New Delhi, April 05: Mycobacterium tuberculosis’s engagement with the host's metabolic pathways is a known strategy employed by the pathogen to shift the balance in its favor. A team of researchers from DBT-Translational Health Science and Technology Institute (DBT-THSTI), Faridabad, and Jadavpur University, Kolkata analyzed high throughput proteomics data reflecting the response of the Macrophage-like THP1 cell line to M. tuberculosis infection.
The team integrated temporal proteomics data in genome-scale metabolic models (GSMM) giving context-specific GSMMs. PMA differentiated THP1 cells were infected with H37Ra, H37Rv, BND433 and JAL2287 strains of M. tuberculosis and the host response was studied at different time points after infection. Difference in quantitative dynamics of host metabolites showing common and/or unique response to infection with laboratory and clinical mycobacterial strains can be delineated using this methodology.

The group developed a modified flux balance analysis (FBA) which uses GSMMs to explore potential strategies to change the flux state of virulent M. tuberculosis infected macrophages as against their avirulent counterparts. This methodology gives a correlation between different flux states, the extent of which was interpreted as the extent of rewiring of GSMMs.

The accuracy of the results from the proposed methodology was confirmed using published gene knockout experimental data. The results showed that more than one reaction has to be rewired simultaneously to alter virulent to an avirulent response. The identified modules presented influence across the investigated strains and time points suggesting that these reactions could be therapeutically targeted.

The results will help in deeper understanding of the time-dependent modulations in host metabolism in response to M. tuberculosis invasion. Also, this novel methodology of extracting important information on metabolic reactions using proteomics data can be extended in other biological systems as well.

Complete paper

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