CHEMICAL BIOLOGY

Our research interests lie in the application of small molecules to biological systems, which involves new and exciting multidisciplinary approaches incorporating molecular biology, organic synthesis, analytical chemistry, NMR spectroscopy, computational chemistry and biochemistry to solving medicinally relevant problems. We are particularly interested in marine natural products and fluorescent natural products, their biological activity, biosynthesis and most importantly, their modes of action as drugs and applications in biotechnology.

CHEMICAL BIOLOGY OF NATURAL PRODUCTS

We focus on changing the way people think about drug discovery by changing the way we work with the interactions between small molecules and biomolecules. This requires the development of new tools that accelerate our understanding of how drugs facilitate change in living systems. This paradigm shift in the relationship between chemical diversity and biological activity will lead to the reinvigoration of the pharmaceutical industry through the rapid development of new drugs based on natural products.

PHAGE DISPLAY AND YEAST SURFACE DISPLAY

The genetic manipulation of bacteriophages and yeast to display foreign proteins on their surface as part of a cDNA or genomic library. Such “libraries” are very useful for the unbiased and rapid identification of proteins that bind to small molecules. We named this field “Reverse Chemical Proteomics”. Working in this area requires crossing disciplinary boundaries so progress can be slow at times but always exciting and challenging. Current projects include:
- identification of the human, bacterial and Plasmodium targets for bioactive natural products;
- isolation and structure elucidation of new natural products;
- synthesis of biotinylated and fluorescently labelled probes;
- construction of high quality gDNA and cDNA libraries for phage display and yeast surface display and methods for biopanning.

BIOMIMETIC SYNTHESIS OF NATURAL PRODUCTS

Nature not only provides small molecules to modulate protein function but also provides clues on efficient methods of constructing (biosynthesising) small molecules. Applying these principles to ageladine A, we developed a 3-step synthesis of this compact natural product that was highlighted in C&E News and was much shorter than an 11-step synthesis published in the same year. Current projects include:
- biomimetic and semi-synthesis of natural products and analogues.
Discoveries in my group resulted in the commercialisation of a fluorescent natural product (epicoconone) and the establishment of a spin-off company (Fluorotechnics) that listed on the Aust. Stock Exchange in 2008. We have also discovered other new highly-fluorescent natural products from marine sponges, microbes and plants. Projects in this area all involve commercially-relevant research to address specific needs in medicine, biotechnology and research where tailored fluorophores can improve current techniques or open the door to completely new areas. Projects include:

- discovery of new fluorescent natural products;
- synthesis of analogues of the fluorescent natural products such as ageladine A and epicocconone;
- synthesis of analogues of the GFP chromophore with dual emission;
- design, synthesis and computational chemistry of novel fluorescent probes.

The last project includes suicide turn-on or switchable fluorophores that can be used to covalently label specific enzyme types and used to visualise the location of the enzymes inside cells and then use the fluorophore as a mass tag to identify the exact protein modified using MALDI mass imaging and standard proteomics techniques.

Selected Publications
