Structural Biology, Biomarkers and Drug Discovery

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Group Overview

Our research focuses on the molecular basis of cancer causation and progression, and seeks to characterise the mechanisms of cancer targets, as well as discover new diagnostic and therapeutic agents.

Our Research Group

Cancer is a family of diseases that involve uncontrolled cell division and tissue invasiveness upon the accumulation of gene mutations in proto-oncogenes and tumour suppressors. Understanding the structural and molecular mechanisms involved provides opportunities to detect cancer earlier and treat more effectively.

Our groups' interdisciplinary studies are directed toward understanding desmosomal adhesion, nuclear receptors, signalling and trafficking proteins and immune receptors. Cancers being studied include brain and nervous system, oesophageal , colorectal, breast, leukaemia and immune inflammation.

These studies make use of advanced methods being developed using mass spectrometry, microarrays, NMR and X-ray crystallography facilities.

Current projects

We are elucidating how proteins including FAPP2 bind to and reshape the Golgi membrane into thin tubules that are pinched off to traffic to the cell surface. A wedge mechanism explaining how tubules are formed by the insertion of pleckstrin homology domains into the bilayer is being developed.

The changes in the conformation and activity of a Ser/Thr kinase which is amplified during breast cancer progression are being analysed by nuclear magnetic resonance spectroscopy (NMR), small angle X-ray scattering (SAXS) and X-ray crystallography. The effects of calmodulin and inhibitor binding include conformational changes that propagate across the enzyme structure and suggest novel sites for intervention.

The mechanisms of membrane recruitment by oncogenic protein phosphatases are being characterised by NMR. We have obtained resolved NMR spectra of several targets by solution condition screening, enabling characterisation of their solution structures and interactions. The lipid binding surfaces and specificities are diverse, and localise the proteins to distinct subcellular and membrane destinations.

The structures of the components of the beta barrel assembly machine (BAM) proteins used by pathogenic bacteria are being revealed by NMR and small angle X-ray scattering. Understanding how proteins are folded up inside the membrane that surrounds bacteria may provide new targets for the discovery of next generation antibiotics to combat a wide range of infectious diseases.

We have developed a new bionanoparticle system to purify and solubilise transmembrane proteins without detergents, thus circumventing one of the major bottlenecks of drug discovery for transmembrane receptors. A styrene maleic acid co-polymer transfers membrane proteins directly into 11 nanometer diameter discs that are soluble, stable and easy to work with, and stabilise membrane proteins with their activities and structures intact.