Abstract

The mycobacterial cell envelope is a chemically composite array of molecular units that has a significant role in the pathogenesis of *Mycobacterium tuberculosis* (*M. tuberculosis*). Biosynthesis and perpetuation of this complex system in mycobacterial pathophysiology remains poorly understood. Interestingly, about 3% of the *M. tuberculosis* proteome comprises of methyltransferases (MTases). The cross-proteomic comparison of MTases of *M. tuberculosis* H37Rv strain with 15 different mycobacterium species has identified an MTase which is exclusively present in pathogenic mycobacteria and not in opportunistic and non-pathogenic mycobacteria.

The in-silico data as well as the functional pathway analysis of Rv000S suggested that it is involved in fatty acid biosynthesis/metabolism pathway with a novel function in modifying the cell wall components. To further delineate the functional role of Rv000S, *Mycobacterium smegmatis*, a non-pathogenic surrogate of *M. tuberculosis*, was used due to logistic constraints. Rv000S was shown to alter growth pattern of recombinant *M. smegmatis* expressing Rv000S, resistance and increased survival under surface stress, acidic condition and antibiotics treatment. Additionally, *M. smegmatis* expressing Rv000S induced necrotic cell death of macrophage after infection and significantly modulated the host immune responses by decreasing the proinflammatory TNF-α and increasing the anti-inflammatory IFN-γ production. This thesis is an attempt to show that members of Methyltransferase family proteins and enzymes are important in imparting virulence, antigenicity and modulation of host pathogen interaction in tuberculosis. Therefore, a systemic functional analysis of these proteins will be helpful in designing effective preventive and therapeutic strategies against tuberculosis.