Islet Cell Transplantation

Diabetes is a disease in which the body’s ability to maintain a tight control on serum glucose levels is impaired. This impairment results from a “supply to demand” mismatch. In type 1 diabetes (T1D, autoimmune diabetes), β cell directed autoimmunity leads to progressive destruction of the insulin-secreting β cells, eventually resulting in a paucity of insulin. Insulin is the hormone that stimulates cell and tissue utilization of glucose. Therefore, in the absence of sufficient insulin, blood glucose levels become uncontrolled. In type 2 diabetes (T2D), the underlying derangement lies in the reduced tissue insulin sensitivity, resulting in a less effective glycemic control in the presence of the same level of insulin.

Regardless, because diabetes is the clinical manifestation of an insulin supply and demand mismatch, therapies aimed at increasing the “supply” would likely be effective in treating both types of diabetes. β cell replacement directly increases the mass of β cells, the cell type that produces insulin. Islet transplantation is a form of β cell replacement in which the insulin-producing islets are extracted from cadaveric donor pancreata and transplanted into a diabetic recipients. Compared with exogenous insulin therapy, islet transplantation allows maintenance of normal blood glucose levels by secretion of just the appropriate amounts of insulin based on glucose sensing, therefore avoiding life-threatening hypoglycemia.

In 2002, 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 enroller for CIT trials for the two targeted populations. A total of 18 T1D patients have been transplanted with allogeneic human islets, and are currently between 3-6 years of post-transplant follow up. All recipients achieved the primary end points as defined by the studies, i.e. elimination of hypoglycemic episodes and achievement of hemoglobin A1C <7.0%. These recipients continue to show robust islet graft function during their extended follow up.

Currently, the Human Islet Transplant Program at the Northwestern Comprehensive Transplant Center has completed the CIT sponsored trials of allogeneic islet cell transplantation, and is currently in the follow-up phase of these recipients. In addition, based on our extensive experience in the use of alemtuzumab (Campath-1H) as an induction agent in our solid organ transplant protocols, we have designed a new clinical trial of allogeneic human islet cell transplantation using a combination of alemtuzumab and etanercept as the induction therapy for cellular depletion and anti-inflammatory therapies.

The new study, registered at ClinicalTrials.gov (NCT01897688, STU00059469, “A Phase 3 Single Center Study of Islet Transplantation in Non-uremic Diabetic Patients”) was approved by the Food and Drug Administration (FDA) as an Investigational New Drug (IND) in June, 2012, and is currently actively enrolling subjects. After much preparation, in 11/2014, we successfully transplanted our first recipient under this new study protocol and demonstrated superb safety profile of this induction regimen. In addition, the subject quickly achieved insulin independence within 4-5 weeks after a single islet infusion with evidence of robust insulin production.

In addition to having professed in the above-described standardized procedures adopted by the CIT Consortium for allogeneic islet cell transplantation, we, in collaboration with the broader research community at Northwestern and beyond, continue to search for innovative strategies to improve the outcome of β cell replacement for the treatment of diabetes.

The Human Islet Manufacturing Team is currently led by Dr. Xiaomin Zhang. The clinical study coordinating team is composed of Ms. Natalie Monson and Ms. Patrice Al-Saden, RN, who ensure timely coordination and superb communications between the study group and all regulatory parties (FDA, IRB) as well as with all of our patients.

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