出口重复蛋白（Erp），也称为P36、Pirg和Rv3810，是一种M. tuberculosis的胞外/分泌蛋白，已被证明是重要性病原体的决定性因素。Erp蛋白在营养限制条件下高度上调。Erp基因的破坏（Erp-）在M. tuberculosis和M. bovis BCG中导致了显著的毒力衰减，而在H37Rv和BCG菌株之间没有观察到生长特性的差异（Berthet et al., 1998）。Attenuation of the growth of erp in M. tuberculosis only in the infected macrophage and not in vitro, suggests that the Erp protein somehow modulates the environment within the host macrophages. Despite many efforts, the biological roles of this virulence factor during host infection remain elusive.

In order to gain insight into the function of the secretory Erp protein within the host, we have explored interacting partners of Erp from mouse macrophage library. The Erp protein devoid of its signal sequence (ΔAssErp) was used as a “bait” to fish out the “prey” protein encoded by mouse macrophage cDNA library using yeast two hybrid assay. After analysis, homology search and sequencing, nine putative interacting host partners of ΔAssErp were identified. One of the identified putative interacting partners of ΔAssErp was LDHA. ΔAssErp and LDHA interact directly with each other under in vitro, as demonstrated by GST pull down assays and also under in vivo conditions as shown by Co-immunoprecipitations. The deletion of PGLTS, COOH and SRC domains of Erp protein has no effect on the interaction with LDHA whereas deletion of amino terminus abrogates its interaction with LDHA. This result is consistent with our finding that ΔAssErp resides in the cytoplasm whereas the ΔNH2Erp localizes to the nucleus. Furthermore, a doublet of ΔAssErp was observed in the immunorecipients and in the lysates of cells upon over-expression, suggesting posttranslational modification(s) of ΔAssErp protein in the mammalian cells. Also, increased expression levels of LDHA were observed when it was co-transfected along with ΔAssErp. Unlike ΔAssErp of M. tuberculosis, the ΔAssErp protein from non-pathogenic M. smegmatis does not interacts with LDHA and thus render this interaction specific to pathogenic strain. Confocal studies revealed that both Erp and ΔAssErp localized in the cytoplasm of CHOK1 and THP1 macrophage whereas ΔNH2Erp localized predominantly in the nucleus. The Erp
and ΔssErp protein co-localized with LDHA in the cytoplasm whereas ΔNH2Erp being nuclear in localization did not co-localize with LDHA. *In-vitro* activity assay revealed 7 fold increase in the enzymatic activity of GST-LDHA after treatment with purified recombinant ΔssErp protein whereas no significant change in the activity was observed after treatment with purified recombinant ΔNH2Erp protein. Moreover, three fold increase in LDHA activity of THP1 was observed after treatment with purified ΔssErp whereas ΔNH2Erp had no significant effect. Further, LDHA, SPT2 and Erp appeared to indicate that they are associated in a common pathway related to metabolism of sphingosine.

In total, we found that Erp protein of *M. tuberculosis* interacts with LDHA and modulates its activity. Further studies are required to understand the mechanism involved in the Erp mediated upregulation of LDHA activity and to understand the significance of the Erp and LDHA interaction in the intracellular survival of *M. tuberculosis* within the host. Also, the post translational modification(s) of Erp in the mammalian system needs to be identified and their role in the regulation of the interactions and modulation of host cell biology needs to be explored further.