Research Project Title
Reverting Antibiotic Resistance in Multi-drug Resistant Bacteria

Principal Investigator
Associate Professor Kevin Pethe, LKCMedicine

Co-supervisor (if any)
Associate Professor Eric Yap, LKCMedicine

Project Description

Background
The emergence and spread of multi-drug resistant (MDR) among pathogens is recognized as a global emergency for both hospital-acquired and community-acquired bacterial infections. Hospital-acquired bacterial infections (HABI) are becoming increasingly common worldwide. The epidemic affects 1.7 million hospitalized patients in the US only, resulting in a human cost over 99,000 deaths per year - the vast majority being imputable to drug-resistant bacteria.

Drug resistance among gram negative superbugs is particularly worrying because this class of pathogenic bacteria is usually intrinsically resistant to multiple antibiotic classes owing to the thickness of the cell membrane and the expression of efflux pumps.

The aim of this project is to explore alternate strategies to reverse drug susceptibility in MDR gram negative bacteria.

Proposed work
1. Study the link between thiamine metabolism and drug susceptibility.
   We have previously shown that pharmacological perturbation of thiamine-dependent enzymes promotes antibiotic susceptibility in gram-negative bacteria. The molecular mechanisms leading to the increase in drug susceptibility will be characterized, with the idea of developing potent drug combinations.
2. Develop a strategy to target plasmid stability in MDR gram-negative bacteria.
   Multi-drug resistant is often mediated by large plasmids carrying multiple determinant of resistance. Plasmids are transmitted at very high frequency to the daughter cells upon cell division. The objective is to identify small-molecule drugs that inhibit plasmid segregation in order to reverse drug susceptibility.

Contact Us
If you have questions regarding this project, please email the Principal Investigator.
Associate Professor Kevin Pethe
kevin.pethe@ntu.edu.sg