Protein Crystallography and Engineering

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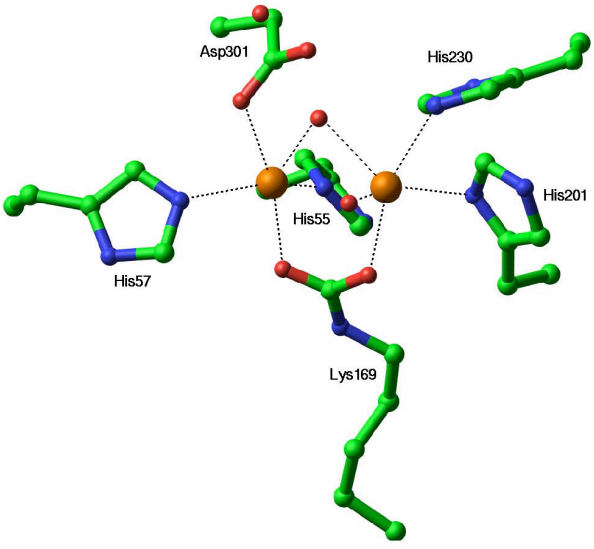
The group works at the interface between chemistry and biology. Our major interest is in working out how proteins function and how they might be modified for new and useful purposes. The laboratory routinely uses X-ray crystallography to obtain structures that can be used to better understand protein function. Directed evolution is used to produce mutant proteins that frequently have interesting properties that can be utilized in industrial and environmental applications. These mutants can also be analysed using a variety of techniques, including X-ray crystallography, to further understand the detailed mechanics of protein function.

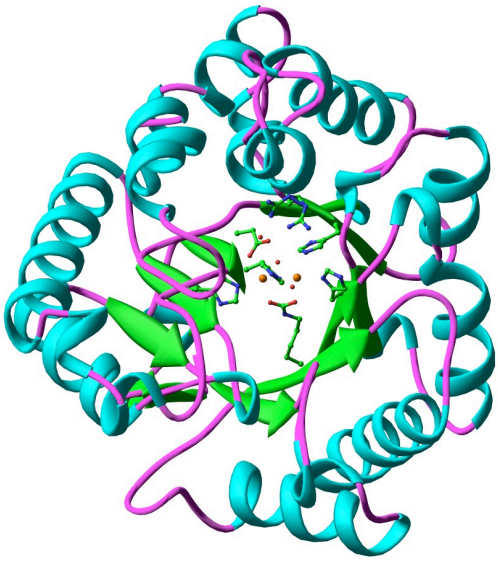
In the past year, methods have been developed to allow *Escherichia coli* to grow by using common pesticides, like Paraoxon, as the sole source of phosphorous. This greatly facilitates the directed evolution of pesticide degrading enzymes.

Enzyme Engineering with an Organophosphate Degrading Enzyme

The organophosphate degrading enzyme from *Agrobacterium radiobacter* (OPDA) is a bacterial enzyme that shows some utility in bioremediation. The protein was initially discovered in the laboratory of John Oakeshott in the Division of Entomology, CSIRO. In the past years we have obtained the structure of OPDA while more recently our attention has been directed towards evolving the enzyme so that it efficiently degrades a wide range of substrates. The location of mutations that enhance the catalytic activity of the protein has increased our understanding of the enzyme mechanism and given some insights into how enzymes evolve. *(with H. Yang, S. Yu-McLoughlin, P.D. Carr, J.-W. Liu)*



Close-up of the active site amino acid residues and metal ions at the 'catalytic heart' of the protein OPDA.



Schematic view of the protein OPDA which is being investigated for its potential use in the bioremediation of pesticide residues of economic importance in Australia.

The β Subunit of the IL-5 Receptor – Identifying the Interaction Site

IL-5 is a regulator of growth, differentiation, and activation of the white blood cell eosinophils. These cells are of major importance in the body's response to invasion by parasites and asthma inducing aeroallergens. In previous years, the structure of the β receptor interleukin-5 (IL-5) was determined. Efforts to exploit the new structure have proceeded this year. Structure based site-directed mutagenesis of the β common receptor successfully identified amino acid residues that are crucial for binding the cytokines IL-3, IL-5 and GM-CSF. These studies confirmed the existence of a novel ligand-binding interface composed of two non-contiguous fibronectin-III domains. *(with P.D. Carr, J. Murphy, and I.G. Young [JCSMR, ANU])*

Structure Function Studies of Regulatory Proteins of Nitrogen Uptake in Bacteria.

Over the last year the structure of the PII signal transduction protein from cyanobacteria has been solved. The structure was also determined of the N-terminal domain of *E. coli* glutamine synthetase adenyl transferase. Both structures were a collaborative effort with a group in the James Cook University in Townsville. (with *P.D. Carr and Y. Xu and S. Vasudevan [James Cook U.])*

http://rsc.anu.edu.au/research/ollis.php