

Summary:

The Present work focuses on understanding the role of *phoP* locus in global heat-shock response of Mtb. The subject of the study was introduced in chapter 1 then, in Chapter 2, we emphasize on understand global effect of *phoP* locus on global heat-shock response. Initially we started with effect of *phoP* on survival of bacterium under heat-stress for extended time points and could observe that *phoP* mutant strain was more susceptible to heat-shock condition compared to wild type strain. Next, we analyzed the total transcriptome of wild type of *phoP* mutant strain of Mtb using microarray platform under normal and heat-shock condition. Microarray data gave us the global view of effect of *phoP* locus on heat-shock responsive gene expression which shows, *phoP* affects 45% of heat-shock responsive genes. Further, chapter 3 focuses on understanding mechanism of action of PhoP in regulating gene expression of heat-shock responsive genes. The results in observed unravel the mechanism of regulation of heat-shock responsive genes. We observed that PhoP has dual mode of regulation, it can act as repressor as well as activation in stress dependent manner. The interaction of PhoP with both global heat-shock repressors HrcA and HspR is crucial for regulation heat-shock responsive genes. The presence of PhoP in found to prerequisite for efficient recruitment of respective heat-shock repressors on the target promoter. In chapter 4, we attempted to understand the molecular details of PhoP-HrcA and PhoP-HspR protein-protein interaction so that we could identify the PhoP residues involved in interaction. We could biochemically validate the model generated using ZDOCK server but more efforts are undergoing to know the particular residues of PhoP involved in protein-protein interaction.