CENTER *for* APPLIED MOLECULAR MEDICINE

University of Southern California Physical Sciences in Oncology Center

2015 Monthly Seminar Series

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"Biomechanical Modeling of Decellularized Liver Perfusion"

FRIDAY, MAY 29, 2015

NOON - 1:00 P.M.

Q & A to follow

PIZZA AND BEVERAGES WILL BE SERVED FOR ATTENDEES AT 11:45 A.M.

HARKNESS AUDITORIUM

HSC - Clinical Sciences Building, **2nd Floor**
2250 Alcazar Street, Los Angeles, CA

ABSTRACT:

Regenerative medicine has the potential to alleviate severe donor organ shortages for patients with end-stage liver failure. Bioengineered liver constructs could also serve as test platforms for pharmaceutical research, liver disease, metastasis, and development. Organ decellularization, a promising bioscaffolding technique, is the removal of all cellular components from an organ leaving behind intact extracellular matrix (ECM). Since the vasculature is retained, decellularized scaffolds have the potential to generate bioengineered liver constructs at the whole-organ scale. Scaffold perfusion through a cannulated portal vein generates a variety of mechanical forces that act across multiple length scales, from pressure and shear stress in vascular channels to interstitial flow and ECM tension in the parenchyma. Since many liver cell types, including hepatic stem/progenitor cells, hepatocytes, endothelial cells, stellate cells, cholangiocytes, and portal fibroblasts, are sensitive to mechanical stimuli, we hypothesize that providing optimal biomechanical conditions inside the scaffold is important for successful generation of viable tissue.

Currently little is known about the biomechanical environment in decellularized tissue. The goal of this research is to quantify the mechanical microenvironment in decellularized liver, for varying organ-scale perfusion conditions, using a combined experimental/computational approach. Needle-guided ultra-miniature pressure sensors were inserted into liver tissue to measure parenchymal fluid pressure ex-situ in portal vein-perfused native (n=5) and decellularized (n=7) ferret liver, for flow rates from 3-12 mL/min. Pressures were also recorded at the inlet near the portal vein cannula. Experimental results were fit to a multiscale computational model to simulate perfusion conditions inside native versus decellularized livers for all flow rates. The multiscale model consists of two parts: an organ-scale electrical analog model of liver hemodynamics and a tissue-scale model of pore fluid pressure, pore fluid velocity, and solid matrix stress throughout a 3D hepatic lobule. Distinct models were created for native versus decellularized liver. Results show that vascular resistance decreases several fold as a result of decellularization. Similarly, the hydraulic conductivity of decellularized liver, a measure of tissue permeability, was approximately 5 times that of native liver. In future this modeling platform can be used to guide the optimization of biomechanical conditions in decellularized scaffolds for liver bioengineering.

Funded by:
NCI/NIH 5U54CA143907-05

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