

Research Theme: Synthetic microbiology

Research Project Title: Genome-guided discovery of marine natural products

Principal Investigator/Supervisor: Liang Zhao-Xun

Co-supervisor/ Collaborator(s) (if any): NA

Project Description

a) Background:

Microbial natural products are renowned for their complex chemical structures and potent biological activities. Many microbial natural products have been developed into commercially valuable compounds such as pharmaceutical agent, pesticide, food preservative and cosmetic ingredient. After several decades of extensive screening of terrestrial microbes, the current field is plagued with the problem of “re-discovering” already known microbial compounds. In contrast, the ecologically unique microbial communities from the marine environment are emerging as a promising and underexplored resource for discovering novel natural products. Between 1965 and 2015, more than 16,000 marine compounds have been isolated and more than 300 patents have been granted. Seven FDA-approved drugs and about two dozens of drug candidates currently in various stages of clinical trials are derived from marine natural products.

In the last two years, we have isolated a large number of microbial strains from the tropical marine environment of Southeast Asia, with some isolated by using non-traditional cultivation methods. Most of the strains belong to the phylum of actinomycetes that are known for their unsurpassed ability in producing structurally diverse bioactive compounds. Genome sequencing revealed that some of the strains contain highly unique biosynthetic gene clusters, hinting the capability of the microbes to produce novel compounds. Motivated by the potential of discovering novel and commercially valuable compounds, we will explore this unique collection of marine microbes with an interdisciplinary team of microbiologists, chemists and bioinformaticians. To mitigate the re-discovery problem, we will employ a genomics-guided approach that begins with the mining of microbial genomes for identifying “high potential” strains. We will expedite the discovery of novel bioactive compounds from the “high potential” strains by leveraging on a platform that combines high-throughput metabolite-profiling and gene cluster activation. By the end of the five-year project, we expect to patent a number of new marine natural products, with some of them exhibiting potent bioactivity to be further assessed as drug leads.

b) Proposed work:

1. Dereplication and prioritization of marine microbial strains.
2. Genome sequencing and mining of novel biosynthetic gene clusters.
3. Isolate and characterize novel secondary metabolite (with the help of in-house chemists)
4. *Discover novel secondary metabolites by activating silent biosynthetic pathways by using synthetic biology tools.*



Supervisor contact: If you have questions regarding this project, please email the Principal Investigator:
SBS contact and how to apply: Associate Chair-Biological Sciences (Graduate Studies) : AC-SBS-GS@ntu.edu.sg Please apply at the following: http://admissions.ntu.edu.sg/graduate/R-Programs/R-WhenYouApply/Pages/R-ApplyOnline.aspx