Research Theme: Drug discovery, Isolation and Characterization of Natural Products

Research Project Title: Mode-of-Action of Druggable Biologics from Medicinal Plants

Principal Investigator/Supervisor: Professor James P. Tam

Collaborator: Dr Prakash Arumugam, Bioinformatics Institute, A*STAR

Project Description

Background

From time immemorial, herbs have fascinated humans and have served as a rich source of molecules that exert both beneficial and harmful health effects. The powerful anti-malarial drug artemisinin is derived from *Artemisia annua* (sweet wormwood). Hemlock, a potent poison is derived from the herb *Conium maculatum* (poison hemlock). While scientific research in herbal medicine has largely focused on small molecules, recent work has sparked an interest in plant-derived peptides (MW considerably >500 Da) and their potential use as biologics and anti-infectives. Several classes of cysteine-rich peptides (CRPs) have been isolated from plants such as defensins (antimicrobial), thionins (antimicrobial), leginsulins (hormone), knottins (protease inhibitors) and cyclotides (peptide-based scaffolds). Genome analysis of two model plants *Arabidopsis thaliana* and *Oryza sativa* (rice) suggest CRP-encoding genes constitute 2-3 % of all genes indicating that a large subset of CRP’s remain undiscovered. Although cysteine rich-peptides have been shown to show robust biological effects, their precise Mode-of-Action remains poorly understood. Chemogenomic profiling in yeast is a powerful technique in that can unravel Mode-of-Action of bioactive compounds, pathways that provide resistance to toxicity of the compound and novel functions of genes.

Proposed work

The major aims of this project are: (1) Determination of the Mode-of-Action of bioactive cysteine-rich peptides by chemogenomic profiling in budding yeast. (2) Detailed characterization of peptides that have anti-ageing and anti-infective properties. The proposed work will utilize a combination of genetic, molecular, biochemical and imaging tools that are amenable for the extremely tractable yeast model system. Part of the research (including chemogenomic profiling) will be done in Dr Prakash Arumugam's lab at Bioinformatics Institute, A*STAR.

Supervisor contact: If you have questions regarding this project, please email the Principal Investigator: jptam@ntu.edu.sg SBS contact and how to apply: Associate Chair-Biological Sciences (Graduate Studies) : AC-SBS-GS@ntu.edu.sg Please apply
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