Targeting Host Immuno-Metabolic Circuits for Designing Interventions against TB

Abstract
An effective host immune response is important to control Mycobacterium tuberculosis (Mtb) insult, and to contain its latent persistence. Recent studies have revealed that cellular metabolic pathways fuel the cell fate decisions and regulate the maturation and effector functions of immune cells. Using chemical genetics approach we have found that activating metabolic sensors such as AMP-activated protein kinase (AMPK) and Sirtuin 1 (SIRT1) by FDA approved drugs / supplements could rewire host fitness against Mtb infection. This indicates a deep engagement of Mtb pathogenicity with host’s immuno-metabolic machinery. We hypothesize that the functional connections between immunity and pathways controlling metabolic signaling could be harnessed to advance the host-directed therapy (HDT) pipeline, leading to the development of clinically relevant anti-tuberculosis arsenal. The data related to this effort will be presented.


