Mineralized Synthetic Polymer Scaffolds for Jaw Bone Tissue Regeneration

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Statement of Purpose: There is an unmet clinical need to improve the available methods to repair craniofacial jaw bone and tooth defects. A multidisciplinary bioengineering approach is required to come up with clinically relevant therapies in humans. Currently available FDA approved bone substitutes like NanoBone from Artoss, chronOS from DePuy, Puros from Zimmer, Bio-Oss from Geistlich are based on hydroxylapatite embedded in silica gel, beta-tricalcium phosphate, Allogenic (cadaver) and Xenogenic (Bovine), respectively. But none of the device outperform the rest in the market. With the collaborative effort between Kohn Lab at the New Jersey Center for Biomaterials (NJCBM) and Yelick Lab at Tufts University we are able to develop macro and microporous scaffolds made from a degradable polymer (E1001(1k)) with a calcium/phosphate mineral phase at NJCBM and test the regenerative potential of human dental stem cell seeded E1001(1k) scaffolds for repair of critical sized mandibular defects. This study is highly innovative and utilizes novel approach to bioengineer composite bone and planned scale up to medium and larger sized animal models.

Methods: Highly porous, tissue engineering scaffolds were prepared using E1001(1k) with and without calcium phosphates (e.g., β-TCP) by a combination of freeze-drying, porogen leaching and phase separation techniques. E1001(1k) tyrosine-derived polycarbonate terpolymers as a tunable class of polymers that have good engineering properties while also being resorbable *in vivo* (Lewitus et al. 2011)[1]. We also tested the biocompatibility of E1001(1k) scaffolds for human dental pulp stem cells (hDPSCs), by examining *in vitro* cultured scaffolds seeded with hDPSCs. The scaffolds were of following dimensions: 5mm diameter and 1mm thickness. Standard operating procedures (SOPs) on scaffold fabrication were developed.

Results: The resulting scaffolds (see Figure 1) exhibited >90% porosity, and displayed: 1) a bimodal pore distribution (micropores <20μm, macropores 200-400μm); 2) a highly interconnected and open pore architecture; 3) a highly organized microstructure where the micropores are oriented and aligned along the walls of the macropores; and 4) pore size range and architecture resembling trabecular bone.

Whole mount fluorescence actin staining *in vitro* cultured constructs showed excellent hDPSC viability, scaffold attachment, spreading and infiltration throughout the macropores and micropores of the scaffold (see Figure. 2). Based on these promising results, we next tested the ability for hDPC seeded E1001(1k)-β-TCP scaffolds to support alveolar bone formation in a critical sized rat mandibular ramus defect.

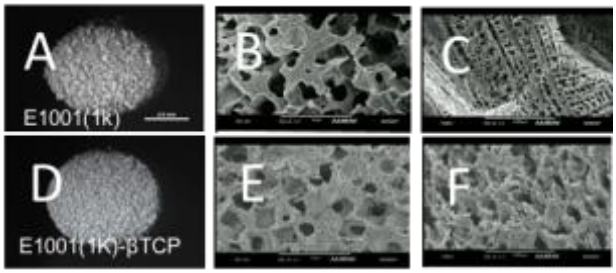

Figure 1. Tyrosine-derived polycarbonate (TyrPC) scaffolds. (A-C) E1001(1k) scaffolds. (D-F) E1001(1k)/ β-TCP scaffolds.

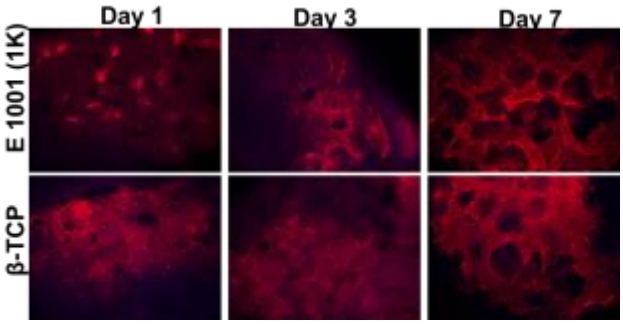

Figure 2. Human dental pulp cells cultured in vitro on E1001 (1k) polymer scaffolds.

Conclusions: Tissue engineering scaffolds based on E1001(1k)/CaP showed interconnected ultra large macropores and micropores ideal for vascular ingrowth and proliferation of cells. The scaffolds possessed hierarchical structure and biocompatibility suitable for cell growth as demonstrated by in vitro study with human dental pulp stem cells (hDPSCs). Additional studies are being performed to incorporate different calcium phosphate mineral phase as well as to scale up the study to large animal models.

References:

1. Lewitus, D., Smith, K.L., Shain, W., Kohn, J., 2011. Ultrafast resorbing polymers for use as carriers for cortical neural probes. Acta Biomater. 7(6), 2483-2491.