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Stem cell therapy for myocardial infarction: Challenges and prospects

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Myocardial infarction causes death worldwide with the greatest incidence being in the United States. Although there have been many advances in myocardial re-perfusion strategies and novel pharmacological approaches, therapies for treating acute and chronic myocardial ischemic damage remain limited. This means that no currently available heart failure treatment has demonstrated an ability to generate new muscle tissue within the scared regions of the heart. Stem cell, however, offers new hope to patients who have otherwise limited choices. Therefore, this review aims at exploring the use and peculiarities of stem cell therapy for myocardial infarction. But the success of stem cell therapy for clinical use needs the validation of several issues ranging from selection of appropriate stem cells, routes of transfer, establishment of conducive trans- differentiation milieu with associated cytokines, means to evaluate/track response to cell therapy to compliance with regulatory and ethical issues besides addressing biological and technical issues surrounding stem cell therapy.

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The effect of overexpression of Pdx1 on the differentiation of induced pluripotent stem cells derived from fibroblast of diabetic patient into pancreatic cells

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Objectives: Pancreatic and duodenal homeobox 1 (PDX1), a member of the homeodomain- containing transcription factor family, is a key transcription factor important for both pancreas development and mature β cell function. Induced overexpression of Pdx1 resulted in a significant upregulation of insulin and other pancreas-related genes. The generation of insulin-producing pancreatic β-cells from human iPS cells in vitro would provide an unprecedented cell source for cell transplantation therapy in diabetes without the ethical obstacle of embryonic stem cells and would bypass immune rejection.

Materials & Methods: Pdx1 overexpressed hiPS cells were produced by Lentiviral transduction system and the infected cells were selected by puromycin. A differentiation process was carried out according to Kroon et al., 2008 protocol with some modifications that converts human induced pluripotent stem cells to endocrine cells capable of synthesizing the pancreatic hormones insulin, glucagon, somatostatin. This process mimics in vivo pancreatic organogenesis by directing cells through stages resembling definitive endoderm, primitive gut-tube endoderm, posterior foregut, pancreatic endoderm and endocrine precursor which lead to cells that express endocrine hormones. We characterized the differentiation process in each stage at the RNA and protein levels using real-time PCR, western blotting, immunofluorescence and flow cytometry.

Results: The results indicated high expression level of each stage-specific marker including SOX17, FOXA2, and GSC in DE stage, HNF4A in PG stage; PDX1 and HNF6 in PF stage, NKX6-1, NGN3, NKX2-2, PTF1A in PE stage and pancreatic hormones such as insulin, glucagon, somatostatin were detected.

Conclusion: These results demonstrated that over expression of Pdx1 is an important new strategy for the efficient generation of functionally immature insulin-producing β-islet cells from hiPS cells.

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