Research

Stem Cells and Diabetes

Diabetes is a debilitating chronic disease spiralling out of control, affecting more than 380 million people in the world. People with diabetes commonly develop severe complications such as blindness, cardiovascular diseases, kidney failures and lower limb amputations, leading to an astronomical healthcare burden. Despite intensive research, early mechanisms underlying human pancreatic β cell failure during the development of diabetes remain unclear. Species-specific differences in pancreas development, islet architecture and distribution pattern of islet cells necessitate a human model for diabetes research.

The Teo Lab seeks to leverage on human pluripotent stem cells (hPSCs) and their directed differentiation into pancreatic cells and cell types affected in diabetic complications to dissect the pathology of diabetes and its complications (Figure 1). The three main thrusts of the lab are:

1) **Modelling and studying human pancreas development *in vitro***
   hPSCs will be differentiated into human pancreatic cells to study the development and formation of functionally mature β cells. This is aimed at identifying critical steps, key pathways and mechanisms which guide human β cell development and maturation. It is hoped that one would be able to produce sufficient mature functional human β cells for cell replacement therapy to achieve physiological control of blood glucose levels.

2) **Studying mechanisms by which genes and gene variants cause diabetes**
   hiPSCs derived from patients with maturity onset diabetes of the young (MODY), a monogenic form of diabetes, will be used to study human β cell development, maturation and function. hiPSCs derived from diabetic patients with a risk allele that could potentially confer diabetes susceptibility will be differentiated into pancreatic cells to functionalise gene variants associated with diabetes. The tracking of early diabetes progression *in vitro* seeks to pinpoint mechanisms of β cell demise at the earliest stage(s). This is otherwise not possible given that clinical manifestation of overt diabetes in humans takes decades to occur and patient material is inaccessible.

3) **Studying mechanisms underlying diabetic complications**
   hiPSCs derived from diabetic patients with and without complications, such as diabetic nephropathy, will be differentiated into kidney cells to elucidate genetic and epigenetic perturbations which occur in cells/tissues/organs constantly exposed to hyperglycemia.
Figure Legend: Differentiation of hiPSCs derived from diabetic patients into various cell types for *in vitro* disease modelling of diabetes and its complications. (Teo et al., Cell Metab, 2013)