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Application of Mesenchymal Stem Cells in Diabetic Therapy

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Abstract : Pancreatic β-cells are the predominant insulin-producing cell types within the Islets of Langerhans and insulin is the primary hormone which regulates carbohydrate and fat metabolism. Apoptosis of β-cells or insufficient insulin production leads to Diabetes Mellitus (DM). Current therapy for diabetes includes either medical management or insulin replacement and regular monitoring. Replacement of β- cells is an attractive treatment option for both Type-1 and Type-2 DM in view of the recent paper which indicates that β-cells apoptosis is the common underlying cause for both the Types of DM. With the development of Edmonton protocol, pancreatic β-cells allo-transplantation became possible, but this is still not considered as standard of care due to subsequent requirement of lifelong immunosuppression and the scarcity of suitable healthy organs to retrieve pancreatic β-cell. Fetal pancreatic cells from abortuses were developed as a possible therapeutic option for Diabetes, however, this posed several ethical issues. Hence, in the present study Mesenchymal stem cells (MSCs) were differentiated into insulin producing cells which were isolated from Human Umbilical cord (HUC) tissue. MSCs have already made their mark in the growing field of regenerative medicine, and their therapeutic worth has already been validated for a number of conditions. HUC samples were collected with prior informed consent as approved by the Institutional ethical committee. HUC (n=26) were processed using a combination of both mechanical and enzymatic (collagenase-II, 100 U/ml, Gibco) methods to obtain MSCs which were cultured in-vitro in L-DMEM (Low glucose Dulbecco's Modified Eagle's Medium, Sigma, 4.5 mM glucose/L), 10% FBS in 5% CO2 incubator at 37°C. After reaching 80-90% confluency, MSCs were characterized with Flowcytometry and Immunocytochemistry for specific cell surface antigens. Cells expressed CD90+, CD73+, CD105+, CD34-, CD45-, HLA-DR-/Low and Vimentin+. These cells were differentiated to β-cells by using H-DMEM (High glucose Dulbecco's Modified Eagle's Medium,25 mM glucose/L, Gibco), β-Mercaptoethanol (0.1mM, Hi-Media), basic Fibroblast growth factor (10 µg /L,Gibco), and Nicotinamide (10 mmol/L, Hi-Media). Pancreatic β-cells were confirmed by positive Dithizone staining and were found to be functionally active as they released 8 IU/ml insulin on glucose stimulation. Isolating MSCs from usually discarded, abundantly available HUC tissue, expanding and differentiating to β-cells may be the most feasible cell therapy option for the millions of people suffering from DM globally.

Keywords : diabetes mellitus, human umbilical cord, mesenchymal stem cells, differentiation
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