

# Dr Dominic Campopiano

## Senior Lecturer in Organic Chemistry

e-mail: [Dominic.Campopiano@ed.ac.uk](mailto:Dominic.Campopiano@ed.ac.uk) tel: 0131 650 4712

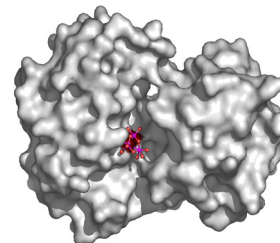
Research Interests: natural product biosynthesis, enzymology, protein structure, antibiotics, defensins, antimicrobial resistance, iron uptake, innate immunity



Our research group studies the structure, function and mechanism of action of various enzymes, proteins and natural products involved in interesting biological processes. We are particularly interested in the interactions between bacterial pathogens and their human hosts.

### Enzyme structure/function

We are interested in a range of protein targets which are involved in essential metabolic reactions such as drug detoxification, metal uptake and vitamin-dependent, post-translational modifications e.g. Glutathione S-Transferases (GSTs), Ferric binding proteins (FBPs), Biotin Protein Ligases (BPLs).



### Defensins

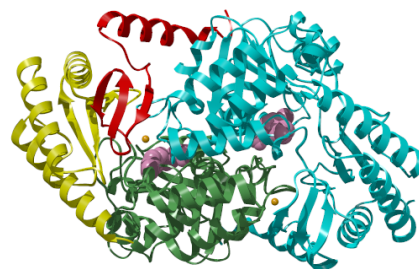
Mammals have a range of self-defense mechanisms as part of their innate immunity. Defensins are a small family of antimicrobial peptides (AMPs) characterized by their +ve charge, conserved cysteine residues, disulfide bonds and 3D fold. In collaboration with various colleagues within "Team Defensin" we have characterised various peptides including Defr1, a novel mouse defensin. Defr1 kills a broad range of pathogenic bacteria and is a dimeric peptide held together by an unusual intermolecular S-S bond.

### Antibiotic resistance

We are part of a team "The UK Cystic Fibrosis Microbiology Consortium" which brings together scientists and clinicians with complementary expertise funded by grants from the Big Lottery Fund and the Cystic Fibrosis Trust, ([www.cfmicrobiology.org.uk/](http://www.cfmicrobiology.org.uk/)). Together we are characterising the mechanisms of resistance to antimicrobial agents in the major CF pathogens, with a view to develop novel antimicrobial agents. *Burkholderia* infections are extremely hard to treat since they are resistant to most antibiotics. In collaboration with Profs John Govan and Miguel Valvano (London, Ontario) we have discovered a weak link in the armour of this pathogen. Mutation of a gene cluster which encodes a putative lipopolysaccharide (LPS)-modifying pathway is lethal to *Burkholderia cenocepacia*. I am organiser of the 2008 RSC conference "Antibiotics – where now?" ([www.rsc.org/ConferencesAndEvents/RSCConferences/antibiotics08/](http://www.rsc.org/ConferencesAndEvents/RSCConferences/antibiotics08/)).

### Sphingolipid biosynthesis

We are also interested in how bacteria, mammals and fungi produce sphingolipids – these are key components of the cell membrane and play roles in regulation and metabolism. In collaboration with Prof. Jim Naismith (St. Andrews), we have determined the structure of Serine palmitoyltransferase (SPT) in the sphingolipid biosynthetic pathway. This work provides a platform for future studies to explore the molecular basis of human disease and the mechanism of a complex enzyme.



### SELECTED RECENT PUBLICATIONS

1. B. A. Yard, L. G. Carter, K. A. Johnson, I. M. Overton, M. Dorward, H. Liu, S. A. McMahon, M. Oke, D. Puech, G. J. Barton, J. H. Naismith & D. J. Campopiano The Structure of Serine Palmitoyltransferase; Gateway to Sphingolipid Biosynthesis. *J. Mol. Biol.*, 2007, **370**, 870-886.
2. X. P. Ortega, S. T. Cardona, A. R. Brown, S. A. Loutet, R. S. Flanagan, D. J. Campopiano, J. R. W. Govan & M. A. Valvano. A putative gene cluster for aminoarabinose biosynthesis is essential for *Burkholderia cenocepacia* viability. *J. Bacteriol.*, 2007, **189**, 3639-3644.
3. B. Shi, R. Stephenson, D. J. Campopiano, & M. F. Greaney. Discovery of Glutathione S-Transferase inhibitors using dynamic combinatorial chemistry. *J. Am. Chem. Soc.*, 2006, **128**, 8459-8467.
4. D. J. Campopiano, D. J. Clarke, N. C. Polfer, P. E. Barran, R. J. Langley, J. R. W. Govan, A. Maxwell & J. R. Dorin. Structure-activity relationships in defensin dimers. *J. Biol. Chem.*, 2004, **279**, 48671-48679.
5. D. Alexeev, H. Zhu, M. Guo, W. Zhong, D. J. B. Hunter, W. Yang, D. J. Campopiano & P. J. Sadler. A novel protein-mineral interface. *Nature Structural Biology*, 2003, **10**, 297-302.