Prof M Carr - Molecular basis of tuberculosis pathogenesis.

Research in my group is focussed on determining the structures, functions, interactions and mechanisms of action of proteins and protein complexes involved in key biological processes of significant medical importance. A major component of this work has been the successful use of NMR-based methods to determine new protein structures and to investigate protein-drug, protein-protein and protein-DNA interactions. The ongoing research in my group aims to integrate the information obtained from molecular, cellular and structural biology-based approaches to provide a detailed understanding of the function of proteins involved in disease states, which is an essential prerequisite for a rational, knowledge-based approach to drug discovery and development. In addition, through close collaboration with pharmaceutical companies such as UCB-Celltech we aim to make a major contribution to the design and development of important new drugs, such as therapeutic antibodies targeted at secreted signalling proteins (cytokines, chemokines, etc.) or cell surface receptors.

Tuberculosis remains one of the most significant bacterial diseases of humans, with about one third of the world's population infected resulting in over 2 million deaths annually. Research in my group is focussed on determining the structures, functions and mechanisms of action of major *M. tuberculosis* and *M. bovis* protein virulence factors, including a number of members of the ESAT-6/CFP-10 family, components of the novel secretory system for the ESAT-6.CFP-10 complex and MPB70. We have recently shown that several of the secreted proteins under investigation play key roles in pathogen to host cell signalling and identification of host cell proteins that interact with these mycobacterial proteins, together with determination of their affects on host cell behaviour, are major focuses of ongoing research. This work is a collaboration with groups at the National Institute for Medical Research (Dr Roger Buxton), University of Kent (Dr Richard Williamson), University College, Dublin (Prof. Stephen Gordon) and with several colleagues at Leicester (Dr Bernard Burke, Dr Helen O'Hare, Dr Galina Mukamolova and Prof. Mike Barer). My research group is also an active member of the *Mycobacterium Tuberculosis* Structural Genomics Consortium, which involves over fifty research laboratories across the world.

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