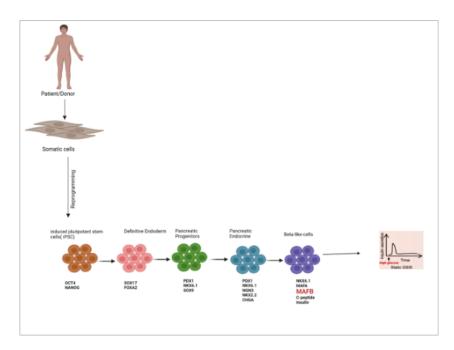
## **Summer Research Program 2025 – Projects**

## **Project #9**

**Title:** Role of MAFB in the maturation and functionality of induced human pluripotent stem cell-derived pancreatic  $\beta$  cells

**Description:** Impaired insulin secretion contributes to the pathogenesis of 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, insulin-producing β cells generated from induced human pluripotent stem cells have potential as a therapy for insulin-dependent diabetes. Thus, great effort has been concentrated on developing in vitro differentiation protocols to realize this therapeutic potential. However most of the differentiation protocols generate insulin-positive pancreatic β cells with immature phenotype, such as low or absence expression of islet-enriched transcription factors like MAFA and MAFB, and consequently impaired glucose-stimulated insulin secretion (GSIS) as compared with their in vivo counterparts. Using MAFB knock out iPSC line with CRISPR-Cas9 technology, we aim to investigate the specific role of this transcription factor in the maturation and functionality of hPSC-derived pancreatic β cells using a 2D differentiation protocol.

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**Figure**. Schematic of the induced hPSC-derived pancreatic  $\beta$  cell differentiation protocol with relevant-stage gene expression markers.