Program in Tissue Engineering

Jason Wertheim, MD, PhD

The overreaching goal of the Northwestern University Comprehensive Transplant Center’s Program in Tissue Engineering is to advance the state of the art in organ regeneration to develop a small animal model capable of supporting a tissue engineered organ for an extended period of time. The Northwestern University Comprehensive Transplant Center recognizes the seriousness of the organ shortage dilemma and is investigating cutting-edge solutions to this problem. Nationally 112,045 patients are waiting for solid organ transplantation, yet the number of transplants performed annually falls short of this need by 75%. In the absence of suitable donors for solid organ transplantation, organ failure leads to associated health problems, increased health care expenditures and death. Organ shortage is a national issue with local impact. Last year there were just over 1,050 solitary kidney, liver, or heart transplants performed in Illinois yet 311 patients died in the state alone, and more than 6,650 nation-wide, waiting for an organ.

Our research proposes a multidisciplinary solution to the organ shortage by utilizing a tissue engineering approach to rehabilitate the extracellular matrix (ECM) of these unusable organs. Just-in-time organs, reconstituted with recipient derived progenitor cells, would abrogate the need for long waitlist times and associated waitlist mortality, reduce the reliance on organs from living donors, and obviate the need for immunosuppression. Conceptually, these organs would be prepared from a donor matrix using a recipients own cells at the first signs of organ dysfunction. The re-engineered organ would then be ready for implantation when progressive organ failure indicates the need for transplantation.

The traditional paradigm in tissue engineering has been to grow cells on synthetic, polymer scaffolds to recreate the organ or tissue of interest. The limitation of this approach is the scale-up to thicknesses over 100 micrometers. Beyond this, diffusion of nutrients and oxygen is not sufficient to support cellular life, and a vascular system must be incorporated into the tissue to supply nutrients. It has been technically difficult to design a synthetic micro-vasculature resembling small, terminal capillaries and to combine these structures with functional cells. Our approach challenges this paradigm by using the natural ECM as a scaffold to support the growth of new cells capable of repopulating and rehabilitating a scarred organ. Together we have partnered with the McCormick School of Engineering at Northwestern University, Wake Forest Institute for Regenerative Medicine, the University of Pittsburgh and Cellular Dynamics International, a leader in high-volume production of human induced pluripotent stem cells.

Though human trials are years away, we have begun initial, proof-of-principle studies using rat kidneys, livers and hearts. More than 99% of DNA is removed from the matrix as determined by real-time PCR. Hematoxylin and eosin staining and electron microscopy of decellularized kidneys show large spaces where cells once occupied. After decellularization, the next step in the production of engineered kidneys is to incorporate endothelial cells and renal parenchyma cells into the kidney matrix. Preliminary studies from our group suggest that decellularized rat kidney scaffolds can be repopulated with human endothelial cells derived from induced pluripotent stem cell technology (Figure). The key personnel in the Comprehensive Transplant Center working on this project are Drs. Michael Abecassis, Jason Wertheim, Jenny Zhang, and Mireia Caralt. We are actively looking to hire research associates to be a part of the Tissue Engineering Laboratory. For more information, to become part of the laboratory or to collaborate please contact Dr. Jason Wertheim (jwerthei@nmh.org).