

## **Beneficial effects of parenteral GLP-1 delivery by cell therapy in insulin-deficient streptozotocin diabetic mice.**

### **Abstract**

Parenteral delivery of long-Acting glucagon-like peptide-1 (GLP-1) mimetics has received much attention as a therapeutic option for diabetes. However, cell therapy-based GLP-1 treatments may provide a more physiological regulation of blood glucose. The present study assessed the effects of chronic GLP-1 delivery by cell therapy, using the GLP-1-secreting GLUTag cell line, in normoglycemic and streptozotocin-induced diabetic mice. GLUTag cell aggregates were transplanted into the subscapular region of mice. Over 30 days, cellular transplantation gave rise to encapsulated and well-vascularized growths, which contained immunoreactive GLP-1. Cell implantation was well tolerated and had no appreciable metabolic effects in normal mice. However, transplantation significantly ( $P<0.001$ ) countered excessive food and fluid intake in diabetic mice and maintained normal body weight. Circulating glucose ( $P<0.01$ ) and glucagon ( $P<0.05$ ) were significantly reduced and plasma insulin and GLP-1 dramatically increased. This was associated with significantly ( $P<0.01$ ) improved glucose tolerance in diabetic mice. Histological examination of the pancreata of these mice revealed elevations ( $P<0.001$ ) in islet and  $\beta$ -cell area, with reduced ( $P<0.001$ )  $\alpha$ -cell area. Increased  $\beta$ -cell mass reflected the enhanced proliferation relative to apoptosis. These studies emphasize the potential of chronic GLP-1 delivery by cell therapy as a potential therapeutic option for diabetes.

**Keyword:** Beta-cell; Diabetes; Glucagon-like peptide-1 (GLP-1); Glucose tolerance; Insulin secretion; Streptozotocin.