Developing a regulatory macrophages (Mreg)-based tolerance in islet transplantation for treatment of type 1 diabetes

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Project Keywords:
1. Islet transplantation
2. Type 1 diabetes
3. Cellular Therapy

Project Description:

The long-term goal of our multidisciplinary research group is to transplant the majority of patients with type 1 diabetes with insulin secreting tissue pancreatic islets before they develop debilitating secondary complications. A major barrier to this therapy is the requirement for life long immunosuppression to prevent graft rejection. For successful islet transplantation, the overall burden of immunosuppression must be substantially reduced or eliminated so that the benefits of improved glycaemic control are not outweighed by chronic complications from immunosuppressive therapy. To achieve this, clinically applicable strategies for immunomodulation need to be developed.

The overall objective of this project is to produce a cell-based therapy that can be developed ex vivo that will suppress the cell mediated response to the graft and thereby reduce or eliminate the requirement for immunosuppression. It is our hypothesis that Mreg generated ex vivo will suppress the cellular immune responses in islet transplantation, therefore leading to a state of functional tolerance. We propose to develop this strategy in a model of islet allotransplantation. However because of the need for an expanded donor pool we propose to evaluate the suitability of this strategy for islet xenotransplantation as well. The fundamental goal in this project is to develop a cellular therapy to provide islet allo- and xeno-graft protection, thereby to provide a curative treatment for the majority of diabetic patients.