Research Theme: Cell Signaling and Stem Cell Biology

Research Project Title: Evaluating the role of Rho GTPases during differentiation of human pluripotent stem cells into pancreatic cells

Principal Investigator/Supervisor: Koh Cheng Gee
Co-supervisor/ Collaborator(s) (if any): Adrian Teo (IMCB, ASTAR)

Project Description
The Rho family of GTPases plays diverse roles in cytoskeletal dynamics, cell polarity and cellular locomotion. Common members of the family include Cdc42, Rac1 and RhoA. During mammalian development, cells emanate from the epiblast and the embryo undergoes gastrulation. This involves extensive cellular movement where Cdc42, Rac1 and RhoA play roles in filopodia elongation, lamellipodia extension and actin depolymerization (Mezzacappa et al., 2012). Recently, it has been reported that the loss of Rac1 in the mouse epiblast perturbs germ layer formation, leading to migration defects and extensive cell death. Rac1 is found to cross-talk with PI3K-Akt signaling to regulate cell survival (Migeotte et al., 2011). Besides this report, the role of Rho GTPases in early endoderm development and differentiation is still largely unexplored (Loebel and Tam, 2012). Beyond endoderm development towards pancreas formation, Rho GTPase has also been reported to be involved in coordinating pancreas branching morphogenesis (Zygmunt and Spagnoli, 2013). Further, the blockade of Rac1 is known to affect pancreatic beta cell migration from the ductal epithelium through E-cadherin-mediated cell-cell adhesion (Greiner et al., 2009). Rho-ROCK signaling is also implicated in pancreatic beta cell function (Hammar et al., 2009; Nakamura et al., 2006). Given the dearth of knowledge in the understanding of the role of Rho GTPases in human embryonic development, definitive endoderm and pancreas formation, this Ph.D. project seeks to address these fundamental developmental processes. The laboratory of Dr. Adrian TEO at IMCB, A*STAR, is focused on the directed differentiation of human pluripotent stem cells (hPSCs) into pancreatic cells whereas the laboratory of Associate Professor KOH Cheng Gee at SBS, NTU, is specialized in the biology of Rho GTPases. Hence, this Ph.D. candidate is well positioned to leverage upon the complementary expertise of both laboratories to study this interesting biological question.

Supervisor contact:
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