The interaction of the macrophages with a pathogen determines the outcome of infection. Importantly, modality of the cell death of infected macrophages governs the cascade of TB pathogenesis. Necroptosis helps a virulent pathogen to multiply and escape from the infected cells and infect other bystander cells. The relevance of the host HO-1 in cellular defense with particular emphasis on the Mtb induced necroptosis has been summarized in **Chapter 1.** Importantly, many published studies suggest both positive and negative regulation of HO-1 in modulation of Mtb induced necroptosis. Therefore in **Chapter 2** of the thesis, we have generated multiple lines of evidence to conclude that induction of necroptosis is dependent on the bacillary load and virulence of Mtb. We can conclude that RD-1 region mediated virulence is required for initiation of programmed necrosis in the host cells. We have also demonstrated a direct nexus of the bacillary load in triggering programmed necrosis. Mycobacterial infection leads to increased ROS that derives the formation of the necrosome and activation of p-MLKL that eventually leads to rupturing of cells (Roca and Ramakrishnan, 2013; Zhao et al., 2017). In **Chapter 3** of thesis, we have analyzed whether Mtb infection induces the canonical signaling pathway of necroptosis *in-vitro* and *in-vivo*. Using co-immunoprecipitation of RIP1 and RIP3 necrosome formation and its terminal MLKL enzyme activation, we have demonstrated that upon Mtb infection with high MOI of 1:20, Mtb induces necroptotic cell death which is canonical and depends upon the activation of RIP1, RIP3, and MLKL. In **Chapter 4** of thesis, we report for the first time that the host anti-inflammatory regulator, HO-1 acts at a post-translation level in the host necrosome assembly. We have shown that RIP3 protein is modified by K63 ubiquitination through post-translation modification which is dependent on the HO-1 enzyme activity. After using a pharmacological inhibitor of HO-1 enzyme (ZnPP), we found that RIP1 and RIP3 necrosome formation is reduced which consequently decreases the Mtb induced necroptosis in host cells.. This suggests that HO-1 is a regulator of Mtb induced host necroptosis.