

## College PhD Studentship in Microbial Science Research

**Studentship Number:** BBSRC/10/04

**Primary Supervisor:** Dr G Mukamolova  
Tel: 0116 229 7053  
Email: [gvm4@le.ac.uk](mailto:gvm4@le.ac.uk)  
Department of Infection, Immunity & Inflammation

**Co-supervisor:** Professor M D Carr [mdc12@le.ac.uk](mailto:mdc12@le.ac.uk)  
Department of Biochemistry

**Host Department:** Department of Infection, Immunity & Inflammation  
University of Leicester

**Project Title:** Mycobacterial resuscitation-promoting factors (Rpf): roles and mechanisms in infected macrophages

### **Project Description**

Nearly 2 million people die every year from tuberculosis and one third of the entire world population carries the infection in a quiescent form known as latency. The mycobacterial cells associated with latent tuberculosis are believed to be in a special non-replicating state known as dormancy. The precise mechanisms underlying the transition to the dormant state and in particular resuscitation remain unknown. Resuscitation-promoting factors are a family of secreted muralytic enzymes produced, which have been implicated in many processes, including resuscitation of dormant cells, intracellular growth and modulation of the cytokine response of infected macrophages.

The main goal of the project is to investigate the functions of individual Rpf proteins from the model microorganism *Mycobacterium marinum* in infected macrophages. Experimental approaches will include the expression and purification of recombinant Rpfs, generation of specific antibodies, localization studies; generation of deletion mutants and analysis of their phenotype *in vitro* and *in vivo*, and characterisation of potential protein-protein interactions of Rpf proteins with other secreted proteins. Expression patterns of individual Rpfs will be studied at both the RNA (qRT-PCR) and protein (immunoblot and fluorescence microscopy) levels.

**Application deadline: March 10<sup>th</sup> 2010.**

Relevant publications:

1. Mukamolova, GV, Turapov, OA, Young, DI, Kaprelyants, AS, Kell, DB, Young, M. (2002) A family of autocrine growth factors in *Mycobacterium tuberculosis*. **Mol.Microbiol.**46: 623-35
2. Mukamolova, GV, Murzin, AG, Salina EG, Demina, GR, Kell, DB, Kaprelyants, A S, Young M. (2006) Muralytic activity of *Micrococcus luteus* Rpf and its relationship to physiological activity in promoting bacterial growth and resuscitation. **Mol. Microbiol.** 59: 84-98.
- 3.Kana BD, Gordhan BG, Downing KJ, Sung N, Vostroktunova G, Machowski EE, Tsenova L, Young M, Kaprelyants A, Kaplan G, Mizrahi V. **Mol Microbiol.** (2008) 67(3):672-84. The resuscitation-promoting factors of *Mycobacterium tuberculosis* are required for virulence and resuscitation from dormancy but are collectively dispensable for growth *in vitro*.
4. Mukamolova, GV, Turapov, OA, Malkin J, Woltmann G, Barer, MR(2010) Resuscitation Promoting Factors reveal an occult population of tubercle bacilli in sputum. **Am J Respir Crit Care Med.**, 181: 174-180.