Title: Nutritional virulence: how is the metabolism of Mycobacterium tuberculosis adapted to the pathogenic lifestyle?

Application deadline: Applications accepted all year round

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Funding: **Self-funding only**

In 2011 there were 8.7 million new cases and 1.4 million deaths worldwide from tuberculosis. Understanding how Mycobacterium tuberculosis causes disease is a vital part of developing improvements to treatment and prevention. The intracellular nutrition of M. tuberculosis is poorly understood but it is clear that bacterial metabolism is linked to virulence.

Research in my group focuses on the regulation of central carbon and nitrogen metabolism. Recently we have shown that M. tuberculosis has a complete TCA cycle that is regulated by the activity of protein kinase G, a protein known to be associated with virulence. Protein kinase G also regulates glutamate metabolism. These pathways appear to be particularly vulnerable in M. tuberculosis, making potentially interesting for inhibition as a new strategy for drug development.

Ongoing research aims to explore the reason for this vulnerability and improve the understanding of M. tuberculosis metabolism during infection and metabolic interactions with the host.

Students within my group receive training in modern techniques of microbiology, biochemistry and molecular biology, in addition to the broad training programme offered to all PhD students at the University. There is a concentration of Tuberculosis research groups in the University and students become involved in collaborations within Leicester, the rest of the UK and Europe.

Recent review:

Mycobacterium tuberculosis and the intimate discourse of a chronic infection.

Russell DG. Immunol Rev. 2011 Mar;240(1):252-68. Free PMC Article

Relevant papers from my lab:

1. Rieck B, Degiacomi G, Zimmermann M, Cascioferro A, Boldrin F, Lazar-Addler N, Bottrill A, le Chevalier F, Frigui W, Bellinzoni M, Lisa M, Alzari P, Nguyen L, O'Hare, H (2017) PknG senses amino acid availability to control metabolism and virulence of Mycobacterium tuberculosis, PLoS Pathogens 13(5) http://journals.plos.org/plospathogens/article?id=10.1371/journal.ppat.1006399

2. Ventura M, Rieck B, Boldrin F, Degiacomi G, Bellinzoni M, Barilone N, Alzaidi F, Alzari PM, Manganelli R, O'Hare HM. (2013) GarA is an essential regulator of metabolism in Mycobacterium tuberculosis. Mol Microbiol. 90(2):356-66.

3. Wagner T, Bellinzoni M, Wehenkel A, O'Hare HM, Alzari PM (2011) Functional plasticity and allosteric regulation of alpha-ketoglutarate decarboxylase in central mycobacterial metabolism. Chemistry & Biology 18(8) 1011-1020.

4. Nott TJ, Kelly G, Stach L, Li J, Westcott S, Patel D, Hunt DM, Howell S, Buxton RS, O'Hare HM, Smerdon SJ (2009) An intra-molecular switch regulates phospho-independent FHA domain interactions in Mycobacterium tuberculosis. Science Signaling 2 (63) ra12..