

P042 Reduced and Oxidised Structures of ResA reveal a Redox-Driven Protein Substrate Selection Mechanism in Cytochrome c Biosynthesis

**Allister Crow, Richard Acheson, Nick Le Brun
and Arthur Oubrie**

University of East Anglia

C-type cytochromes are near-ubiquitous proteins involved in a range of biological processes. Roles for c-type cytochromes include the efficient transfer of electrons within, and between, respiratory complexes, enzyme catalysis, and sensing and sequestration of small molecules such as nitric oxide. Numerous enzymes involved in the processes of the nitrogen cycle contain at least one c-type cytochrome.

To better understand the processes by which c-type cytochromes are assembled, we have solved the structure of a soluble, functional domain of *Bacillus subtilis* ResA; a membrane-anchored thiol:disulfide oxidoreductase that maintains the Cys-Xxx-Xxx-Cys-His motifs of newly synthesised c-type apo-cytochromes in the reduced, dithiol, state in preparation for heme insertion by dedicated heme lyases. The structures of the oxidised and reduced states of the protein reveal the molecular basis for ResA's low redox potential as well as redox-linked conformational changes at the protein surface. The postulated protein-substrate interaction surface of oxidised ResA is relatively smooth and hydrophobic while the reduced state has a more basic (negative) character conferred by the opening of a deep cleft beside the active site. The cleft exposes a previously buried glutamate residue at its base. ResA might therefore preferentially select redox partners on the basis of its redox state.