LEE KONG CHIAN SCHOOL OF MEDICINE

NANYANG TECHNOLOGICAL UNIVERSITY SINGAPORE

Imperial College London

LKCMedicine Research Lecture Series

Genetic and Nutritional Control of Beta Cell Connectivity



Prof Guy Rutter

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Professor and Head of Section of Functional Genomics, Department of Medicine, Imperial College London, UK

Hosted by LKCMedicine Dean Prof James Best

Date: 29 November 2017, Wednesday

Time: 5pm – 6pm

Venue: Seminar Room 5-1, Level 5
Lee Kong Chian School of Medicine
Clinical Sciences Building
11 Mandalay Road, Singapore 308232

Synopsis

Persistently elevated levels of glucose and fatty acids are known to contribute to failed insulin secretion during the development of Type 2 diabetes. Prof Rutter and his team have shown that glucolipotoxic conditions impair cell-cell communication ("connectivity"), which impairs insulin secretion (Hodson et al, 2013). Recently (Johnston et al, 2016) the study has combined optogenetics and rapid Ca2+ imaging across the islet syncytium to demonstrate that a subset (~5%) of beta cells ("hubs") coordinate the activity of "follower" cells. Photo-painting using a light sensitive-RFP revealed that hub cells are enriched for glucokinase, but show low levels of Nkx6.1 and insulin gene expression. These cells also display enhanced mitochondrial membrane potential in response to high glucose. Interrogation of single beta cell RNASeq data (Xin et al PNAS, 2016) confirms the existence of a subset of cells with a similar transcriptomic configuration. Hub cells are unusually susceptible to metabolic stresses including high fatty acid/glucose levels, and cytotoxic cytokines, suggesting that they may be targeted in diabetes. Since deletion of GWAS genes for diabetes including ADCY5 and TCF7L2 affect cell-cell communication, future work will explore the possibility that genes at other loci, including STARD10 (Carrat et al, 2017) also act in part by altering hub cell-led beta cell connectivity.