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<td>Koh, Tracy</td>
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Supervisor: Dr Yusuf Ali                       Co-Supervisor: Dr Zheng Xiaofeng

Project Title: Does Fat-Inducing Protein FIT2 cause Insulin-Producing Cell Dysfunction and Diabetes?
Category: 6
Lee Kong Chian School of Medicine
Student: Koh Tracy                Project ID: LKCM14008

URECA
Undergraduate Research Experience on CAmpus

Elucidating the Role of Fat-Inducing Transmembrane Protein 2 (Fit2) in Insulin-producing Beta-cells (β-cells)

INTRODUCTION
Fat-Inducing Transmembrane protein 2 (Fit2/Fitm2) is an evolutionarily conserved transmembrane protein. Located on the membrane of the endoplasmic reticulum (ER), Fit2 has been shown to play an important role in the packaging of triglycerides into lipid droplets (LD) within adipocytes (Fig.1). Pancreatic beta-cells (β-cells) secrete insulin. In diabetes β-cell dysfunction is driven partly by lipid stress (lipotoxicity). Fit2 is expressed in β-cells but its function remains elusive.

METHODS AND RESULTS

OBJECTIVES
We hypothesise that Fit2 plays a protective role in β-cells by sequestering lipids, thereby reducing β-cell lipotoxicity. To test our hypothesis, we aim to knockdown (KD) Fit2 expression in β-cells to determine its effect on 1) lipid droplet packaging, 2) cell death and 3) cellular lipid metabolism.

METHODS AND RESULTS (cont’d)

I. Evaluating the efficiency of different FIT2 KD constructs in β-cells.
Three commercially available Fit2 shRNA sequences (80, 81 and 83) targeting Fit2 mRNA were tested in Min6 cells (β-cell line) after infection with the respective shRNA-containing lentiviruses.

II. Effect of FIT2 KD on LD formation, survival and gene expression of fat metabolism-related genes in Min6 cells

Fit2 KD cells were treated with oleate to determine effect on 1) lipid droplet formation, 2) cell death and 3) cellular lipid metabolism.

CONCLUSION & FUTURE WORK
Among the three KD constructs tested, 80 was most efficient in silencing Fit2 expression in Min6 cells. For subsequent experiments, only the 80 BSA clone was used. Silencing of Fit2 decreases LD formation but increases cell death in Min6 cells, suggesting the Fit2-mediated LD formation is protective in β-cells. Surprisingly, reduction of Fit2 resulted in a significant change in BSL2 gene expression. Fat storage-Inducing transmembrane protein 2 is required for normal fat storage in adipose tissue.

REFERENCES