

The Generation of Insulin Producing Cells from Human Mesenchymal Stem Cells by miR-375 and Anti-miR-9

Authors : Arefeh Jafarian, Mohammad Taghikani, Saied Abroun, Amir Allahverdi, Masoud Soleimani

Abstract : Introduction: The miRNAs have key roles in control of pancreatic islet development and insulin secretion. In this regards, current study investigated the pancreatic differentiation of human bone marrow mesenchymal stem cells (hBM-MSCs) by up-regulation of miR-375 and down-regulation of miR-9 by lentiviruses containing miR-375 and anti-miR-9. Findings: After 21 days of induction, islet-like clusters containing insulin producing cells (IPCs) were confirmed by dithizone (DTZ) staining. The IPCs and β cell specific related genes and proteins were detected using qRT-PCR and immunofluorescence on days 7, 14 and 21 of differentiation. Glucose challenge test was performed at different concentrations of glucose as well as extracellular and intracellular insulin and C-peptide were assayed using ELISA kit. In derived IPCs by miR-375 alone are capable to express insulin and other endocrine specific transcription factors, the cells lack the machinery to respond to glucose. The differentiated hMSCs by miR-375 and anti-miR-9 lentiviruses could secrete insulin and c-peptide in a glucose-regulated manner. Conclusion: It was found that over-expression of miR-375 led to a reduction in levels of Mtpn protein in derived IPCs, while treatment with anti-miR-9 following miR-375 over-expression had synergistic effects on MSCs differentiation and insulin secretion in a glucose-regulated manner. The researchers reported that silencing of miR-9 increased OC-2 protein in IPCs that may contribute to the observed glucose-regulated insulin secretion. These findings highlight miRNAs functions in stem cells differentiation and suggest that they could be used as therapeutic tools for gene-based therapy in diabetes mellitus.

Keywords : diabetes, differentiation, MSCs, insulin producing cells, miR-375, miR-9

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