191f Protection of Microencapsulated Islets from Hypoxia by Perfluorocarbon

Amy S. Lewis, Robert J. Fisher, Abdulkadir Omer, Gordon C. Weir, and Clark K. Colton

Type 1 diabetes is a disease that results from a person's impaired ability to produce insulin, a protein that regulates blood glucose concentration. Insulin is produced by β-cells in the Islets of Langerhans, which are aggregates of cells averaging about 150μm in diameter and constituting about 1 to 2% of the pancreas volume. The efficacy of islet transplantations as a treatment for diabetes has been demonstrated in humans by the Edmonton Protocol, but obstacles remain for wide scale application. One major issue is that successful islet transplantation requires permanent use of multiple immunosuppressive agents that may have serious side effects as well as a substantial financial burden. Microencapsulation is used for full or partial protection of transplanted islets from immune rejection. The microcapsule creates an additional mass transfer resistance for oxygen transport to islets, which can lead to a hypoxic core within the islet that results in tissue death and reduced function. Prior results have shown that the culture of islets in media containing perfluorocarbon (PFC) increases islet survival and function by providing protection from hypoxia due to increased solubility of oxygen in PFC. In this study we evaluated the ability of alginate microcapsules containing perfluorocarbon emulsion, which increase oxygen permeability due to a factor of 25 increase in oxygen solubility, to protect islets or INS-1 cells from hypoxia and thereby to increase beta cell survival and function.

A theoretical reaction-diffusion model was developed to predict the oxygen partial pressure profile, extent of cell death, and rate of insulin secretion in alginate microcapsules containing an islet or INS-1 cells implanted in the peritoneal cavity or exposed to specified pO_2 values, with or without PFC. Results show that hypoxic conditions should be reduced, therefore enhancing islet viability and insulin secretion in PFC capsules. Calculations have also predicted that the minimum oxygen value observed at the core of a capsule containing single dispersed cells is significantly higher than with one single intact islet (diameter 150μm) indicating that single dispersed islet cells or smaller islet cell aggregates are beneficial in enhancing oxygen transport to encapsulated tissue.

PFC emulsions (70% w/v) were prepared in a microfluidizer from a fat emulsion and perfluorodecalin. Alginate was dissolved in the PFC emulsion to produce PFC alginate. Microcapsules containing islets or INS-1 cells were formed by dropwise addition of alginate or PFC alginate into $CaCl_2$ or $BaCl_2$. After 1 day of culture in a limited oxygen environment, the viability of islets or INS-1 cells within the microcapsules was determined by measuring the oxygen consumption rate (OCR). OCR measurements of microencapsulated islets after one day of culture in a low oxygen environment indicated that the viability of the islets in plain alginate microcapsules is reduced compared to the viability of those in PFC alginate microcapsules. Increased survival of INS-1 cells was observed when encapsulated in PFC-alginate as compared to plain alginate and cultured in a low oxygen environment. In conclusion, the elevated oxygen partial pressure profile in PFC alginate microcapsules increases survival of islets as compared to plain alginate microcapsules.