THE HARTWELL FOUNDATION

2010 Individual Biomedical Research Award

Review of Proposed Research

Investigator: **Pamela Itkin-Ansari, Ph.D.**
Assistant Professor
Departments of Pediatrics

Institution: **University of California, San Diego**

Proposal: **Novel Approaches to Improving Survival of Encapsulated Islets for the Treatment of Juvenile Diabetes**

The requirement for multiple blood glucose measurements each day and insulin injections in type-1 diabetes creates a special challenge in the management of the disease for children and adolescents, along with a large financial burden on affected families. About 1 in 400 children in the US have juvenile or type-1 diabetes and for reasons that are not entirely clear, the incidence of the disease is rising. By proposing a safe, minimally invasive and effective human islet transplantation therapy for children that does not require immunosuppression, she offers an innovative solution to ending the illness and the emotional toll of the disease. In juvenile diabetes insulin producing β-cells in pancreatic islets are destroyed by the patient's own immune system. Unfortunately, periodic administration of insulin in response to elevated glucose is not sufficient to prevent the serious medical consequences of this disease. Islet transplantation into the liver has been evaluated as a diabetes therapy in adults. However, it is considered too risky for children because transplant patients must take potent drugs to suppress the immune system for the rest of their lives. In 2009, Pamela reported in a mouse model of type-1 diabetes that an innovative encapsulation device could hide mouse islets from the destructive effects of the immune system and importantly, could be used to successfully treat the disease without reliance on immunosuppressive drugs. The encapsulated islets functioned well when placed just under the skin and continued to secrete insulin in response to a glucose load. To overcome the high sensitivity of the human islets to the low oxygen environment during transplantation, which typically is known to cause many of the cells to die, she proposes to optimize survival of encapsulated human islets by providing a medically approved oxygen carrying agent that can be loaded into the device with the islets. She intends to maintain the supply of oxygen to transplanted cells indirectly, by using a new class of drugs to accelerate blood vessel formation around the encapsulation device. If she is successful, her encapsulated cell technique will not require tissue matching and will not have a requirement for immunosuppression thus transforming the health and quality of life for diabetic children. Her vision for the future of this encapsulation strategy includes applications for treating other devastating childhood diseases that would benefit from cell transplantation.