Research Theme
Metabolic Disorders

Research Project Title
The Role of FIT2/FITM2 in Pancreatic Beta-cell Physiology and Diabetes

Source of Funding
MOE Tier 2 Grant

Principal Investigator
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Project Description
Fat storage-Inducing Transmembrane proteins belong to a unique family of evolutionarily conserved proteins localized to the endoplasmic reticulum (ER) that are involved in intracellular lipid droplet formation. FIT proteins have been shown to mediate the partitioning of cellular lipids into micelle-encased droplets. FIT1 is primarily expressed in skeletal muscle, with lower levels found in heart, and FIT2 is ubiquitously expressed in tissues, with the highest levels in white and brown adipose tissue. FIT proteins, especially FIT2, are crucial for intracellular lipid regulation. The absence of FIT2 in a global knockout mouse confers embryonic lethality. Given its importance, the potential role of FIT proteins on lipid droplet formation and ultimately pancreatic β-cell function is an enigma that needs to be addressed.

Lipid droplets are evolutionarily conserved organelles for fat storage within cells and have been observed in insulin-secreting pancreatic β-cells. However our knowledge on their biogenesis and function in these highly specialized cells are relatively poor. Guided by strong preliminary results, we hypothesize that the novel Fat-storage-inducing Transmembrane protein 2 (FIT2/FITM2) modulate β-cell lipotoxicity by sequestering cellular lipids (TG/FFA), thereby reducing ER stress, β-cell apoptosis and ultimately diabetic pathogenesis (Fig 1). We will systematically interrogate our hypothesis by pursuing two specific aims: (i) Elucidating the mechanism(s) of FIT2 action on lipid (TG/FFA) sequestration and pancreatic β-cell function; (ii) Uncovering the role of FIT2 in diet-induced obesity and diabetic pathogenesis. In addition to improving our understanding of β-cell lipid sequestration, the proposed research will establish and validate a new approach to study the effect of obesity-driven dyslipidemia on β-cell function in vivo, addressing a critical need in experimental tools for future in vivo studies.
Contact Us

If you have questions regarding this project, please email the Principal Investigator.

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