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Abstract - Master Thesis Project, the Pharmacy Programme

Differentiating human pluripotent stem cells towards pancreatic lineage using chemical tools

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Type 1 diabetes mellitus is an autoimmune disease, which results in the permanent destruction of insulin producing β -cells of the pancreas. Diabetes is primarily treated by the regular monitoring of blood glucose, along with exogenous insulin injections when necessary. Successful transplantation of β -cells eliminates the need for this sort of treatment. However, due of a shortage of β -cell donors as well as the risks associated with required long-term immunosuppression, it is not yet ideal. Replacement of insulin producing cells with β -cells originating from embryonic stem cells (ESCs) represents a more ideal alternative.

Embryonic stem cells, derived from the inner cells mass (ICM) of the blastocyst, are self-renewing pluripotent cells which can differentiate into a variety of cell types. The study of how ESCs give rise to pancreas and β -cells might lead to ways of generating new pancreatic β -cells which could be used as therapy for diabetes.

The purpose of this thesis is to further characterize compounds which have been previously identified from high-content screening. A stepwise protocol mimicing the signals used during embryonic pancreatic development is used to differentiate human embryonic stem cells. Several compounds which are able to induce the differentiation of hESCs to pancreatic progenitors (PP) and endocrine progenitors are identified. This study focuses on the cell-based assay to study how their related signaling affects the biological process. Gsk 3 β inhibitor, NF 279 and AG 30 were the most potent compounds for the generation of PP in vitro.