Proceedings of German Society for Stem Cell Research (PGSSCR)

Comparison of stemness and endocrine differentiation potential of human pancreatic islet derived and human bone-marrow derived stromal cells

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Published on 16 May 2007

Introduction:

Cell-based therapy of type 1 diabetes mellitus resides on beta cell replacement and islet regeneration strategies. Various cell types of embryonic, foetal and adult origin have been investigated. So far, the most adequate alternative cell source is still to be defined. Human islet pancreatic derived cells (hIPC) have been demonstrated to differentiate in vitro into beta cell phenotypes. In previous work we have shown that stromal hIPCs display mesenchymal stem cell features. Here, we compared the stemness character of hIPCs and human bone-marrow derived mesenchymal stem cells (hMSC) as well as the in vitro potential of these two cell populations to differentiate into insulin producing cells.

Materials and methods:

Gene expression pattern was analysed in hIPCs and hMSC by means of cDNA microarray hybridization (Affymetrix U133 Plus 2.0 chip) and stem cell marker genes were confirmed by RT-PCR. hIPCs and hMSC were expanded and cultivated in specific pancreatic endocrine promoting conditions (high glucose serum free medium, Activin-A, s-cellulin, hHGF, exendin-4 and nicotinamid). After 5 days in differentiation medium, islet gene markers were investigated by means of RT-PCR and immunocytochemistry in both cell populations.

Results:

Both cell types expressed key genes of a cluster of stemness-associated genes (Oct1, Hmgb1, Meis2, Hoxb5, cbfa1 and cbfa2) though with varying expression signal levels. In addition, both hIPCs and hMSCs could undergo an endocrine differentiation pathway shown by isl-1, Ngn3, Pax4, NeuroD1, Pdx-1, Glut2, insulin, glucagon, somatostatin (SST) and pancreatic polypeptide (PP) expression, although to a lower extend in hMSC. Mature insulin and c-peptide proteins were identified in both cell populations.
Conclusion:

Our results provide evidence for similar stemness character of the two stromal populations. Both, hIPCs and hMSCs can be induced in vitro to differentiate towards a pancreatic endocrine phenotype. However, the more extended endocrine differentiation capacity of hIPCs suggests an endocrine “imprinting” in these cells compared to hMSCs, supporting the hypothesis that hIPCs represent an intermediate phenotype with epithelial-mesenchymal commitment. Further studies are needed to elucidate if stromal cells can be induced to replace beta cells or to support islet regeneration and which population constitutes the most adequate cell source in the context of cell-based approaches in type 1 diabetes.