BBSRC Strategic Research Priority

Food security

- Microbiology

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PhD project title: Serine/threonine protein kinase mediated regulation of protein secretion in mycobacteria

University of Registration: University of Leicester

Project outline

1. Project outline describing the scientific rationale of the project (max 4,000 characters incl. spaces and returns)

   Tuberculosis remains a major global threat as it affects humans and production animals. *Mycobacterium tuberculosis* and *Mycobacterium bovis*, the causative agents of tuberculosis in human and animals, are highly successful pathogens which secrete multiple virulence factors. Despite great progress in understanding the role of secreted proteins in virulence of mycobacterial pathogens, molecular mechanisms controlling their secretion are poorly understood. In particular, several recent *M. tuberculosis* proteomics studies showed that many components of secretion systems and secreted proteins themselves are phosphorylated, suggesting that this post-translational modification may play a regulatory role.

   *M. tuberculosis* and *M. bovis* possess eleven serine/threonine protein kinases and two of them, PknA and PknB, are essential for the growth of these pathogens. Our recent findings suggest that PknB can phosphorylate several components of secretion systems and secreted proteins involved in mycobacterial virulence, development of pathology and transmission.

   The proposed project will elucidate the importance of serine/threonine protein phosphorylation for secretion of mycobacterial proteins.

   Recent papers from our laboratories in a related area:

Techniques that will be undertaken during the project

The project will involve the following methods:
Genetic manipulation of mycobacteria, generation of deletion and over-expression mutants
Growth assays
Proteomics and phosphoproteomics analysis of secreted proteins
Generation of recombinant proteins and phosphorylation assays
Pull-down assays and mycobacterial protein fragment complementation assays