Tuberculosis (TB), caused by the intracellular pathogen *Mycobacterium tuberculosis* (*M. tb*), is responsible for around two million deaths per year worldwide. *M. tb* possesses myriad of mechanisms to infect and survive within the host. *M. tb* employs methyltransferases (MTases) to hijack the host transcriptional machinery through epigenetic regulation. Interestingly, around 3% of the *M.tb* genome encodes methyltransferases. Acquisition of the novel gene, Rv1515c, through horizontal gene transfer during reductive genomic evolution from non-pathogenic mycobacteria indicates its probable role in TB pathogenesis. Proteome analysis of the 121 methyltransferases of *M. tb* H37Rv, investigated till date, shows that several of these MTases are present only in *M. tb*. Most of the MTases in *M. tb* still remain uncharacterised, and further research is required to explore their mechanistic role in TB pathogenesis. Among these MTases, the hypothetical protein Rv1515 is exclusively present in the *M. tb* complex (MTBC) and is absent in the non-pathogenic strain of mycobacteria. This study explores the functional role of the *M. tb* Rv1515c hypothetical protein in virulence and pathogenesis of *M. tb*. 

*In-silico* analysis of *M. tb* Rv1515c revealed presence of S-adenosyl methionine binding site and conserved methyltransferase domain. *In-vitro* studies confirmed that Rv1515c exhibits DNA binding and DNA methyltransferase activity. Knock-in of *M. tb* Rv1515c gene in the non-pathogenic *M. smegmatis* strain lead to drastic morphological and physiological changes. The recombinant *M. smegmatis* was able to adapt and grow under extreme stress conditions, and exhibited pathogenicity. *In-vitro* treatment of recombinant *M. smegmatis* to macrophage showed enhanced uptake and survival by modulating phagolysosomal maturation. Recombinant *M. smegmatis* exhibited virulence by suppressing the host defence systems through lowering of NO (Nitric oxide), ROS ( Reactive oxygen species) production and suppressing apoptosis in the macrophages. Rv1515c modulated pro-inflammatory cytokines, inhibited antigen presentation and suppressed co-stimulatory molecules. Interestingly, recombinant *M. smegmatis* survived for longer duration and caused pathological conditions in several organs of the infected mice. We also observed that *M. tb* Rv1515c could reduce the effector T cells by increasing the Treg cells and downregulated activation markers on the macrophages. Notably, Rv1515c induced polarisation of macrophage towards M2 lineage in the peritoneal macrophage which favoured persistence of mycobacterial infection. Cumulatively, these results highlight the significant role of Rv1515c in *M.tb* pathogenesis and in modulating the host immune responses. 

This thesis demonstrates the role of Rv1515c in host-pathogen interactions during mycobacterial pathogenesis which may aid in devising novel therapeutic interventions against TB.