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Localized Immunosuppression Therapy for Islet Cell Encapsulation

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ABSTRACT

Type 1 diabetes, an autoimmune disease in which the body's immune system destroys the insulin-producing beta cells necessary for managing a person's blood glucose levels, affects 1.25 million Americans. A potential treatment for this disease is islet cell transplantation where Islets of Langerhans, containing the beta cells, are transplanted from a normal donor to a diabetic recipient to regulate blood glucose levels and provide insulin independence. Similar to whole organ transplantation, immune modulation through immunosuppression therapy is necessary for successful transplantation of islets without rejection. However, long-term systemic immunosuppression therapy can be toxic to the patient and the islets. Because of this, there is a need for alternative strategies where immune protection is provided locally through islet encapsulation or localized delivery of immunomodulatory agents. In this study, we investigated the toxicity of the inactive and active forms of an FDA approved immunosuppressant drug by assessing the morphology, viability, and protein expression of human islets embedded in a novel collagen encapsulation material. Overall, there was decreased islet cell death and improved morphology with i) decreasing drug concentration from 1.0 mg/mL to 0.01 mg/mL; ii) use of the inactive form of the drug vs the active form of the drug; and iii) incorporation of the drug into the collagen encapsulation material rather than the culture medium. Islet encapsulation strategies incorporating localized immunosuppression has the potential to be a successful solution for improving islet longevity and function following transplant without impacting the patient systemically.

KEYWORDS

Type 1 diabetes, islet cell transplantation, localized immunosuppressive therapy, immune response