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Regeneration of Alveolar Bone for Dental Implant

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Introduction

Regeneration of alveolar bone for dental implant remains a major issue, particularly for patients suffering from severe bone adsorption and irregular socket trauma. Recapitulating embryological development is becoming an attractive approach for engineer organ or three-dimensional tissues from stem cells. In this study, we aimed to develop an injectable "cartilaginous" graft with adequate mechanical resistance and ideal bone remodeling potential. The cartilaginous graft was composed of a particulate de cellularised cartilage matrix (PDCM), chondro genically primed bone mesenchyme stem cell (BMSC) bricks (CB), and enriched platelet-rich plasma (P) gel. In immunodeficient mice, we found that angiogenesis occurred quickly inside PDCM-CB-P constructs after implantation, thereby improving tissue survival and bone formation. In rabbit tibia bone defects around implants, we confirmed that CBs not only transformed into bone tissue rapidly, but also significantly promoted bone remodeling and replacement of PDCM, thus realizing osseointegration of dental implants within 3 months. In conclusion, CBs exhibited the potential for endochondral ossification *in vivo*, and application of a cartilaginous template composed of PDCM, CB, and P provided a minimally-invasive, "free material residual" approach to regenerate alveolar bone tissues *in vivo*. This method could have applications in peri-implant bone regeneration [1-3].

About the Study

Regeneration of alveolar bone for dental implants remains a major challenge, particularly for patients suffering from severe bone adsorption and irregular socket trauma. Despite the beneficial effects of solid bioceramics such as hydroxyapatite and beta-tricalcium phosphate, novel minimally-invasive, less immune-reactive substitutes are needed for complete remodelling alternatives to current therapies.

Although decellularised and demineralised bone matrices (DBMs) are effective bone reparative materials, these materials are produced xenogenically or allogeneically, and transmission of infectious microorganisms is a possibility that compromises clinical safety. Moreover, the dense native structure of DBMs reduces the efficiency of *in vivo* remodelling, including angiogenesis. Recapitulating embryological development is becoming an attractive approach for engineering organs or three-dimensional (3-D) tissues from stem cells. Endochondral ossification is the process through which BMSCs aggregate and chondrogenically differentiate, resulting in the formation of a cartilage template. Angiogenic and chemotactic factors are then excreted by transformed BMSCs and further attract host cells to remodel the mineralised cartilage into vascularised bone. For chondrogenic differentiation, harvesting BMSCs from bone marrow, and reconstituting them into cell macroaggregates may significantly enhance the efficiency of chondrogenic differentiation and has been widely studied for cartilage regeneration4. By benefitting from gap junction-mediated intercellular contacts and interactions between cell-extracellular matrices5, the chondrogenic differentiation of BMSCs in the aggregating model was significantly enhanced by exogenous growth factors as compared with that of solid scaffold-based cell transplants6. Therefore, the establishment of clinically applicable "developmental engineering" technology may provide a new approach for peri-implant bone regeneration.

The development of injectable cell macro aggregates may offer a micro-invasive and shapeable approach to alveolar bone regeneration, even for loading dental implants. For alveolar bone regeneration via injectable grafts, adequate mechanical resistance and rapid estrogenic remodeling remain challenges for peri-implant filling. Hydrogels enforced chemically or physically are therefore developed to provide a 3-D niche with enhanced toughness for seeding cells. However, *in vivo* behaviors remain less than satisfactory owing to inflammatory reactions, interior necrosis, and poor osseointegration. Blood clot-mediated socket bone healing has great potential for host remodeling, and platelets carrying multiple factors may play important roles in vascularization and host remodeling. Moreover BMSC-platelet-rich plasma (PRP) compounds exhibit significant bone forming potential in humans; however, contraction and intrinsic mechanical weakness still limit the applications of these materials. Attempts to reconstitute BMSC-PRP mixtures with solid bio ceramics, however, show reduced remodeling potential owing to the toughness and slow biodegradation of the materials. As alternatives to cell-plasma-bioceramic mixtures, "cartilaginous" grafts showing adequate mechanical resistance may show more potential for remodeling and clinical translation [4-5].

Conflict of Interest

The authors declare that there is no conflict of interest associated with this manuscript.

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