

Dr. Chris Mowat
Lecturer in Bioinorganic Chemistry

e-mail: C.G.Mowat@ed.ac.uk

tel: 0131 650 4738

Research Interests: redox proteins, protein crystallography, enzyme mechanisms, bacterial respiration.



Our research is centred upon the enzymology and crystallography of bacterial redox proteins. These include:

Enzymes of the kynurenine pathway

Tryptophan 2,3-dioxygenase (TDO) and indoleamine 2,3-dioxygenase (IDO) are heme-containing enzymes. They catalyse the oxidative cleavage of the L-Tryptophan (L-Trp) pyrrole ring. This is the first (and rate-limiting) step in L-Trp catabolism through the kynurenine pathway. We are investigating a TDO from *Xanthomonas campestris* and an IDO from *Shewanella oneidensis* and have recently obtained the first structure of reduced TDO in a binary complex with the substrate L-Trp (figure, left panel).

Tetrathionate reductase

We have recently determined (to 2.2 Å resolution) the X-ray structure of a unique octaheme cytochrome from the bacterium *Shewanella oneidensis* (figure, middle panel). The protein has an unprecedented structure and we are just beginning to investigate its molecular properties. Recent results suggest the enzyme may be involved in the bacterial nitrogen cycle.

SHP and DHC

Sphaeroides heme protein (SHP) and *diheme cytochrome c* (DHC) (figure, right panel) have been demonstrated to be redox partners *in vitro*. SHP has a labile asparagine heme ligand, which is displaced from the iron upon reduction of the protein. We are currently exploring the possibility of nitric oxide dioxygenase activity in SHP *via* a combination of kinetic, crystallographic and phenotypic experiments.



SELECTED RECENT PUBLICATIONS

1. "Molecular insights into substrate recognition and catalysis by the tryptophan and indoleamine 2,3-dioxygenases" Forouhar, F., Anderson, J. L. R., Mowat, C. G., Vorobiev, S. M., Hussain, A., Abashidze M., Bruckmann, C., Thackray, S. J., Seetharaman, J., Tucker, T., Xiao, R., Ma, L.-C., Zhao, L., Acton, T. B., Montelione, G. T., Chapman, S. K., Tong, L., *Proc. Nat. Acad. Sci. U.S.A.*, 2007, **402**, 473-478.
2. "Structural and Functional Studies on DHC, the Diheme Cytochrome *c* from *Rhodobacter sphaeroides*, and its Interaction with SHP, the *Sphaeroides* Heme Protein" Gibson, H. R., Mowat, C. G., Miles, C. S., Li, B.-R., Leys, D., Reid, G. A., Chapman, S. K. *Biochemistry*, 2006, **45**, 6363-6371.
3. "Multiheme Cytochromes - New Structures, New Chemistry" Mowat, C. G., Chapman, S. K. *Dalton Transactions*, 2005, **21**, 3381-3389.
4. "Octaheme Tetrathionate Reductase is a Respiratory Enzyme with Novel Heme Ligation" Mowat, C. G., Rothery, E. L., Miles, C. S., McIver, L., Doherty, M. K., Drewette, K., Taylor, P., Walkinshaw, M. D., Chapman, S. K., Reid, G. A. *Nat. Struct. Mol. Biol.*, 2004, **11**, 1023-1024.