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Repurposing common non-steroidal anti inflammatory drugs (NSAIDs) could potentially reverse intrinsic antimicrobial resistance in TB

Aims: Non-steroidal anti-inflammatory drugs (NSAIDs), successfully used against a range of human and animal illnesses, were reported to display antibiotic action against replicating, non-replicating and multi-drug-resistant clinical isolates of the tuberculosis (TB)-causing dreadful bacterial pathogen *Mycobacterium tuberculosis*. In this project, we have extended our investigation on NSAIDs anti-tubercular specific endogenous mode(s) and mechanism(s) of action.

Results: Interdisciplinary research methods were used to achieve the objectives of this project. 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.

Conclusions: NSAIDs have the potential to reverse antimicrobial resistance by inhibiting efflux pumps and biofilm formation.

Significance: The exponential increase of antimicrobial resistance in TB has led to an insurmountable economic and scientific challenge worldwide. Drug repurposing offers a direct route to phase III clinical trials, thereby reducing the investment of time and finances. 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 world-leading TB-expert and Academic Head of the ISMB-Mycobacteria Research Laboratory at the Institute of Structural and Molecular Biology. His continued research interest in global infectious diseases (funded by Wellcome Trust, Research Council-UK, EU and International Newton Fund) is focused on developing novel therapeutics as well as repurposing existing drugs to tackle antimicrobial resistance and persistence in TB. He has published around 100 original research articles for a number of internationally acclaimed journals viz. *J. Exp. Med.*, *J. Biol. Chem.*, *Tuberculosis, Biochemical Journal, Journal of Antimicrobial Chemotherapy, FEBS J, Molecular Microbiology, British Medical Journal, British Medical Bulletin, PLOS* and *Journal of Medicinal Chemistry*. As a UK-STEM Ambassador and BSAC-Antibiotic Action Champion, he has volunteered on the Wellcome Trust/Research Council-UK funded program "Researchers in Residence" at local schools in London and has contributed to British Museum science program "News & Views".

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