Long-term reversal of diabetes by the injection of immunoprotected islets.

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Abstract

The intraperitoneal injection of insulin-producing islets immunoprotected by an alginate-poly(amino acid) membrane is a potential method of reversing diabetes without the need for lifelong immunosuppression. Previous attempts to demonstrate this technology in large animals have failed, preventing application in humans. We have determined that key factors responsible for these past failures include cytokine (interleukins 1 and 6 and tumor necrosis factor) stimulation by mannuronic acid monomers from alginate capsules with weak mechanical integrity, which results in fibroblast proliferation. With this insight, we formulated mechanically stable microcapsules by using alginate high in guluronic acid content and report prolonged reversal of diabetes in the spontaneous diabetic dog model by the intraperitoneal injection of encapsulated canine islet allografts. Euglycemia, independent of any exogenous insulin requirement, was noted for up to 172 days. Graft survival, evidenced by positive C-peptide release, was noted for as long as 726 days in a recipient receiving a single injection of immunoprotected islets. Histological evidence of viable islets retrieved from the peritoneal cavity 6 months posttransplant confirmed the biocompatibility and immunoprotective nature of this capsule formulation. The finding that intraperitoneal injection of alginate-immunoprotected islets, a minimally invasive surgical procedure, is effective in prolonged (> 1 year) maintenance of glycemic control, without the need for lifelong immunosuppression, may have significant implications for the future therapy of type I diabetes in humans.

Full text

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Fig. 2 on p.5846

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