CO-CULTURE OF HUMAN MESENCHYMAL STEM CELLS AND HUMAN ISLETS

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Background: Islet transplantation remains an attractive therapy for type 1 diabetes. The progressive loss of insulin independence in transplant recipients associated with islet destruction is a concern. A strategy to mitigate this decrease in beta-cell function is to activate endogenous cellular repair. Bone marrow (BM) derived mesenchymal stem cells (MSCs), for instance, can regenerate pancreatic islets in mice with chemically induced diabetes. The expansion of a similar MSC population from the human pancreas led us to believe the natural fluctuations in beta-cell mass can be regulated by these MSCs. As pancreatic mesoderm produces signals for pancreatic development, we hypothesized that these cells may be bioactive signals for beta-cell survival.

Methods: Human MSCs were isolated from the exocrine pancreas and characterized by flow cytometry. Human islets were obtained from the Clinical Islet Isolation Core and cultured for two to four days in serum free media before microencapsulating in calcium-alginate. MSCs and encapsulated islets were added at a ratio of 1:1 by cell number (1 IEQ ≈ 1000 cells) in DMEM low glucose (5.6 mM) with 10% fetal bovine serum. Samples of these islets were collected at 0, 24 and 72h to assess islet mass, insulin content, glucose sensitive insulin release, and tissue histology.

Results: After 72h in culture, MSC treated and untreated islets demonstrated no difference in DNA (54.5 ± 17.3% vs 54.1 ± 12.2%, n=4) or insulin content (44.0 ± 5.5% vs 39.3 ± 5.5%, n=2) normalized to islets at 0 h. However, islet mass decreased between 24 and 72h while insulin content remained unchanged in MSC treated and untreated islets. Glucose sensitive insulin release of two human islet preparations revealed improved stimulation indices from co-cultured islets compared to islets alone after 24 and 72h.

Conclusion: Culture conditions appear to preserve beta cell mass independent of mesenchymal factors. However, co-culture of mesenchymal stem cells with encapsulated islets may be a way to maintain glucose sensitive islet function in vitro.

Key words: Islet transplantation, Mesenchymal stem cells, Co-culture