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Stem cells and regenerative medicine: A special focus on enhanced differentiation of Stem cells into insulin-producing beta cell like clusters

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Background & Aim: Recently stem cells are an attractive starting source for producing pancreatic lineage derivatives to be used in treatment of DM as a form of cell replacement therapy. The present study is aimed to investigate the effect of histone deacetylase inhibitor (HDACi) in adipose tissue derived stem cells (ADSC) differentiation in to insulin producing cells (IPCs).

Methods: ADSCs differentiation into insulin producing cells (IPCs) was carried out using a modified differentiation cocktail of the previous protocols. First we checked insulin packaging ability of differentiated β -like clusters treated with VPA by dithizone staining and later the effect of VPA on the expression of β -cell developmental and endocrine markers were investigated by quantitative real-time polymerase chain reaction (RT-PCR). In addition, at the end of differentiation, β -cell like clusters were evaluated by immunofluorescence staining for expression of pancreatic endocrine proteins and release of insulin in response to increasing glucose challenge by ELISA.

Result: Addition of 10 mM of valproic acid to the modified differentiation cocktail resulted change in cell morphology, dithizone positive β -cell like clusters as well as about more than 1.5 fold increase in NeuroD1 and insulin1 mRNA expression compared with cells differentiated without valproic acid. Moreover, further immunohistochemical analysis confirmed that differentiated β -cell like clusters were expressed relevant pancreatic endocrine markers, including insulin, somatostatin and pancreatic poly peptides. We found that differentiated IPCs secreted insulin and insulin secretion was further increased in the presence of high glucose challenge.

Conclusion: Based on these results, we conclude that inhibition of histone deacetylase could enhance β -cell like cell differentiation from ADSC and that differentiated IPCs might be an alternative beta cell source for diabetes treatment.

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