Project #9

Role of MAFA and Mitochondria in the maturation and functionality of human pluripotent stem cell-derived pancreatic beta-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 the 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 phenotypes, such as limited expression of islet-enriched transcription factors like MafA, and consequently impaired glucose-stimulated insulin secretion (GSIS). As mitochondria play an important role in β cells functionality, we aim to investigate the role of mitochondria and MAFA in the maturation and functionality of hPSC-derived pancreatic β cells using a six-step scalable 3D directed differentiation protocol.

Mentors

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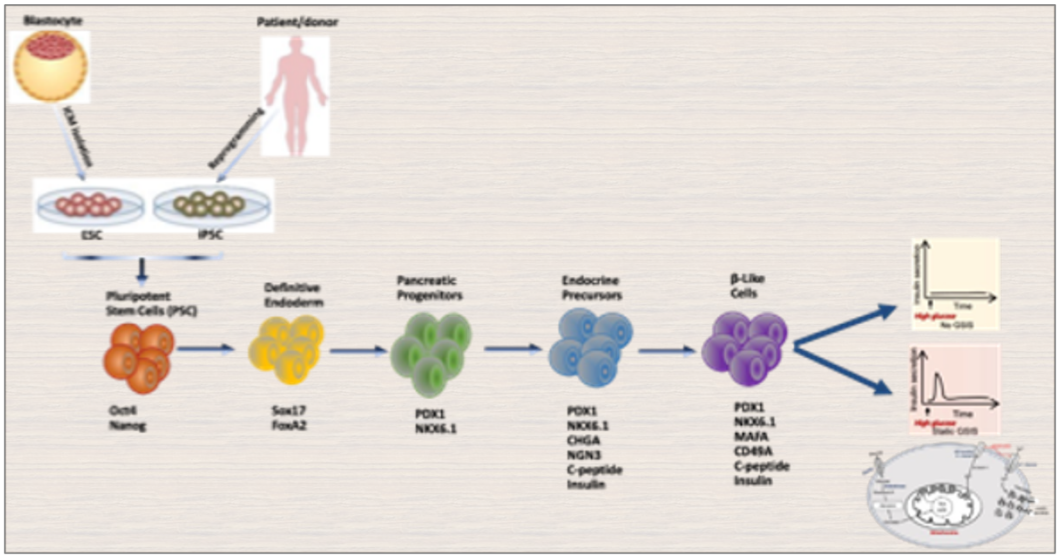

Figure. Schematic of the hPSC-derived pancreatic β cell differentiation protocol with relevant-stage gene expression markers.