THE HARTWELL FOUNDATION

2015 Individual Biomedical Research Award

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Engineering a Cellular Thread for Juvenile Diabetes

Juvenile or type 1 diabetes (T1D) is an autoimmune disease that destroys the insulin-secreting islet (beta) cells of the pancreas responsible for controlling the level of blood glucose. In the U.S., about 15,000 children are diagnosed every year with T1D and the incidence is rising. Unfortunately, there is no effective cure. Tedious and painful insulin injections can keep affected children alive but cannot cure the disease or prevent its many devastating effects that accumulate over the course of their lives. While all therapeutic interventions share the substantial difficulty of overcoming the autoimmune destruction of the insulin-secreting cells, several therapeutic strategies that have been suggested, including: implantation of a glucose-sensitive insulin pump; stimulation of other pancreatic cells to produce beta cells through trans-differentiation; reprograming patient skin-derived pluripotent stem cells into pancreatic islet cells; overcoming autoimmunity by other than drug immunosuppression; and islet cell transplantation, which is currently limited to adults due to the severe shortage of human donor cells. In theory, islet encapsulation should overcome the autoimmune problem, because the insulin producing islet cells are held in an implanted device that protects them from immune rejection while still allowing their active response to the level of circulating blood glucose. The challenge with designing any such device however, is in achieving robust mechanical properties; biocompatibility; and convenient retrieval or replacement of the device. To address this unmet need Minglin proposes a radical new cell encapsulation technology. Derived from the way certain spiders create a silk thread to collect drinking water, his innovation is a string of twisted, tough polymer with a porous hydrogel coating that holds the cells in place that he calls *Cellular Thread*. A biocompatible hydrogel surrounding the string encapsulates the islet cells, enables nutrient transfer to sustain cell life and most important, offers protection from autoimmune attack. The polymer string is designed to be mechanically strong to enable ease of handling, implantation and retrieval. The *Cellular Thread* can be precisely prepared and scaled to deliver a large number of islets without compromising cell packing density. To evaluate the effectiveness of his approach as an intervention for T1D, he will implant the thread loaded with islet cells percutaneously (through the skin) in mouse and dog animal models. If Minglin is successful, *Cellular Thread* will overcome immune rejection and extend the limited sourcing of islets from human donors to the abundant supply available from pigs. In addition, *Cellular Thread* may find application in other diseases as well, where cell transplantation is desirable but currently not feasible.