Tuberculosis is a major cause of mortality worldwide. Protective immunity against *Mycobacterium tuberculosis* is mediated by variety of innate and adaptive immune mechanisms. The immune response against *Mycobacterium tuberculosis* (*M.tb*) is complex. Macrophages play a peculiar role in the host response as they represent both, the primary effector cells for bacterial killing and the primary habitat in which the persisting bacilli reside. Thus, during the infection a dynamic cross-talk occurs between the host and the pathogen in which they reciprocally influence their gene expression profiles. The development of the immune system and the host response to microbial infection rely on the activation and silencing of numerous, differentially expressed genes. In post-genomic era, the availability of variety of experimental animal models has produced enormous information about tuberculosis pathogenesis and immunity. More recently, there has been a growing appreciation on the role of chromatin structure in gene regulation by *cis* regulatory elements and *trans* acting factors. SMAR1 (Scaffold Matrix Attachment Region binding Protein 1) is a MAR (matrix attachment region) binding protein, which interacts with the regulatory region (promoters/enhancers) of genes and potentially controls the transcriptional activity. It has also been shown to play a crucial role in modulating the chromatin structure and controlling gene expression.

The present thesis entitled, “Studies on understanding the regulation of host immune response upon *Mycobacterium tuberculosis* infection”, covers five chapters along with bibliography, summary, future perspectives and appendix. The present study is designed to understand the role of nuclear matrix associated chromatin remodelling protein SMAR1 in tuberculosis infection.

The Chapter 1 introduces the subject of the present thesis, giving an outline of the origin and purpose of the work carried out.

The Chapter 2 has given extensive review of published literature on the subject, followed by the origin, aim and specific objectives of the present thesis work. Details of pathogenesis of tuberculosis, various innate and adaptive immune responses against *M.tb*, modulation of host-pathogen interactions due to *M.tb* antigens (ESAT-6, CFP-10) in macrophages, genome wide studies and the animal model for studying
*M. tb* are discussed. Genomic organization of SMAR1 and its functional role in cellular processes is also elaborated.

The Chapter 3 covers all the materials and experimental procedures used in the study. The study design included detailed information on the techniques, such as generation of transgenic mice, genotyping, *in-vivo* mice infection procedures, *in-vitro* methods, mammalian cell culture and several other molecular methods employed in this study.

The Chapter 4 details the findings of the first objective of the thesis. It describes all the results obtained from *in-vivo* infection experiments performed on SMAR1 transgenic and T cell specific conditional knockout mice. It also focusses on understanding the regulation of IFN-γ gene by SMAR1 at transcriptional level.

The Chapter 5 describes the findings under the second objective of the present work, i.e., to understand the role of *M. tb* secretory antigen ESAT-6 in the regulation of SMAR1 expression. The thesis has been summarized at the end. Bibliography has provided the list of all the references quoted in the present thesis. The Future Perspectives gives the idea about how one can make use of the present observations, extrapolate the findings of this study and the potential role of SMAR1 in the regulation of host immune response at molecular level. The list of publication and manuscripts communicated is appended at the end.