Prof M Carr - Structure-based drug design.

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

High resolution structural information for proteins and protein-ligand complexes now plays a major role in the design, optimisation and patent protection of new therapeutic molecules. In close collaboration with medicinal chemistry, protein biochemistry, molecular biology and therapeutic antibody groups at UCB-Celltech (Dr Richard Taylor, Dr Alistair Henry, Dr Martin Robinson and colleagues) we are using NMR-based methods to determine the structures of validated protein drug targets, to map the binding sites for candidate drugs on proteins, and to determine the orientations and conformations of potential drugs bound to target proteins. This approach has proved to be highly successful and informative for both traditional small molecules and for a wide range of potential therapeutic antibodies (scFv and Fab). We are also developing new, improved and more rapid NMR-based approaches to obtain detailed structural information for large protein-drug complexes (50-100 kDa).

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