Summer Research Program 2024 – Projects

Project #8

Title: Role of islet-enriched transcription factor (Mafb) and Mitochondria and in the maturation and functionality of human pluripotent stem cell-derived pancreatic β-cells

Description: Diabetes mellitus (DM) is a chronic disease characterized by impaired glucose homeostasis resulting from a defect in insulin secretion, action, or both due to the loss or dysfunction of pancreatic β cells. The two major types of DM are type 1 diabetes (T1DM) and type 2 diabetes (T2DM). Since cadaveric islet transplantation using Edmonton protocol has served as an effective intervention to restore normoglycaemia in T1DM patients for months, stem cell-derived β cells have been explored for cell replacement therapy for diabetes. Thus, great effort has been concentrated on developing in vitro differentiation protocols to realize the therapeutic potential of human pluripotent stem cells (hPSC)-derived β-cells. However most of the differentiation protocols generate insulin-positive pancreatic β cells with immature phenotype, such as limited expression of islet-enriched transcription factors like MAFA, and consequently impaired glucose-stimulated insulin secretion (GSIS). As mitochondria plays an important role in β-cells functionality, we aim to investigate the role of mitochondria in the maturation and functionality of hPSC-derived pancreatic β cells using directed differentiation protocols.

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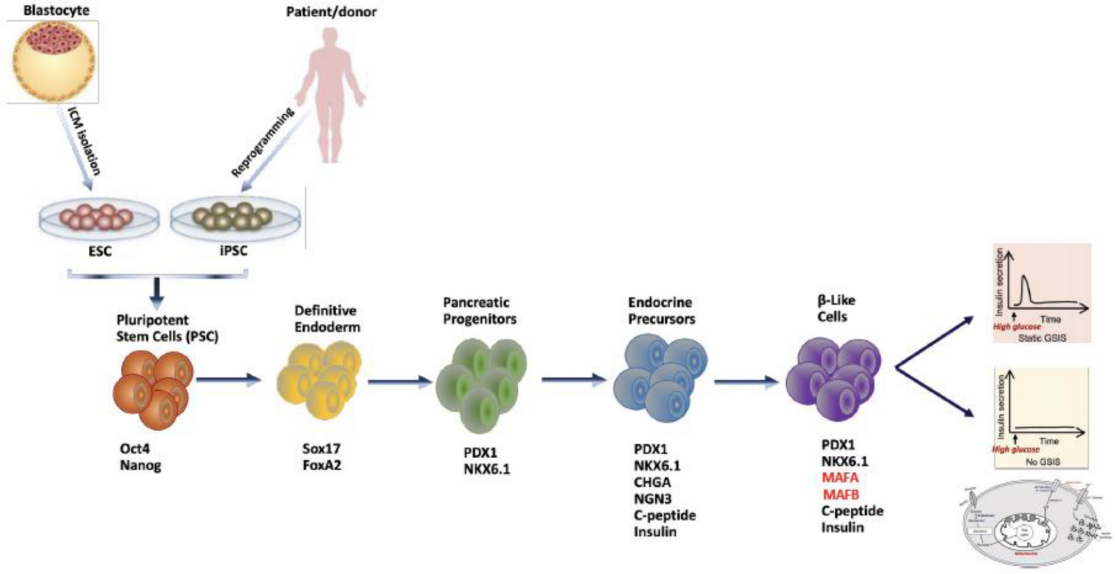

Figure: Schematic of the stepwise differentiation protocol for generation of hPSC-derived β-cells. Relevant-stage markers are also indicated, and they are evaluated at each stage to track the efficiency of differentiation using flow cytometry, immunofluorescence, RT-PCR or Western Blot.