Common non-steroidal anti-inflammatory drugs (NSAIDs) in the fight against tuberculosis (TB)

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Tuberculosis (TB) remains a serious healthcare issue, more than two decades on from the first time it was declared as a global health emergency. Control of the disease has become increasingly difficult because of the alarming rise of antibiotic resistance in Mycobacterium tuberculosis, the etiological agent of TB. Development of new and effective drugs with novel mechanisms of action is thus of paramount importance to tackle antibiotic resistance. Novel chemical entities require at least a decade to be commercially available and repurposing drugs offers a solution to circumvent the investment of time and other resources. Certain common non-steroidal anti-inflammatory drugs (NSAIDs) have proven to be selectively bactericidal against replicating, non-replicating and multi-drug-resistant clinical isolates of M. tuberculosis. Our primary focus is to repurpose Carprofen and investigate their novel mechanisms of action in M. tuberculosis to help design more potent inhibitors in the future. To this effect we have followed both target-based and whole-cell approaches. Whole-cell transcriptomic analyses have revealed the effects of the drugs on a selected set of genes involved in key metabolic pathways that also play essential roles in antimicrobial resistance. Furthermore, the NSAIDs showed influence on the expression levels of proteins involved in cell-wall homeostasis and dormancy mechanisms. The most active NSAID, Carprofen was found to be a bactericidal drug that also inhibited the formation of mycobacterial biofilms and exhibited strong efflux pump inhibitory properties thus demonstrating their great potential in reversing antibiotic resistance.

Biography

Sanjib Bhakta following a BSc (Hons), MSc and a PhD in Molecular Biology & Biochemistry from world class Universities & Research Institutions in India. He joined the Oxford University, Department of Pharmacology as an ISIS Innovation Senior Research Scholar and shortly after he was awarded with a Wellcome Trust International Travelling Fellowship. He has graduated from The Queen’s College, University of Oxford completing a Second Doctoral Degree (DPhil) and received a “Sir William Paton Prize” in Pharmacology. He is currently a Reader in Molecular Microbiology and Director of ISMB Mycobacteria Research Laboratory at the Institute of Structural and Molecular Biology, University of London and UCL. He has published more than 50 original research articles in last 10 years for a number of internationally acclaimed journals. He is a Member of a number of international societies and Editorial Boards of peer reviewed international journals including OMICS group open access journal “Molecular Biology”. He was elected as a Fellow of the Royal Society of Medicine in 2008, received Academic Excellence Award in 2012 and awarded with a Cipla Distinguished Fellowship in Pharmaceutical Sciences in 2014. He is recognized as an “Antibiotic Action Champion” Member of the British Society for Antimicrobial Chemotherapy.

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