Islet Cell Transplantation

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Type 1 diabetes (T1D) is an autoimmune disease in which the immune system attacks one’s own pancreatic β cells, the insulin-producing cells of the body. Consequently, patients become dependent on exogenous insulin to maintain glucose homeostasis. However, insulin therapy while life saving, is not perfect. Most patients treated with insulin still have blood glucose levels above normal, which puts them at risk for long-term complications of diabetes. On the contrary, those who are able to keep their blood glucose levels near normal often develop hypoglycemia, and over years lose the ability to sense hypoglycemia (hypoglycemic unawareness) and therefore are at risk of severe hypoglycemia. Islet cell transplantation replaces the diseased β cells in a T1D patient and allows maintenance of normal blood glucose levels by secretion of appropriate amounts of insulin based on glucose sensing, therefore avoiding life-threatening hypoglycemia. The National Institutes of Health launched a multi-center Clinical Islet Transplantation (CIT) Consortium to determine the feasibility and efficacy of islet transplantation for two target populations: 1) T1D patients with severe hypoglycemic events and normal native kidney function; and 2) T1D patients who have already undergone successful kidney transplantation. Northwestern University is one of the eight clinical centers of the CIT consortium in Northern America and the leading enrollee for CIT trials for the two targeted populations.

Current status of islet transplantation at Northwestern.

In the past two years, a total of 18 T1D patients have been transplanted with islets at Northwestern Memorial Hospital, of which 14 recipients received islet transplant alone and 4 recipients received islet after kidney transplant. The longest follow-up thus far has been two years post-islet transplantation in 2 islet transplant alone recipients and 1 islet after kidney recipient, with all maintaining insulin-independence. Out of the 18 recipients, 8 patients achieved insulin independence with only one islet infusion. No one has required a third islet infusion in order to achieve insulin-independence. The islet transplant significantly decreased hemoglobin A1C in these T1D patients, but more importantly completely eliminated life-threatening hypoglycemic events in all recipients therefore significantly improving quality of life for these patients.

Innovative approaches to islet transplantation at Northwestern.

In practice, there are problems to overcome in islet transplantation before it can be considered a standard therapy for people with T1D. First, as with any organ transplant, the recipient of an islet transplant must take anti-rejection drugs indeﬁnitely. These drugs predispose patients to higher risks of infections and certain cancers. Second, the intra-portal route remains a sub-optimal route for islet transplantation despite improvement of engraftment with anti-inflammatory and anti-thrombotic therapies. Third, scarcity of appropriate donors of pancreata will not fulﬁll the need of patients waiting for islet transplantation. Physicians, scientists and engineers at Northwestern are working closely together to design innovative approaches to overcome these problems. “Tolerance therapies” which coax the immune system of the islet recipients to accept the allogeneic islet grafts as “self” are being developed. These therapies will ultimately allow indeﬁnite survival of the transplanted islet grafts without the need for indeﬁnite immunosuppression. In addition, nanotechnology is being used to develop bio-degradable scaffolds for carrying the islet cells that can be subsequently implanted in a vasculature-rich area of the body, such as the omentum, to avoid overwhelming inﬂammaton and allow optimized islet engraftment. Improved engraftment will signiﬁcantly reduce the islet mass needed to establish insulin independence, therefore decreasing the number of islet infusions and improving donor availability. Lastly, alternative sources of islets are being explored using xenogeneic islets and stem cell technology. We are hopeful that a combination of these multi-disciplinary approaches and cutting edge technology will put Northwestern at the forefront of islet cell transplantation in the near future.