THE HARTWELL FOUNDATION

2009 Individual Biomedical Research Award

Review of Proposed Research

Investigator: **Jonathan T. Butcher, Ph.D.**
Assistant Professor
Departments of Biomedical Engineering

Institution: **Cornell University**

Proposal: **Anatomically Precise Engineered Living Valved Conduits for Pediatric Applications**

Dr. Butcher proposes an innovative tissue engineering approach to heart valve replacement that will accurately mimic patient-specific 3D anatomy, intrinsic tissue requirements, and sustainable growth. During each pumping cycle of the human heart, four valves ensure that blood flows productively and that there is no backward leakage. Abnormalities in valve anatomy, particularly the aortic valve, may cause insufficient blood flow to the body and undue stress on the heart muscle, which unattended can lead to congestive heart failure. Pediatric heart valve disease occurs in approximately 1% of all live births and is the most common congenital anomaly of the heart contributing to death in infants and children. Prosthetic valve replacement (human tissue, animal tissue or mechanical) is the only option. Greater than 100,000 heart valve surgeries are performed in the United States each year (about 15% of all heart surgeries) and the number performed continues to grow. Bioprosthetic valves are unable to grow with the child and can degrade over time, frequently necessitating resurgery; and mechanical valves necessitate lifelong risk of anticoagulation therapy. One alternative (Ross procedure) is to transfer the patient's own living pulmonary valve into the aortic position and implant a prosthetic valve in the less demanding pulmonary position. While the Ross procedure meets requirements for growth of the aortic valve, absence of anticoagulant therapy or tissue antirejection medications, the risk of either valve failing later in life is significant. Thus, there remains an especially critical and unmet need for an aortic valve replacement for children suffering from congenital valve defects. Dr. Butcher proposes a systematic approach to construct a living valve replacement that is designed specifically for the anatomical and mechanical requirements of each patient. He intends to combine imaging *in vivo* and 3D tissue printing of the required valve, followed by natural physical conditioning of the construct. If successful, he envisions meeting the changing growth requirements of a child by implanting a temporary scaffold that will perform mechanically as a functioning valve the instant it is inserted; a scaffold that will degrade non-toxically as the patient's own tissue cells migrate into it and differentiate, secreting the required extracellular matrix to reconstitute what will become a naturally growing valve. His hope is that these innovations will lead to a surgical intervention without substantial risk; one that can resolve heart valve disease, without imposing lifestyle limitations to the recipient.