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A biphasic scaffold design combined with cell sheet technology for simultaneous regeneration of alveolar bone/periodontal ligament complex

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This study describes the design of a biphasic scaffold composed of a Fused Deposition Modeling scaffold (bone compartment) and an electrospun membrane (periodontal compartment) for periodontal regeneration. In order to achieve simultaneous alveolar bone and periodontal ligament regeneration a cell-based strategy was carried out by combining osteoblast culture in the bone compartment and placement of multiple periodontal ligament (PDL) cell sheets on the electrospun membrane. In vitro data showed that the osteoblasts formed mineralized matrix in the bone compartment after 21 days in culture and that the PDL cell sheet harvesting did not induce significant cell death. The cell-seeded biphasic scaffolds were placed onto a dentin block and implanted for 8 weeks in an athymic rat subcutaneous model. The scaffolds were analyzed by μCT, immunohistochemistry and histology. In the bone compartment, a more intense ALP staining was obtained following seeding with osteoblasts, confirming the μCT results which showed higher mineralization density for these scaffolds. A thin mineralized cementum-like tissue was deposited on the dentin surface for the scaffolds incorporating the multiple PDL cell sheets, as observed by H&E and Azan staining. These scaffolds also demonstrated better attachment onto the dentin surface compared to no attachment when no cell sheets were used. In addition, immunohistochemistry revealed the presence of CEMP1 protein at the interface with the dentine. These results demonstrated that the combination of multiple PDL cell sheets and a biphasic scaffold allows the simultaneous delivery of the cells necessary for in vivo regeneration of alveolar bone, periodontal ligament and cementum.

1. Introduction

Periodontitis is a common chronic inflammatory disease that results in degradation of the supporting tissues around teeth, which if left untreated, can lead to tooth loss [1]. Periodontal wound healing following conventional therapy results in repair by collagenous scar tissue and is accompanied by the apical migration of gingival epithelium between the gingival connective tissue and the root surface [2,3]. However, periodontal regeneration requires the formation of periodontal ligament fibers and the insertion of these fibers into newly formed cementum on the root surface, as well as reconstitution of the adjacent resorbed alveolar bone. To this end, dedicated surgical techniques have been developed in order to promote periodontal regeneration and the most widely utilized of these is based around the principles of Guided Tissue Regeneration (GTR) [4,5]. This technique utilizes barrier membranes to selectively promote the repopulation of the periodontal defect by cells capable of periodontal attachment regeneration (periodontal ligament cells, osteoblasts) on the root surface at the expense of those that do not (gingival epithelial cells). However, although this approach is conceptually sound and can be successful in ideal clinical scenarios, the clinical results have been unreliable and predictable regeneration remains elusive [2]. It may be hypothesized that a tissue engineering approach could be utilized to optimize the conceptually sound principles of GTR (selective cell population, space maintenance, wound stabilization) through the use of scaffolds that can deliver the various cells required for periodontal attachment formation to the anatomically desirable locations on the periodontal defect.

Akizuki et al. [6] have proposed a strategy whereby various periodontal cell sheets were applied onto the root surface in order to form new cementum and promote periodontal attachment [6–12]. This tissue engineering strategy involved the use of

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