

P036 Preservation of Islet Mass by Enhanced Intracellular Oxygen Utilization

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Isolated islets are avascular and ischemic from isolation through the period required for revascularisation, resulting in the loss of 35% to 50% of islet mass from ischemic cell death. It is our hypothesis that the induction of intracellular cytoglobin may reduce ischemic cell death by enhancing beta cell oxygen utilization and reducing damage from oxidative stress. Lewis rat islets were transfected with cytoglobin genes resulting in the production of intracellular cytoglobin. Cytoglobin expression significantly reduced islet cell death in culture at 20% and 5% oxygen concentrations and increased insulin secretion ($P < 0.01$) in contrast to untreated islets. Cytoglobin maintained normal oxygen consumption rates in islets cultured for 5 days. Untreated islets increased their oxygen consumption rates as a result of an hypoxia driven shift to anaerobic metabolism and the production of reactive oxygen species. Cytoglobin prevented graft failure from a suboptimal syngeneic islet mass. Allogeneic transplantation resulted in islet rejection within 7 days. The expression of cytoglobin delayed rejection for over 15 days, suggesting that the maintenance of healthy islets reduced the antigenic burden to the host and delayed the induction of immune rejection. Increased islet survival and function by the presence of cytoglobin suggests that cytoglobin induction may be a useful adjunct to islet transplantation.