PknE, a Serine / Threonine kinase from *Mycobacterium tuberculosis* modulates apoptosis and arginase signalling in macrophages

Dinesh Kumar P and Sujatha Narayanan
Department of Immunology, National Institute for Research in Tuberculosis (ICMR), Chennai

Introduction

Pathogenic microbes evade host innate immunity using virulence factors enabling survival and persistence. The mechanisms of immune subversion are of great interest as it provides insights in to the pathogenesis and aids in the development of new therapeutics. *Mycobacterium tuberculosis* (MTB), the causative organism of tuberculosis was found to survive inside the macrophages through the inhibition of apoptosis. The aim of the present study was to identify the apoptotic phenotypes suppressed by PknE of MTB.

Material and methods

The THP-1 cellline was differentiated into macrophages and infected with the strains *M. tuberculosis* H_{37}Rv (wild-type), *M. tuberculosis* H_{37}RvÄPknE (mutant) and complemented H_{37}RvÄPknE. On day 5 post infection microarray analysis was carried out. Subsequently the genes involved in apoptosis, arginase pathway and immune responses, were validated using oligoGE array and qReal-Time PCR.

Results

The deletion mutant of PknE shows a highly activated macrophage transcriptional program. The mutant showed increased pro-apoptotic molecules like BAX, BID of intrinsic pathway of apoptosis with decreased pro-inflammatory cytokines. The decrease in pro-inflammatory response correlated with increased SOCS expression that negatively regulates cytokine signalling. Interestingly, the expression of arginaseI, arginosuccinate lyase and iNOS were decreased.

Conclusion

PknE enhances survival of *M. tuberculosis* inside the macrophages by inhibiting signals that activate apoptosis.

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