THE HARTWELL FOUNDATION

2017 Individual Biomedical Research Award

Robert R. "Bob" Redfield, MD

Assistant Professor
Department of Surgery

University of Wisconsin-Madison

Genetically Engineered Porcine Islets for the Treatment of Type 1 Diabetes

Type 1 Diabetes (T1D), one of the most common chronic childhood diseases affects roughly 200,000 children in the U.S. and will affect an estimated 600,000 children by 2050. T1D occurs when the body's immune system destroys insulin-producing cells of the pancreas, known as pancreatic islets. Insulin injections allow children with T1D to stay alive, but the injections do not cure the disease or prevent its serious effects, including kidney failure, blindness, nerve damage, heart attack, and stroke. Therapies that have the capacity to address the disease itself are urgently needed. Transplantation of human islet cells or a solid pancreas is the current standard of care for select patients with T1D. These treatments, however, have two significant limitations: the requirement for long-term immunosuppression (medications required to prevent rejection) and the limited availability of pediatric human donor organs. Due to these barriers, only 1,000 patients per year in the U.S. undergo pancreas transplantation. Swine, however, may represent a limitless and compatible source of pancreatic islets if they can be genetically engineered to enable their transplant into humans without immunosuppression. To meet this need, Robert proposes to genetically edit Wisconsin Miniature Swine™ (bred to have organs similar to size of children) by engineering the animals to lack critical gene products recognizable by the human immune system, which will facilitate both solid organ and islet transplantation. Using CRISPER technology, He will genetically delete four genes that are critical for the human immune system to recognize swine cells as foreign by human T-lymphocytes. For each of the four genes, using the sequenced swine genome as the template, he will design CRISPR guided RNAs (gRNA) to target desired regions of the gene. To avoid the introduction of foreign genetic material (i.e., non-human and non-swine), gRNA/Cas9 complexes will be used for subsequent transfection. He will determine if the engineered swine islets regulate insulin production and are protected from immune-surveilance in a non-human primate model (diabetic rhesus macaque). If Robert is successful in demonstrating the engineered swine islets can be transplanted into non-human primates without immunosuppression and the monkeys can achieve long-term insulin independence, a limitless supply of pancreatic islets will exist for treating T1D in children. The creation of a genetically engineered swine will also make it possible to perform other solid organ transplants, such as renal transplants for children with end-stage renal disease.