Proceedings of German Society for Stem Cell Research (PGSSCR)

Bone marrow derived mesenchymal stem cells isolated from patients with diabetes mellitus type 1 are able to induce a pancreatic endocrine genes in vitro

Sebok D¹, Eberhardt M¹, Barbero A¹, Linscheid P¹, Timper K¹, Martin ¹, Keller U¹,², Muller B¹,² and Zulewski H¹,²

1Dept. of Research, Div. of Endocrinology, Diabetes and Clinical Nutrition
2University Hospital, Basel, Switzerland

Published on 16 May 2007

Background:

The shortage of human islets as well as allograft rejection hampers islet transplantation for treatment of type 1 diabetes. Recent findings suggest that bone marrow derived mesenchymal stem cells (MSC) have the capacity to differentiate into a variety of cell types including endocrine cells of the pancreas, which could provide an abundant source of autologous cells for this procedure. Our aim was to investigate if MSC isolated from different patients with type 1 diabetes harbour the potential to adopt a pancreatic endocrine phenotype in order to accelerate a bench-to-bedside approach regarding the future use of bMSC for transplantation purposes.

Material and Methods:

MSC were isolated from three patients with diabetes mellitus type 1 and expanded in DMEM with 10% FBS and FGF (5ng/ml). For induction of differentiation, cells were incubated for three days in serum free differentiation medium (DMEM/F12) supplemented with factors known to enhance β-cell differentiation. Total RNA was extracted on days 0, 1, 2 and 3 and subjected to quantitative real time RT-PCR. Immunocytochemistry (ICC) was performed with undifferentiated and differentiated cells from day 3 using an anti human c-peptide antiserum.

Results:

Upon induction of differentiation, the formation of islet-like clusters was observed and quantitative RT-PCR analysis revealed that various key transcription factors needed for the development of pancreatic endocrine cells were either constitutively expressed (Isl-1, Pax6) or up-regulated (Ngn-3, Ipf-1) during the 3 days differentiation period. Additionally, an induction of the islet protein genes (insulin, somatostatin, glucagon and glut-2) was
observed. Furthermore, ICC indicated the presence of C-peptide positive cells in differentiated cells.

Conclusions:

bMSC isolated from patients with diabetes mellitus type 1 are able to differentiate into a pancreatic endocrine phenotype in vitro by sequential expression of key developmental genes. The yield of islet hormones however was very low, indicating that the current strategies for isolation and differentiation need substantial improvements.