

Understanding antibiotics resistance through structural elucidation of MsrE



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Seminar Abstract

The rapid escalation of antibiotics resistance crisis is a major threat to modern societies. The lack of structures which implicate ribosomal protection by the ubiquitous ATP-binding cassette sub-family F (ABC-F) proteins warrants research. MsrE is a horizontal gene transferable ABC-F protein which confers cross-species antibiotics resistance to macrolides and streptogramin B. Structural elucidation of MsrE would give us important insights towards building a mechanistic model for ABC-F mediated ribosome protection.

Bacterial expression, protein purification and cryo-electron microscopy (Cryo-EM) were performed. Biochemical, mutational, microbiological and structural investigations were performed to understand the molecular mechanism. The Cryo-EM structure of ribosome-bound MsrE was successfully determined at 3.6 Å, offering first structural insights into ribosome protection by ABC-F proteins. This enabled structural modelling despite the lack of crystal and existing structures. Based on experimental data and literature review, a model is proposed for antibiotic resistance element (ARE) ABC-F mediated ribosome protection. Preliminary work on a MsrE inhibitor is also lightly touched on.

About the Speaker

Aaron is fascinated with life, biology and the potential for science and technology to elevate the human condition through new therapeutics as well as cost-effective production. He developed his research interests over the years. It started off from his undergraduate years as he took on histology, proteomics data mining to mammalian stem cell research work. These experiences eventually led to bacterial-based protein expression, purification and structural biology during his PhD studies in Nanyang Technological University. He is excited to be in BTI, to meet everyone and to work with all the wonderful equipment here.