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Targeting host signalling AKT kinase pathway to overcome *Mycobacterium tuberculosis* infection

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Statement of the Problem: Tuberculosis (TB) is an ancient disease, but its treatment remains challenging because of development of drug resistance strains (MDR and XDR) by bacteria. Although there is lot of research going on, in development of new antibiotics targeting novel bacterial enzymes, as in case with existing antibiotics, resistance may ultimately rise against these drugs as well. This can be overcome by adopting a fundamentally new treatment approach. One such approach is targeting host rather than bacteria itself i.e. host directed therapeutics (HDT's). In this approach we target host biochemical pathway that is utilized by bacteria for its survival. HDT's might shorten the course of treatment, reduce the number of agents required in combination drug therapy, and simplify treatment of drug-resistant TB by improving the efficacy of second-line therapy and/or preserve lung function of TB patients. In the present study, we have synthesized a novel akt inhibitor which targets PI3K/Akt/mTOR signalling pathway of host.

Methodology: Peritoneal macrophages were isolated from mice infected with tb bacteria for four hrs. Then novel akt inhibitor was added and different biological assays were carried out to evaluate the efficacy of drug as per time point.

Findings: Our drug inhibited effective survival strategies of bacteria by promoting phagolysosome fusion, apoptosis and autophagy, this directly reduced bacterial burden on macrophages. We also observed decrease in cytokine and ROS expression.

Conclusion & Significance: We believe our drug can be used as an adjunctive therapy in treating tuberculosis disease and as we are targeting host pathway the likeliness of developing antibiotic resistance can as be reduced.

Biography

Nikhila Meda has completed her Bachelor of Science from Nizam College in the year 2008 and Master of Science in Biochemistry from Osmania university in the year 2010. She has worked as SRF at CRIDA an ICRA Institute for four years (2010-2014). She has been appointed as a PhD student in the Department of Pharmacy, BITS-Pilani, Hyderabad campus in the year 2015 under the supervision of Prof. D Sriram. She has three scientific publications in well-renowned international journals. She had presented papers at national and international conferences.

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