Day / Date / Time:  
Tuesday  
9th October 2018  
12pm - 1pm

Venue:  
Department of Microbiology and Immunology  
Seminar Room  
@ NUS  
5 Science Drive 2, Block MD4, Level 2, Singapore 117545

Convener:  
Dr John Chen

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Targeting Bacterial Bioenergetics And Central Metabolism For Antibiotic Development

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Abstract

The rapid emergence and spread of multi-drug resistant Mycobacterium tuberculosis and other pathogenic bacteria is a serious concern worldwide that advocates for the development of new classes of antibacterials with a novel mode of action. Current antibiotics derive mainly from natural sources and inhibit a narrow spectrum of cellular processes such as DNA replication, protein synthesis and cell wall biosynthesis. With the spread of drug resistance, there is a renewed interest in the investigation of alternate essential cellular processes, including central metabolic and bioenergetics pathways, as a drug target space for the next generation of antibiotics. However, the validation of those targets is more complex, as essentiality of such targets can be conditional. Interest in targeting central metabolism has also been muted because of a concern about selectivity with human orthologs. Nonetheless, we and others have shown that selective inhibition can be achieved for enzymes that are conserved between bacteria and humans. Oxidative phosphorylation as recently emerged as a relevant target space for the development of new classes of drug for tuberculosis. In this context, I will discuss the relevance of targeting the terminal respiratory oxidases for the development of a rational drug combination for tuberculosis and other mycobacterial diseases. I will also discuss opportunities to target central metabolism in gram positive and gram negative pathogenic bacteria.

Selected Relevant Publications for Reference