Mesenchymal Stem Cells Cultured as Spheroids (MSC-Sph) As a Supportive Strategy for Pancreatic Islet Transplantation

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INTRODUCTION: Type 1 diabetes 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 therapeutic alternative however, both islet isolation technique and allorecognition by immune system undermine beta cell viability. Mesenchymal stem cells (MSCs) are present in all tissues releasing several factors that enhance cell survival and viability. MUSE cells, a specific type of MSCs, express several pluripotency markers, are stress tolerant and do not form teratomas when injected into immunodeficient mice. We set out to assess whether co-transplantation of MSC-Sph cells, enriched from skin primary cultures, influence islet viability and functionality, improving the outcome of transplantation. **MATERIAL AND METHODS**: Primary cultures of human skin tissue were subjected to selective e cycles, with adherent and suspension culture steps to enrich MSC-Sph population. Cells were analyzed by flow cytometry (FC) and qRT-PCR. MSC-Sph cells were co-cultured with mouse splenocytes to assess T-cell proliferation and IFNγ secretion. Mouse islets were kept in co-culture with MSC-Sph conditioned medium and submitted to functional assays. **RESULTS AND DISCUSSION:** FC analysis showed an enrichment of CD105+ population (which represents the MSC-Sph) after selection process, with increase in double-positive CD105+/CD90+, CD90+/CD73+ and CD105+/CD73+ populations. Moreover, no significant enrichment of negative markers (CD34, CD45, HLA-DR) was detected. Nanog mRNA levels were higher in cultures after selection cycles. Secreted mouse IFNγ levels were reduced in splenocyte-MSC-Sph co-cultures. Moreover, our results showed that islet culture with MSC-Sph-conditioned medium did not hamper glucose-stimulated insulin release or islet viability. **CONCLUSIONS:** Even when further experiments are underway to confirm *in vitro* and *in vivo* effects of MSC-Sph on islet viability and functionality, these results indicate that the selective culture cycles of MSC employed give rise to an enriched MSC-Sph subpopulation displaying promising potential for islet transplantation.

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