Synthetic Polymer-Calcium Phosphate Derived Scaffolds for Alveolar Bone Regeneration: Clinical Perspective

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Statement of Purpose: The repair of craniofacial bone defects often requires extensive and complicated surgery that involves the harvesting of autogenous bone from additional donor sites. After harvest, further manipulation of the explants is necessary to tailor fit them to the defect site. The high rate of complications and donor site morbidity associated with these procedures necessitates that advances be made in the field of synthetic biomaterials to solve this problem. The current commercially available bone graft materials require the use of biologics, most notably bone morphogenetic proteins (BMPs), in order to approximate the performance of autografts. To address this problem, macro and microporous scaffolds made from a degradable polymer (E1001(1k)) with a calcium/phosphate mineral phase have been developed within the Kohn Lab at the New Jersey Center for Biomaterials. These porous scaffolds are fabricated using a combination of solvent casting and porogen leaching. The various types of mineral phases can be embedded directly into the polymer matrix or coated on the polymer surface. These scaffolds have been developed and tested extensively at NJCBM with *in vitro* and *in vivo* data supporting their osteoconductivity. With the help of our collaborators from the Yelick Lab at Tufts University, we have demonstrated the regenerative potential of human dental stem cell seeded E1001(1k) scaffolds for *in vivo* repair of critical sized rat mandibular ramus defects. This study has provided the validation and foundation for our continued work and planned scale up of this therapy to medium and larger sized animal models.

Methods: In preparation for scale up to medium sized animal models we have designed new tyrosine-derived polycarbonate (E1001(1k)) scaffolds with the following dimensions:14mm long, 10mm deep, and 8mm wide. These scaffolds were fabricated using Teflon molds and a trimming tool to prepare reproducible and consistent implants. The fabricated guide tool is used to trim the scaffolds to the correct dimensions prior to salt leaching. This process has been reproduced within the Kohn lab for use in several *in vivo* studies to produce scaffolds of varying shapes and size. In addition, our newest designs include the development of reservoirs within these scaffolds using a drill press to a specific depth and size intended to house titanium dental implants as well as cell encapsulating hydrogels for the purpose of simultaneous dental tissue regeneration.

Results: In the critical sized rat mandibular defect model, CT data revealed significant alveolar bone formation after implantation of human dental pulp cell seeded E1001(1k) scaffolds after 6 weeks of implantation in the mandibular angle. The following data in Figure 1 demonstrates the bridging of the 5mm rat critical sized defects.

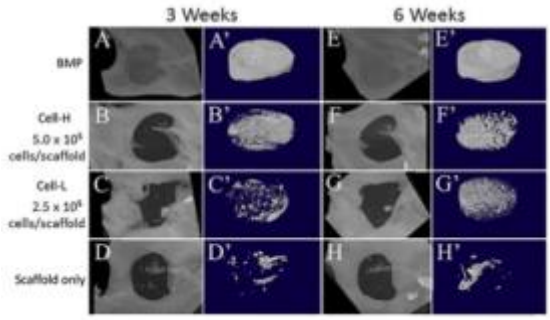

Figure 1. CT evaluation of mandibular bone formation of human DPs cells E1001(1k) constructs compared to BMP loaded and bare scaffolds. (Zhang et al, 2016.)[1]

These animal surgeries performed at Tufts University provided the basis for further exploration of E1001(1k) polymer scaffolds for alveolar bone regeneration. Scale up of these scaffolds is underway (as evidenced in figure 2), in order to demonstrate their effectiveness in a more representative clinical model.

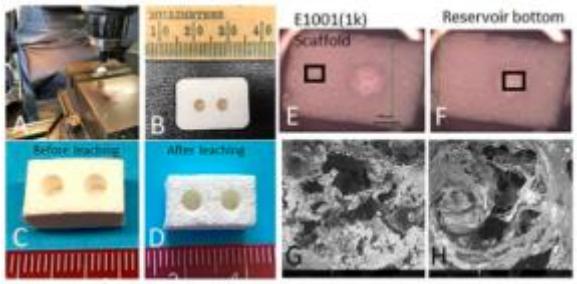

Figure 2. Scale up of porous scaffolds with machined reservoirs. SEM imaging of the bottom of the reservoirs was performed and displayed minimal deformation of the pore structure.

Conclusions: The regenerative capacity of porous E1001(1k)/CaP scaffolds have been demonstrated by extensive *in vitro* and *in vivo* testing between the Yelick and Kohn Laboratories. We are currently working to optimize the material properties and scale up of these scaffolds with the intent of moving to larger animal models. Additional studies are underway to determine the ideal integration of the calcium phosphate mineral phase as well as the most appropriate scaffold architecture to regenerate craniofacial defects.

References: The authors would like to especially acknowledge the following persons: Shuang Chen, Maria Hanshella, Ophir Ortiz, Maziar Shah Mohammadi from NJCBM for their work in scaffold development. As well as, our collaborators from Tufts University: Pamela Yelick and Weibo Zhang for their expertise and continued innovation in tooth and alveolar bone regeneration.

1. Zhang, W., Zhang, Z., Chen, S., Macri, L, Kohn, J., Yelick, P.C., 2016. Mandibular Jaw Bone Regeneration Using Human Dental Cell-Seeded Tyrosine-Derived Polycarbonate Scaffolds. Tissue Eng Part A 22, 985-993.