Harnessing the inhibition of mycobacterial CydDC transporter to block cellular respiration and kill *Mycobacterium tuberculosis*

Tuberculosis, caused by a rod-shaped bacterium *Mycobacterium tuberculosis*, remains a global health burden that claims the lives of more than 1.3 million people each year. The chemotherapy of tuberculosis requires the administration of a drug cocktail for several months. This complicated treatment is exacerbated for drug-resistant tuberculosis, with a limited treatment success rate. However, understanding the physiology and metabolism of this human intracellular pathogen opens up possibilities for developing more effective treatments.

The electron transport chain in *M. tuberculosis* represents a new target space for developing antitubercular drugs with novel mechanisms of action. *M. tuberculosis* requires oxygen for its growth and possesses two oxygen-dependent terminal respiratory oxidases – cytochrome bc_1-aa_3 oxidase and alternative cytochrome *bd* oxidase. Dual inhibition of these terminal oxidases is bactericidal for replicating, non-replicating and drug-resistant *M. tuberculosis*. Despite a huge scientific interest in electron transport chain inhibitors, the biogenesis of cytochrome oxidases in mycobacteria is poorly understood.

In this talk, I will present our preliminary data suggesting that a mycobacterial CydDC ABC-type transporter is required for the enzymatic activity of the cytochrome *bd* oxidase in *M. tuberculosis* and discuss the idea of targeting CydDC as a proxy for cytochrome *bd* oxidase inhibition to block cellular respiration and kill *M. tuberculosis*.