



Lecture Series Seminar

ENGINEERED HEART VALVE TISSUE FORMATION BY BONE MARROW DERIVED STEM CELLS UNDER PHYSIOLOGIC PRESSURE ENVIRONMENTS

Tuesday October 20th, 2009

10:00 am, EC 2300

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Important steps towards clinical applicability of tissue engineered pulmonary valves (TEPVs) are practical cell sources and rapid, robust tissue formation. To achieve this, appropriate *in vitro* mechanical conditioning of TEPVs may be necessary prior to implantation to promote optimal tissue growth. Ovine bone marrow derived stem cells (BMSCs) were isolated and expanded from neonatal sheep. To form the valve geometry, non-woven 50:50 blend, mesh of polyglycolic acid (PGA) and poly-L-lactic acid fibers (PLLA) was cut into three leaflets that were subsequently sewn onto a stent. Scaffold seeding was performed by immersing the TEPV into a hybridization tube for 3 weeks. Two valves (six leaflets) were cultured for an additional 3 weeks in this manner while another two valves were placed in a pulsatile, organ-level bioreactor for dynamic conditioning for 3 weeks. The pressure condition in the system was set to a physiological mean value of 20 mmHg. Significantly higher collagen formation ($P < 0.05$) was observed in the dynamically conditioned groups over static controls. In addition, the DNA content was preserved beyond the initial 3 week culture period when dynamic conditioning was performed. The effect of physiologic pressure environments increased the collagen production rate from 4.76 to 6.42 pg/cell/week (35%). Small strain levels on the scaffold leaflets (< 7%) demonstrated that fluid-induced shear stresses were the dominant stimulatory mechanism for tissue formation. Concomitantly, in computational models, we were able to identify temporal fluctuations in the primary flow direction across specimens. We thus hypothesize that oscillatory shear stresses may play a dominant stimulatory role in the formation of engineered heart valve tissue by BMSCs.

Sharan Ramaswamy pursued doctoral studies in Biomedical Engineering at the University of Iowa, focusing on cardiovascular mechanics. After completing his PhD, Dr. Ramaswamy engaged in post-doctoral research at the NIH in cartilage tissue engineering and the use of MRI as a means to assess/characterize engineered tissue development and cell fate non-invasively. In early 2007, Dr. Ramaswamy took up a research faculty position at the University of Pittsburgh's department of bioengineering, and is affiliated with the McGowan Institute for Regenerative Medicine, where he currently works. His immediate research interests include: heart valve tissue engineering, cardiovascular biomechanics, MRI-based methods for monitoring tissue engineered constructs, CFD modeling in engineered tissue growth studies and bioreactor design/development. He is pleased to be joining FIU's BME department as an Assistant Professor soon.