Dosage and Efficacy Studies On Alginate Encapsulated Pancreatic Islets After Transplantation Into Diabetic Mouse Models
Christina Grace Kummerfeld (Poli Sci), Sherman Chu (Bio Sci)
Faculty Mentor: Dr. Jonathan RT Lakey
Co-Authors: Dr. Rahul Krishnan, Michael Alexander
Department of Surgery

Objective
Limitations of numbers of organ donors, issues of consistency of human islet isolations and the negative complications of chronic immunosuppression have stimulated researchers to explore xenogeneic islet transplantation with encapsulation within alginate hydrogels to protect the transplanted islets from the immune response. We have developed a novel and consistent method of porcine islet isolation and encapsulation within alginate microcapsules. The aim of this study was to evaluate the efficacy of alginate-encapsulated porcine islets in reversing experimentally induced hyperglycemia in two strains of mice after intraperitoneal transplantation in immunodeficient (athymic nude mouse) and the immune-competent (C57Bl/6) mice.

Methods
- Athymic Nude (n=30) were rendered diabetic with a single dose of streptozotocin (150 mg/kg). Athymic Nude (n=10) were left non-diabetic.
- Blood glucose levels were monitored daily with weekly body weight measurements.
- Islets were isolated from 18-22 days old Yorkshire pigs using in vitro culture protocol developed in the lab. After culture period, the islets were encapsulated in 3% alginate (UPLVM, Novamatrix). Encapsulated islets were transplanted intraperitoneally (IP).
- N=10 received 2000 IE/mouse and N=10 received 4000 IE/mouse.
- Explanted islet capsules were tested for viability by Newport green/propidium iodide staining and evaluated for beta cell content sby dithizone staining.

Results
Non-diabetic control mice demonstrated consistently normal blood glucose levels, while untreated diabetic mice showed elevated blood glucose levels throughout the time period (Fig 1). After 2000IEQ and 4000IEQ islets were transplanted, blood glucose levels returned to non-diabetic levels. An oral glucose tolerance test was conducted on the four study groups which showed the transplant groups demonstrating glucose tolerance curves similar to non-diabetic mice, while the diabetic mice showed poor glucose tolerance during the three hour period.

Figure 1. Blood Glucose levels overtime from pre-STZ to three weeks post transplant

Figure 2. Oral Glucose Tolerance Test on four groups of Athymic Nude Mice

Figure 3. Porcine Islet Mouse Transplants A) Transplantation of encapsulated porcine islets into the peritoneal cavity. B) Saphenous vein draw for OGTT

Figure 4. Encapsulated Porcine Islets A) Islets in vivo B) Explanted islets stained with dithizone.

Conclusion
This study demonstrated that encapsulated young porcine islets can survive and function in encapsulated piglet islets in diabetic mice. These results demonstrate the value of encapsulated islet transplantation as a possible permanent cure for type I diabetes.

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