

Research Theme: Cell Biology / Biochemistry
Research Project Title: Cellular Stress Response in Metabolic Syndrome
Principal Investigator/Supervisor: Asst Prof Guillaume Thibault
Co-supervisor/ Collaborator(s) (if any): NA
Project Description
<p>BACKGROUND</p> <p>The unfolded protein response (UPR) is a complex adaptive stress response of the endoplasmic reticulum (ER) that maintains ER function for cell survival. The UPR is typically activated by the accumulation of aberrant proteins within the ER lumen, but also by aberrant lipid mixtures. Excessive accumulation of lipids causes metabolic abnormalities and cells death including loss of pancreatic insulin-producing beta cells. Recently, we identified a broad range of cellular defects that induce ER stress, presumably via aberrant lipids at the ER (https://doi.org/10.1083/jcb.201909165). From these observations, we hypothesize that communication between the ER and other cellular compartments is critical to maintain ER membrane integrity and to prevent unresolved ER stress associated with metabolic diseases. Our findings will identify novel players, which might serve as potential therapeutic targets of metabolic diseases.</p> <p>PROPOSED WORK</p> <p>In the context of metabolic diseases, we still poorly understand how the UPR is activated from ER stress and what are the cellular consequences. The PhD candidate will carry out a genome-wide high-throughput screen to identify new players of the pathway. The screen methodology is very well established in the lab. Newly identified factors will be further narrow down using different in vivo reporters, including reporters of ER membrane biophysical properties. The shortlisted factors will be further investigated using cell biology, genetic, and biochemistry approaches. Finally, conserved factors will be validated in mammalian cells.</p> <p>The PhD candidate will work together with an experience team of experts. Find more about the Thibault lab at www.thibaultlab.com.</p>
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If you have questions regarding this project, please email the Principal Investigator: thibault@ntu.edu.sg
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