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### Repurposing common Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) could potentially reverse intrinsic drug resistance in superbugs

The rise of antimicrobial resistance is leading to ever-more untreatable illness. Intracellularly surviving bacterial pathogens have endogenous machinery to evade host defenses as well as antibiotic treatment. Drug efflux and formation of biofilms are the two key fundamental mechanisms of intrinsic resistance which render many antibiotics ineffective against them. *Mycobacterium tuberculosis* has unique multi-drug transporter protein complexes that allow the pathogen to take up nutrients for survival, while allowing it to extrude deleterious ones so as the signaling molecules for quorum-sensing leading to biofilm formation. Our work has shown that the Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) have anti-bacterial action against *Mycobacterium tuberculosis*. The most potent NSAID so far, at sub-inhibitory concentrations, inhibited whole-cell efflux pumps activity at par with/better than potent efflux pump inhibitors such as verapamil and chlorpromazine. In addition, the NSAID inhibited mycobacterial biofilm formation significantly. Analysis of the extracellular polymeric substances of treated biofilm showed macromolecular alterations compared to the untreated controls. Furthermore, transcriptomic analysis revealed modulation of key metabolic pathways in NSAID-treated *M. tuberculosis* revealing novel endogenous targets of the drug. The over-the-counter immunomodulatory drug's new antibiotic action has paved an alternative route for tackling antimicrobial resistance in TB.

### Biography

Sanjib Bhakta is a Reader (Associate Professor) in Molecular Microbiology and Biochemistry, Strategic Dean (International and Partnership) and Program Director of MRes Global Infectious Diseases at the Institute of Structural and Molecular Biology, Birkbeck University of London and UCL. His continued research interest in infectious bacterial diseases is focused on developing novel therapeutics as well as repurposing existing drugs to tackle antibiotic resistance and persistence in tuberculosis (TB), a global health and economic emergency. To date, he has published more than 100 original research articles for a number of internationally acclaimed journals.

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