Hierarchically porous Slit3-releasing Composite Scaffold for Bone Tissue Engineering

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Statement of Purpose: This research concerns development of novel three-dimensional, highly porous, and interconnective scaffolds with high osteogenesis and angiogenesis properties for bone tissue engineering. Currently, autologous and allogeneic bone grafts are the mainstream strategy for the treatment of large bone defects. However, these strategies are limited because of their high cost, risk of infection and inflammation, low availability. Developing artificial scaffolds has been being a promising strategy to support defected sites and promote bone recovery. The optimum bone scaffold should be biocompatible, biodegradable, with comparable porosity, mechanical stiffness, and interconnectivity to the natural tissue. However, such an Ideal platform has not been achieved due to several limitations of the currently used biomaterials and fabrication techniques[1].

Methods: The scaffold platform will be a composite biomaterial of Poly(lactic-co-glycolic acid) polymer (PLGA) and hydroxyapatite Nanoparticles (n-HA). This composite demonstrates good mechanical properties and outstanding ability to enhance bone regeneration [2]. Moreover, the composite matrix will be coated with the slit3 protein, which plays a significant role in the osteogenesis and angiogenesis processes around H-type blood vessels in bone tissues. Slit3 is hypothesized to trigger the growth of blood vessels, stimulate osteoblast migration and proliferation, and suppress bone resorption [3]. The scaffold will be synthesized using solvent casting and particulate leaching method on a 3D printed removable mold. The mold will be designed to form macropores within the platform (~ 500 µm), while the SCPL will be optimized to create micropores (~ 80 µm). Scaffold's structural, mechanical, physicochemical properties will be assessed using AFM, SEM, XPS, EDX, Strain-stress mechanical test, and water contact angle goniometer. Also, the biological performance of the proposed scaffold will be evaluated by testing its cytotoxicity, angiogenesis, and osteogenesis of the scaffolds will be assessed via MTT, alkaline phosphatase activity (ALP), and the tube formation assays.

Results: As shown in figure 1, we have developed a scaffold based on polycaprolactone (PCL), montmorillonite nanoclay, and nano-hydroxyapatite-clay fibers using a pressurized gyration (PG) method. This biocompatible scaffold demonstrated high cell viability and bone growth enhancement. Here, we aim to produce a biodegradable 3D structure, with controllable porosity, and use it as a protein-releasing platform to enhance bone regeneration.

Conclusion: This work is expected to result in a controllable method to fabricate 3D scaffolds for bone tissue engineering applications. Also, this work will be the first work that focuses on employing H-vessels-related signaling mediators within scaffolds to accelerate the healing of large bone defects.

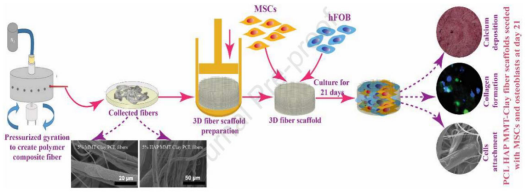

Figure 1. Nanoclay-hydroxyapatite-PCl fiber scaffold for bone tissue engineering manufactured using pressurized gyration.

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