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A modified technique for pancreatic islet transplantation into the submandibular gland: an experimental study

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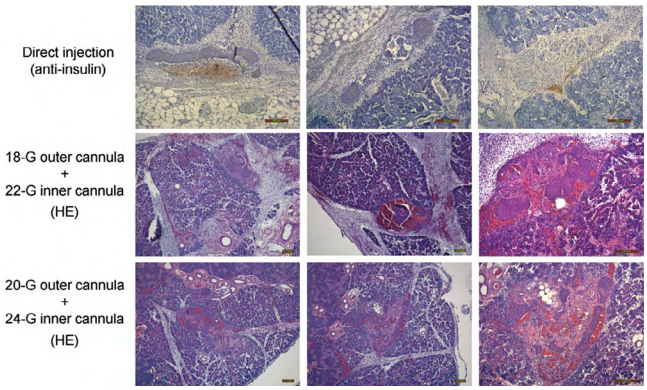
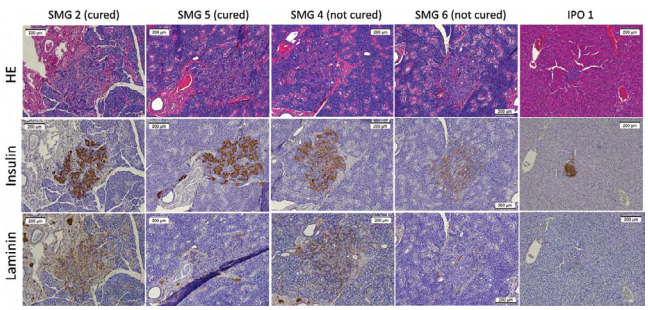
Pancreatic islet transplantation is a promising therapy for type 1 diabetes. Islet transplantation is clinically performed through intraportal infusion, which is associated with several drawbacks, including poor engraftment. The histological resemblance between the submandibular gland and the pancreas renders it an attractive alternative site for islet transplantation. In this study, we refined the technique of islet transplantation into the submandibular gland to achieve good morphological features (Figure 1). Then, we transplanted 2,600 islet equivalents into the submandibular glands of diabetic Lewis rats. Intraportal islet transplantation was performed in diabetic rats as a control. Blood glucose levels were followed for 31 days and an intravenous glucose tolerance test was performed. Immunohistochemistry was used to demonstrate the morphology of transplanted islets. Follow-up after transplantation showed that diabetes was cured in 2/12 rats in the submandibular group in comparison to 4/6 in the control group. The intravenous glucose tolerance test results of the submandibular and intraportal groups were comparable. IHC showed large islet masses in the submandibular gland in all examined specimens with positive insulin staining (Figure 2). Our results show that submandibular gland tissue can support the islet function and engraftment but with considerable variability. Good morphological features were achieved using our refined technique.





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118.5

Insulin independence after intraportal islet transplantation in patients with kidney allograft and type 1 diabetes mellitus

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Background: Islet after kidney transplantation (IAK) could be an alternative to pancreas transplant in patients with T1DM but clinical outcomes of IAK are inconsistent and the experience is very limited. Here, we present our pilot study of islet after kidney transplantation, which provided insulin independence and optimal blood glucose control.
Material: Islet transplantation was performed 5 (2-5.5) years after initial kidney transplant in four T1DM patients and at a median age of 50(45-59) with median BMI of 25(23-26) and median HbA1c of 8.6(6.8-10.2). Median serum creatinine and eGFR were 1.5 (0.9-2.1) and 50 (31-91), respectively. All those patients received basiliximab induction and standard for kidney transplant maintenance immunosuppression. One additional patient received islets infusion 2 days after kidney transplantation with anti-thymocyte globulin induction. Etanercept was administered subcutaneously as peri-transplant anti-inflammatory therapy.
Results: Single islet infusion led to insulin independence in all five patients. Currently four patients remain insulin independent with serum HbA1c <6 for 24, 15, 11 and 4 months after the transplant. Another patient with a high BMI of 30 required a second islet transplant four months after the first one, maintaining insulin independence for the subsequent 5 years. Patients achieved optimal clinical outcome with islet mass and donors comparable to those offered to islet transplant alone recipients with a mean IEQ transplanted of 396,000 (6,121 IEQ/k) and donor BMI 36 (33-37). None of the patients have experienced short or long term adverse events related to islet transplantation. Kidney graft function remained stable without progression of proteinuria.
Conclusion: Islet after kidney transplantation allows for the restoration of insulin independence in type 1 diabetic patients without compromising kidney graft function.
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