Multipotent Mesenchymal Stem Cells as Tools for Optimization of Human Pancreatic Islet Transplantation

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INTRODUCTION: Type 1 diabetes mellitus is a chronic disease caused by autoimmune destruction of pancreatic beta cells, leading to insulin deficiency and consequent metabolism impairment. Pancreatic islet transplantation is a viable therapeutic alternative, however, both islet isolation as well as recipient immune system promote beta-cell apoptosis contributing to reduction in graft viability. Mesenchymal stem cells (MSCs) are present in all tissues releasing several factors which enhance cell survival and viability. MUSE-like cells, a specific type of MSCs, express several pluripotency markers, are stress tolerant and do not form teratomas upon injection into immunodeficient mice. This project aims to assess whether co-transplantation of MUSE cells, enriched from skin primary cultures, influence pancreatic islets viability, thereby improving the outcome of transplantation.

MATERIAL AND METHODS: Primary cultures of human skin tissue were derived and submitted to selective culture cycles, comprising adherent and suspension culture steps. Cells were subjected to flow cytometry (FC) analysis using antibodies against CD105, CD29, CD90, CD73 and CD45. Nanog gene expression was evaluated by qRT-PCR. Isolated mice islets were kept in culture with MSC conditioned medium and submitted to functional assay.

RESULTS AND DISCUSSION: FC analysis showed an enrichment of CD105+ population (which represents the MUSE-rich population) after the selection process, with an increase in double-positive CD105+/CD90+, CD90+/CD73+ and CD105+/CD73+ populations. Moreover, no significant enrichment of CD45+ population, a hematopoietic precursor cells marker, was observed. Nanog mRNA levels were increased after each selection cycle in MUSE-like cells. RIA assays showed that culture with MUSE-like conditioned medium does not hamper glucose-stimulated insulin release by the islet cultures.

CONCLUSIONS: Even though further experiments are still underway in order to confirm the presence of MUSE cells and their effects in pancreatic islets, our results indicate that the process of cell selection is effective for enrichment of the desired population and does not interfere with beta-cell function in vitro.

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