CC-3052 accelerates bactericidal activity by Isoniazid and modulates expression of host genes involved in immune responses in experimental *M. tuberculosis* infection

Treatment of tuberculosis is increasingly complicated by the emergence of multi-drug resistant *M. tuberculosis* (Mtb) strains. We hypothesized that the modulation of host immunity by selective inhibition in TNF-α production in macrophages will alter the environmental pressure of the bacilli, rendering them more responsive to antibiotics. To test our hypothesis we used experimental animal models of infection via aerosol with Mtb. Animals were treated with Isoniazid, in the presence or absence of a small immune modulator molecule CC3052 that reduces TNF-α production. To understand how CC-3052 affects gene expression in the Mtb-infected mouse lungs, RNA samples were prepared from lungs at 21 and 28 days post-infection and were analyzed by microarray.

Our observations suggest that by modulating the expression of TNF-α and other cytokines in macrophages, CC3052 modifies bacillary physiology, leading to improved bactericidal activity of anti-TB drugs.