Structural Studies of Mycobacterial Protein Kinases and Phosphatases

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Mycobacterium tuberculosis pathogenicity relies on the peculiar ability of this microorganism to survive and replicate in human macrophages, establishing persistent infection. To understand the pathogen response to the host's environment, we are studying signaling proteins that are presumed to play an important role in the processes that regulate the complex life cycle of mycobacteria.

Two genes encoding the Ser/Thr kinases PknA and PknB, which have been described as essential by saturation mutagenesis [1], are found in a single conserved operon that also includes the gene pstp encoding the only Ser/Thr phosphatase in the mycobacterial genome. The crystal structures of PknB [2] and PstP have recently been determined in our laboratory. Both structures confirm the extraordinary conservation of the protein folds and catalytic mechanisms across the evolutionary distance between eukaryotes and prokaryotes.

We will present a comparative study of these proteins and further characterisation of protein-protein and protein-ligand interections that could be involved in a putative signaling pathway of *M .tuberculosis.*

[1] Sassetti, et al., *Mol. Microbiol*. 2003, **48**, 77-84. [2] Ortiz-Lombardia, et al*., J. Biol. Chem.,* 2003, **278**, 13094-13100.

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