System. The temperature-responsive polymer-grafted (poly N-isopropylacrylamide) dishes were rinsed with cold water to remove ungrafted monomer and sterilized with ethylene oxide[21].
- Cells and cell culture
  Human periodontal ligament cells were isolated from an extracted tooth. After extraction, periodontal tissue was scraped from the middle third of the root with a scalpel blade. The harvested tissue was placed into culture dishes containing = Dulbecco's modified Eagle's minimal essential medium, supplemented with 10% fetal bovine serum and 100units/mL of penicillin-streptomycin. Then, those outgrowth cells were cultured in a humidified atmosphere of 5% CO_2 at 37°C for 48 hours to allow attachment of the cells to the dishes. The dishes were washed to eliminate debris and the medium was changed three times per week. To harvest the cell sheet, human periodontal ligament cells were plated on temperature- responsive culture dishes(35 mm in diameter) at a cell density of $1x10^5$ and cultured at 37°C supplemented with 50mg/mL ascorbic acid 2-phosphate, 10nM dexamethasone and 10nM β-glycerophosphate that function as an osteodifferentiation medium[5,21].
- Culture of PDL cells in a bioreactor
  A titanium pin which coated with hydroxyappatite (HAP) was placed in a hollow plastic cylinder leaving a gap of 3mm around the pin. Culture medium was continuously pumped through the gap. Single cells suspension, obtained from human, were seeded first into plastic vessels under a flow of growth medium for 18 days. [5,21]

PRECAUTIONS WHEN PREPARING LIGAPLANTS

A cushion of sufficient thickness favours the formation of PDL and on the other, the prolonged cell culturing may favour the appearance of non-PDL cell types.

In order to preserve the cell differentiation state and to obtain adequate cell stimulation, the bioreactor has been constructed with the aim to resemble the PDL situation during cell growth; cells are positioned in a narrow space between the ligaplant and surrounding hollow cylinder. It was thereby anticipated that the PDL phenotype would be favoured implicating a tight attachment of cells to the implant. So, the preparation of the ligaplants should have minute mechanical movements of the medium flow and space between the implants and the culture should be optimal and the duration of the surface treatment should also be optimal to obtain the successful ligaplants which brings big improvements to the implant system[5].

SUCCESS OF THE LIGAPLANTS??

Tissue-specified characteristics were acquired after implantation: a new-cementum like layer, typical for regenerated PDL, orientation of cells and fibres across the non-mineralized peri-implant space.PDL organization that induced the cooperation of the tissues surrounding the ligaplant site. Bone formation was induced around ligaplants, suggesting an osteogenic potential of the new PDL[5].

The development of a regenerative PDL depends on site-specific signaling, which in turn is mediated by an anatomic code, written in expression patterns of homeogene-coded transcription factors. So, the homeoproteins influence the synthesis of cell surface and signaling components, and signals from the cell surface feedback to modulate homeogene expression, whereby cell identities are established according to the anatomic site and tissue type. Homeogene Msx2 has in fact been implicated in the singregation of mineralized bone versus non-mineralized PDL[22]. For the inhibition of mineral formation of PDL, a role of asporin (an SLRP protein that is present in the extracellular matrix) has been introduced.[5,23,24,25]

ADVANTAGES OF LIGAPLANTS

Ligaplants can alleviate problems that implant commonly faced such as gingival recession and bone defects of the missing tooth site. Therefore implant can be applied in cases of periodontal bony defects, situation that conventional implants could not be installed. Ligaplant system mimics the natural insertion of natural tooth roots in alveolar bone. Ligaplants become firmly integrated without interlocking and without direct bone contacts, despite the initial fitting being loose in order to spare the PDL cell cushion. Bone formation was induced and movements of ligaplants inside the bone suggesting an intact tissue communication between bone and the implant surface[5].

DISADVANTAGES OF LIGAPLANTS

The culturing of ligaplants should be cautious about the temperature, the obtained cells that used for culturing, the duration of the culturing and others. If some problem evokes during the culturing, the ligaplants may fail as other non-periodontal cells may develop. Besides that, with limited facilities and members to perform this research, the cost of this type of implant is high. The factors affecting the host to accept the implant or the growth of PDL in the socket is unpredictable, which may result in failure of implant.

CONCLUSION

Ligaplants as tooth replacement has decisive advantages as compared with osseosintegration devices, due to their periodontal tissue regeneration. The ligaplants surgery is relatively easy, because the implant is not tightly fitted to its site. Besides that, patient may not have to undergo bone grafting, inconvenience and discomfort with the ligaplants placement.

REFERENCES

1. Gomez Flores M, Hasegawa M, Yamato M, Takagi R, Okano T, Ishikawa I. Cementum-periodontal ligament complex regeneration using the cell sheet technique. *J Periodont Res* 2008. **43**, 364-371
2. Devlin, H. & Sloan, P. Early bone healing events in the human extraction socket. *International Journal of Oral maxillofacial Surgery* 2002. **31**, 641-645
3. Mizuno, H., Hata, K., Kojima, K., Bonassar, L. J., Vacanti, C. A. & Ueda, M. A novel approach to regenerating periodontal tissue by grafting autologous cultured periosteum. *Tissue Engineering* 2006. **12**, 1227-1235
4. Gay, I. C., Chen, S. & MacDougall, M. Isolation and characterization of multipotent human periodontal ligament stem cells. *Orthodontics and Craniofacial Research* 2007. **10**, 149-160
5. Gault P, Black A, Romette J-L, Fuente F, Schroeder K, Brune T, Berdal A, Wurtz T. Tissue-engineered ligament: implant contructs for tooth replacement. *J Clin Periodontol* 2010. **37**, 750-758
6. Shionhara, J., Shibata, T., Shimada, A. & Komatsu, K. The biomechanical properties of the healing periodontium of replanted rat mandibular incisors. *Dental Traumatology* 2004. **20**, 212-221
7. Yamada, H., Maeda, T., Hanada, K. & Takano, Y. Re-innervation in the canine periodontal ligament of replanted teeth using an antibody to protein gene product 9.5: an immunohistochemical study. *Endodontics and Dental Traumatology* 1999. **15**, 221-234
8. Maeda, T. The regeneration of the periodontal Ruffini endings. *Journal of Oral Tissue Engineering* 2004. **1**, 2-18
9. Seo, B. M., Miura, M., Gronthos, S., Bartold P, M., Batouli, S., Brahim, J., Young, M., Robey, P. G., Wang, C. Y. & Shi, S. Investigation of multipotent postnatal stem cells from human periodontal ligament. *Lancet* 2004. **364**, 49-55
10. Sonoyama, W., Liu, Y., Fang, D., Yamaza, T., Seo, B. M., Zhang, C., Liu, H., Gronthos, S., Wang, C.Y., Shi, S. & Wang, S. Mesenchymal stem cell-mediated functional tooth regeneration in swine. *PLoS One* 2006. **1**, e79
11. Ripamonti, U. Recapitulating development: a template for periodontal tissue engineering. *Tissue Engineering* 2007. **13**, 51-71
12. Malekzadeh R, Hollinger JO, Buck D, Adams DF, McAllister BS. Isolation of human osteoblast-like cells and in vitro amplification for tissue-engineering. *J Periodontol* 1998. **69**, 1256-1262
13. Kojima K, Bonassar LJ, Roy AK, Mizuno H, Cortiella J, Vacanti CA. A composite tissue-engineered trachea using sheep nasal chondrocyte and epithelial cells. *FASEB J* 2003. **17**, 823-828
14. Zweers MC, Schalkwijk j, van Kuppevelt TH et al. Transplantation of reconstructed human skin on nude mice: a model system to study expression of human tenascin-X and elastic fibre components. *Cell Tissue Res2005.* **319**, 279-287
15. Yaszemaki MJ, Payne RG, Hayes WC, Langer R, Mikos AG. Evolution of bone transplantation: molecular, cellular and tissue strategies to engineer human bone. *Biomaterials* 1996. **17**, 175-185
16. Wikesjo, U. M., Huang, Y. H., Polimeni, G. & Qahash, M. Bone morphogenetic proteins: a realistic alternative to bone grafting for alveolar reconstruction. *Oral and Maxillofacial Surgery Clinics of North America* 2007. **19**, 535-551
17. Sennerby, L., Rocci, A., Becker, W., Jonsson, L., Johansson, L. A. & Albrektsson, T. Short- term clinical results of nobel direct implant: a retrospective multicenter analysis. *Clinical Oral Implants Research* 2008. **19**, 219-226
18. Ekfeldt, A., Eriksson, A., & Johansson, L., A. Peri-implant mucosal level in patients treated with implant-supported fixed prostheses: a 1-year follow-up study. *International Journal of Prosthodontics* 2003. **16**, 529-532
19. Phileppe C. Gault & Waroquier-Clerout, R.Tooth auto-transplantation with double periodontal ligament stimulation to replace periodontslly compromised teeth. *Journal of Periodontology* 2002. **73**, 575-583
20. Giuseppe Polimeni, Andreas V. Xiropaidis & ULF M. E. Wikesjo. Biology and principles of periodontal wound healing/ regeneration. *Journal of Periodontology* 2000. **41**, 30-47
21. Pinkerton M N, Wescott DC, GaffeyBJ, Beggs KT, Milne TJ, Meikle MC. Cultured human periodontal ligament cells constitutively express multiple osteotropic cytokines and growth factors, several of which are responsive to mechanical deformation. *J Periodont Res* 2008. **43**, 343-351
22. Yoshizawa, T., Takizawa, F., Iizawa, F., Ishibashi, O., Kawashima, H., Matsuda, A., Endo, N. & Kawashima, H. Homeobox protein MSX2 acts as a molecular defence mechanism for preventing ossification in ligament fibroblasts. *Molecular and Cellular Biology* 2004. **24**, 3460-3472
23. Gomez-Skarmeta, J. L., De la Calle-Mustienes, E. & Modolell, J. The Wnt-activated Xiro-1 gene encodes a repressor that is essential for neural development and downregulates Bmp-4. *Development* 2001. **128**, 551-560
24. Cheng, S. L., Shao, J. S., Charlton-Kachigian, N., Loewy, A. P. & Towler, D. A. MSX2 promotes osteogenesis and suppresses adipogenic differentiation of multipotent mesenchymal progenitors. *Journal of Biological Chemistry* 2003. **278**, 45969-45977
25. Yamada, S., Tomoeda, M., Ozawa, Y., Yoneda, S., Terashima, Y., Ikezawa, S., Saito, M., Toyosawa, S. & Murakami, S. PLAP-1/asporin, a novel negative regulator of periodontal ligament mineralization. *Journal of Biological Chemistry* 2007. **282**, 23070-23080