

<b>Research Theme: Cell Biology / Microbiology</b>
<b>Research Project Title: Dissect an essential human cellular stress pathway by synthetic biology</b>
<b>Principal Investigator/Supervisor: Asst Prof Guillaume Thibault</b>
<b>Co-supervisor/ Collaborator(s) (if any): NA</b>
<b>Project Description</b>
<p><b>BACKGROUND</b></p> <p>Stress pathways monitor intracellular systems and deploy a range of regulatory mechanisms upon stress. One of the best characterized pathways with wide implications in diseases, the unfolded protein response (UPR), is the endoplasmic reticulum (ER) guarding to maintain homeostasis. In eukaryotes, the UPR comprises of three highly conserved transducers leading to the regulation of hundreds of gene targets by activating UPR-specific transcription factors. Developed UPR inhibitors to treat diseases have serious potential long term side effects on the functions of the pancreas, the immune system, and the liver as the UPR program is too broad to be inhibited from the upstream players. Thus, being unable to inhibit a subset of downstream players part of the UPR program might yield better success but the characterization of such players, in different stress conditions, is still poorly understood. We propose to reconstruct the human minimal pathway required to restore homeostasis in a synthetic <i>Saccharomyces cerevisiae</i> system based on inter-species network alignments and identification of the conserved components of the program.</p> <p><b>PROPOSED WORK</b></p> <p>Using a combination of multidisciplinary approaches, the PhD candidate will identify and validate the minimum conserved components of the human UPR branch PERK. The PERK UPR pathway will be incorporated in yeast using Synthetic Chromosome Rearrangement and Modification by LoxP-Mediated Evolution (SCRaMbLE) system. Findings from our novel synthetic yeast system will be critical to develop targeted therapeutic approaches to prevent chronic ER stress while maintaining homeostasis. The PhD candidate will use biochemistry, cell biology, and genetic approaches.</p> <p>The PhD candidate will work together with an experience team of experts, including overseas collaborators. Find more about the Thibault lab at <a href="http://www.thibaultlab.com">www.thibaultlab.com</a>.</p>
<p><b>Supervisor contact:</b>  <b>If you have questions regarding this project, please email the Principal Investigator:</b>          thibaul@ntu.edu.sg</p>
<p><b>SBS contact and how to apply:</b>          Associate Chair-Biological Sciences (Graduate Studies): <a href="mailto:AC-SBS-GS@ntu.edu.sg">AC-SBS-GS@ntu.edu.sg</a>          Please apply at the following:  <a href="http://admissions.ntu.edu.sg/graduate/R-Programs/R-WhenYouApply/Pages/R-ApplyOnline.aspx">http://admissions.ntu.edu.sg/graduate/R-Programs/R-WhenYouApply/Pages/R-ApplyOnline.aspx</a></p>