### Research Theme: Lipid Regulation and Cell Stress

### Research Project Title: From Dietary Excess to Degenerative Diseases: Finding the Missing Links in Autophagy

**Principal Investigator/Supervisor:** Asst/Prof Guillaume Thibault  
**Co-supervisor/ Collaborator(s) (if any):** A/Prof Rachel Susan Kraut

#### Project Description

**a) Background**

Obesity has reached epidemic proportions in many parts of the world from industrialized to developing countries. In Singapore, 10% and 30% of adults were obese and overweight, respectively, in 2010, more than doubled the levels of 1992. Thus, metabolically related illnesses such as diabetes and neurodegeneration are becoming a major issue and are pushing up healthcare costs. In order to combat these conditions and develop treatments, a better understanding of physiological responses to excess fat in the diet, and cellular mechanisms of metabolic feedback is urgently needed.

Based on preliminary results and literature review, we propose that the availability of lipids from the diet influences clearance mechanisms related to vesicle trafficking, such as the regulation of vesicle fusion. To address the influence of dietary lipids on vesicle trafficking, we will investigate lipid uptake and transport from gut to brain, and will explore their effects on feeding, endoplasmic reticulum stress, autophagy, and metabolism as a whole. Moreover, we will focus on metabolic defects in neurons and other cell types, and assay neuronal death associated with lipid-associated perturbations of vesicularly mediated degradation. This project will provide a solid foundation to further explore fundamental questions related to imbalanced diet and resulting metabolic and neurological diseases.

**b) Proposed work**

The student will develop methods using super-resolution stimulated emission depletion (STED) microscopy to study possible effects of excess dietary lipids, and specific lipid species, on vesicle trafficking, including monitoring uptake and transport of these lipids, and tracking the fate of lipid droplets (LD) in autophagy. The model organisms used for this study will be Drosophila and C. elegans.

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