

Title: Regulation of protein secretion by serine/threonine protein kinases in mycobacteria

Application Deadline: Applications accepted all year round

Supervisor: Dr Galina Mukamolova

Email: gvm4@le.ac.uk

Funding: Self-funding only

Summary:

Mycobacterium tuberculosis, the causative agent of tuberculosis, possesses 11 serine/threonine protein kinases (STPK). STPK are involved in mycobacterial, growth, division, virulence and biofilm formation. Recent proteomics studies revealed that many proteins involved in secretion are phosphorylated. These include TatA, FtsY and proteins of ESX1 type VII secretion system. While FtsY and TatA are essential for growth of *M. tuberculosis*, EsxA and EsxB are critical for *M. tuberculosis* virulence. However, the precise role of phosphorylation in function of these secretion proteins is unknown.

The proposed project will be aimed to investigate the influence of phosphorylation on function of secretion systems and protein-protein interactions. Experimental will include generation of deletion and conditional mutants in mycobacteria, mycobacterial two hybrid system, production and purification of recombinant proteins, in vitro phosphorylation, proteomics and secretomics, infection studies.

Publications

1. Barthe, P Mukamolova GV, Roumestand C, Cohen-Gonsaud M. (2010). The structure of the PknB extracellular PASTA domain from *Mycobacterium tuberculosis* suggests a ligand-dependent kinase activation. *Structure*, 18(5): 606-15.
2. Turapov O, Loraine J, Jenkins CH, Barthe P, McFeely D, Forti F, Ghisotti D, Heseck D, Lee M, Bottrill AR, Vollmer W, Mobashery S, Cohen-Gonsaud M, Mukamolova GV. (2015). The external PASTA domain of the essential serine/threonine protein kinase PknB regulates mycobacterial growth. *Open Biology*, 5(7): 150025.