Enhanced Mesenchymal Stem Cell Response on Biodegradable Poly(ε-Caprolactone) Nanowires for Applications in Bone Tissue Engineering

Porter, JR[1]; Popat KC[1]

[1]School of Biomedical Engineering, Department of Mechanical Engineering, Colorado State University, Ft. Collins CO, USA

Statement of Purpose: Critical sized defects in bone, whether caused by tumor resection, trauma, or implant surgery have presented insurmountable challenges to the current gold standard treatment for bone repair. Tissue engineered scaffolds offer promise in addressing these challenges and have been increasingly sophisticated and multifunctional since their inception about 15 years ago.[1] The primary purpose of a tissue-engineered scaffold is to incite and promote the natural healing process of bone which typically does not occur in critical sized defects. Further, the scaffold must be biocompatible and biodegradable to allow native tissue integration, and the scaffold should mimic the micro/nano-hierarchical geometric structure of native bone. Several recent studies have shown enhanced bone cell response to controlled micro/nano-architecture[2, 3] In addition to being biomimetic, a scaffold that is capable of eluting bioactive molecules (eg. BMPs, TGF-b, etc. to accelerate extracellular matrix production and tissue integration) or drugs (eg. antibiotics, cisplatin, etc. to prevent undesired biological response such as sepsis or cancer recurrence) in a controlled and sustained manner is highly desired. Various FDA approved polymers have been investigated for scaffold materials due to their tuneable mechanical properties, enhanced biocompatibility, and controllable biodegradability. In this work, we present a simple, solvent-free method for template synthesis of micro-aggregated nanowire surfaces from poly(ε-caprolactone) (PCL). Cell studies using a pre-osteoblast cell line indicates that these nanowire surfaces are cytocompatible and enhance cell functionality. Further, degradation and release rate studies indicate that these surfaces show promise for controlled drug delivery applications. More detailed studies are now directed towards using mesenchymal stems cells (MSCs) and characterizing the release of relevant bioactive molecules.

Methods: PCL substrates were melted on commercially available alumina membranes (ANOPORE™) at 65°C to form micro-aggregated nanowire surfaces. The nanowire templates were released by dissolving the membrane in NaOH. Preliminary cell viability was assessed using the mouse pre-osteoblast cell line MC3T3. Short-term studies (7 days) were conducted to evaluate cytocompatibility, adhesion, and proliferation of cells on these surfaces. Long-term studies (4 weeks) were conducted to asses the ability of these surfaces to enhance phenotypic behavior of the cells. Enzymatic and hydrolytic degradation as well as bioactive molecule release studies were conducted to assess the potential of these surfaces in controlled drug delivery applications.

Results: Micro-aggregated nanowire surfaces were fabricated using a simple solvent-free temple synthesis. **Fig. 1** shows an SEM image of the PCL nanowire surface. Cell studies indicated that the nanowire surfaces are cytocompatible, and promote adhesion and proliferation of the MC3T3 cell line. **Fig. 2** shows SEM image of MC3T3 cells after 1day (left) and 7 days (right) of culture on nanowire surfaces. The flattening and spreading of the cell seen from day 1 to day 7 indicates favorable phenotypic behavior. Since PCL is biocompatible, biodegradable, highly crystalline and has a low melting temperature, is has been investigated for melt encapsulation and release of bioactive molecules.[4] Enzymatic and hydrolytic degradation as well as release studies indicate that nanostructured PCL surfaces were capable of sustained release of biomolecules over the course of the study. **Fig. 3** shows the daily non-cumulative concentration of bovine serum albumin (model biomolecule) in PBS released from the nanowire surfaces for up to 7 days. Further studies are now directed towards using MSCs and more relevant bioactive molecules.

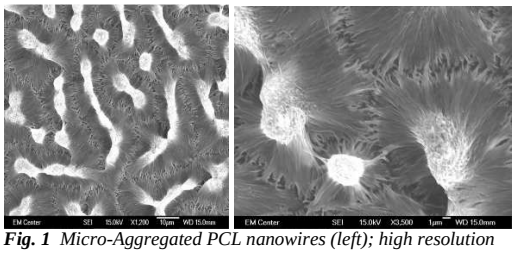

Fig. 1 *Micro-Aggregated PCL nanowires (left); high resolution SEM of nanowires (right)*

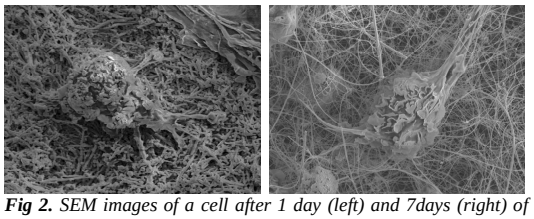

Fig 2. *SEM images of a cell after 1 day (left) and 7days (right) of culture on PCL nanowire surfaces.*

Conclusions:

In this study, we have demonstrated that PCL nanowire surfaces can be used as a favorable template for bone cell adhesion, growth, and differentiation. Further, these surfaces may also be used for controlled and sustained delivery of biomolecules and drugs.

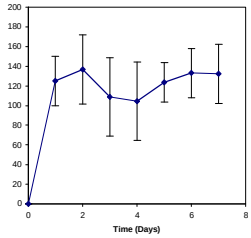

Fig. 3 *Albumin released from PCL nanostructured surface*

References:

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