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| Research Theme: |
| Research Project Title: Dissecting the Output of the Unfolded Protein Response in <i>C. elegans</i> |
| Principal Investigator/Supervisor: Guillaume Thibault |
| Co-supervisor/ Collaborator(s) (if any): |
| Project Description |
| <p>a) Background: Metabolic diseases such as obesity and nonalcoholic fatty liver disease (NAFLD) are emerging disorders that affect the global population. One facet of the disorders is attributed to the disturbance of the membrane phospholipid ratio. The endoplasmic reticulum (ER) is the main organelle for protein and lipid synthesis. Perturbation of ER homeostasis through change in membrane phospholipid composition results in activation of the unfolded protein response (UPR) and causes translational and transcriptional changes in an organism. There are three UPR transducers in mammals, which are ATF6, IRE1, and PEK1 that mediate cellular processes related to the UPR. Most studies have implicated roles of UPR in proteotoxic stress caused by misfolded protein accumulation and little has been done on lipid perturbation mediated ER stress. We utilized DNA microarray to identify changes in UPR signaling during lipid perturbation induced by silencing phosphoethanolamine methyltransferase (<i>pmt-2</i>) gene in <i>C. elegans</i>. Our data show that a distinct group of UPR-related genes are activated during lipid bilayer stress and absence of one UPR sensor may lead to compensation by alternative UPR transducers. Among these, we have demonstrated that autophagy is upregulated in a IRE1-dependent manner upon lipid bilayer stress.</p> <p>b) Proposed work: The candidate will pursue the characterization of the UPR transcriptional programme upon LBS that are dependent on ATF6, IRE1, and PEK1.</p> |
| Supervisor contact: If you have questions regarding this project, please email the Principal Investigator: thibault@ntu.edu.sg |
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