The widespread use and misuse of antibiotics, both clinically and agriculturally, has led to a dramatic increase in the prevalence of antibiotic-resistant strains of pathogenic bacteria, particularly in hospitals. New resistance mechanisms are transferring rapidly between different species of bacteria, imparting broad-spectrum antibiotic resistance to an ever-increasing microbial population. If this disturbing trend continues, deaths from previously treatable bacterial infections will soon return to levels experienced in the early 20th century, before the dawn of the antibiotic era.

Our group works at the exciting and challenging interface between chemistry and biology to identify, isolate, characterise and develop next-generation antibiotics that are effective against these deadly superbugs. Projects are available spanning a range of areas, from natural products chemistry and organic synthesis, to chemical biology and chemical proteomics. Please see the descriptions below for two specific project examples, or feel free to contact me to discuss other possible projects.

**MICROBIAL BIODISCOVERY**

Natural products have long been a mainstay of the pharmaceutical industry, with almost 70% of the FDA approved antibiotics either derived from, or inspired by, natural products. These figures are not surprising when you consider that natural products have evolved through millions of years of natural selection in biological systems to interact with biological systems. The technology for pursuing natural products has matured considerably over the last three decades, making it possible to investigate the chemistry and biology of structurally novel and diverse metabolites present at sub-milligram levels in complex extracts.

In this project, you will use the latest HPLC, LCMS and NMR techniques to isolate, elucidate and characterise potent and/or selective new antibiotics from a range of unique microorganisms provided by our collaborators at Microbial Screening Technologies in Sydney. You will assay these new antibiotics against a range of clinically important microorganisms, both in-house and in collaboration with leading national and international infectious disease researchers. The cellular targets and modes of action of these antibiotics will also be investigated in collaboration with other group members (see following project).
PHAGE DISPLAY

The substantial costs associated with getting a new drug to market mean that early prioritisation of leads is essential. The most significant challenge facing modern antibiotic chemotherapy is the impact of multidrug-resistance, so a key factor in the prioritisation equation must be "mode of action". New antibiotic scaffolds that operate by the same compromised pathways as known antibiotics are clearly less attractive than those that operate by entirely new uncompromised pathways. The prioritisation of natural product antibiotics presents significant challenges as their cellular targets and modes of action are generally not known. Inevitably, these molecules end up being published as basic science or simply abandoned, squandering countless invaluable antibiotic drug leads.

In this project, you will use T7 phage display to identify the cellular targets of both new and historic (abandoned) antibiotic natural products, allowing their modes of action to be determined and facilitating their prioritisation and development as chemotherapeutic agents. This multidisciplinary project draws on a range of techniques from chemistry and biology, including organic synthesis, molecular biology and biochemistry. Projects are also available to construct new bacterial T7 phage display libraries from a range of clinically important pathogens and other model organisms. Please contact me for further details!

Selected publications


cbms.mq.edu.au/~apiggott