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Materials Science and Engineering
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PhD Proposal

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Osteoblasts response to surface properties of mineralized nanofiber shish kebab templates

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Bone tissue engineering has attracted wide attention as more than 500,000 bone graft procedures are performed annually. Critical bone defects, usually greater than 5 mm, require bone grafts for such as autografts, allografts, and xenografts. Even though each of these methods has shown successful bone regeneration, they have their own disadvantages including limited availability and donor site morbidity for autografts and biocompatibility issues for allografts and xenografts. A current strategy that is widely explored is use of synthetic scaffolds. The ideal bone scaffold is bioactive by harnessing the cell's ability from the host to regulate osteogenesis and must be biocompatible. However, it remains a challenge to use synthetic materials to replicate the nanoarchitecture of natural bones.

Bone is a highly organized structure that ranges from nano to macro scale. In fact, there are seven hierarchically structures that make up bone. This project proposes to design a novel synthetic bone scaffold that mimics the natural structure of bone on levels 1-4. The first structure of bone is the sequence of amino acids forming polypeptide chains. The second level is a triple helix structure formed by three polypeptide chains coiled together called tropocollagen. In the third level, multiple tropocollagen are assembled and staggered creating gap zones, which are mineralized with hydroxyapatite, forming mineralized fibers. The fourth level is an array of mineralized fibril structure, in which osteoblasts directly interact with to secrete bone matrix. Upon an osteogenic environment, osteoblasts deposit collagen and mineralize the matrix. As a result, many scaffolds and templates have been molecular engineered to interact with osteoblasts to promote osteogenesis at this structural level.

One critical aspect involved to evaluate osteogenesis in bone tissue engineering is the ability to nucleate minerals and grow into hydroxyapatite crystals. The localization of cations and anions to a specific

interface leads to the initial nucleation of mineral deposition. The accumulation of ions allows the nucleated minerals to grow and form hydroxyapatite crystals. A promising strategy to replicate this mineral nucleation and growth *in vitro* is to use simulated body fluid (SBF). Previous studies have shown that immersion of a charged polymer in SBF can mimic this process. The charged polymer attracts the ions from the saturated SBF to provide a nucleation surface. This is followed by an accumulated mineral growth from the SBF solution. Previous studies have shown that amorphous calcium phosphate can be initially formed from SBF and eventually transitions into crystalline hydroxyapatite over time. However, one of the main challenges is to control the orientation and spatial distribution of mineralized hydroxyapatite crystals in an organized and periodic structure similar to that of bone.

I propose to evaluate the biomimetic bone scaffold/template that is able to nucleate minerals in a periodic manner *in vitro*. In this system, electrospun polycaprolactone (PCL) nanofibers, resembling collagen fibrils, can be crystallized into nanofiber shish kebabs (NFSK) with PCL-polyacrylic acid block copolymer chemistry (BCP). The PCL region of the BCP is crystallized onto the PCL nanofibers leaving an unbound negatively charged PAA region, which allows for mineralization in SBF. BCP NFSK will be synthesized to control the orientation and spatial distribution of hydroxyapatite during the mineralization process, which has not been currently done but is important as it can directly lead to controlled organic-inorganic interfacial area and mineral content. By controlling these parameters, mineralized NFSK have the potential to promote osteoblast differentiation and upregulate osteogenesis in bone defects.