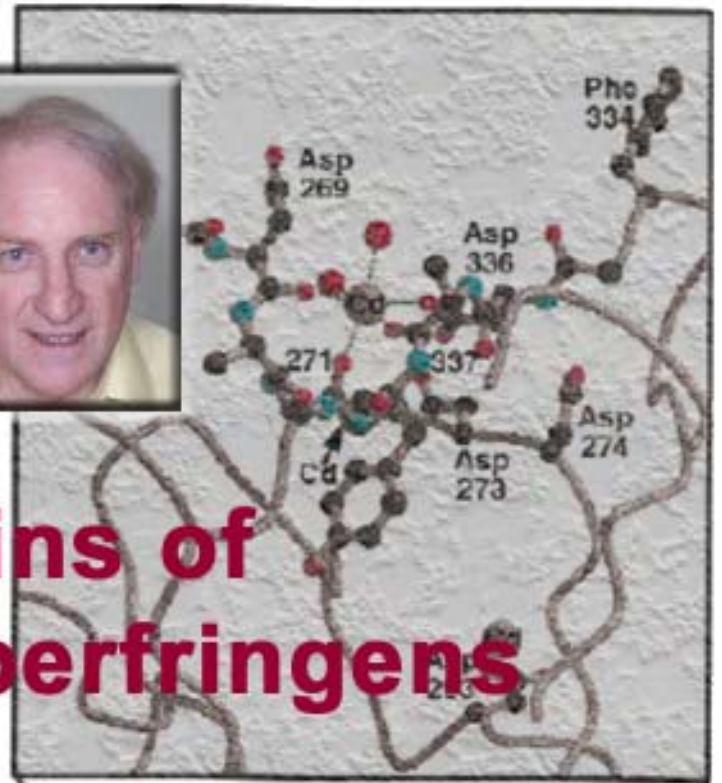


David S Moss

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Bacterial toxins of *Clostridium perfringens*

We have a research programme directed at determining the structures of the major toxins of *Clostridium perfringens* and understanding how they function.

We have used X-ray crystallography to solve the structure of the alpha-toxin from *C. perfringens*. This enzyme, which is a phospholipase-C, is the key virulence determinant in gas-gangrene. It hydrolyses phospholipids of cell membranes and triggers secondary messenger pathways in the cell leading to cell death. Crystal structures containing three metal ions in the active site show the molecule in an open conformation which we believe it to be catalytically active. We have proposed a model for the interaction of the toxin with the cell membrane. Another structure (with only two zinc ions in the active site) shows a closed form of the enzyme where entry to the active site is blocked. We are using fluorescence spectroscopy to investigate the disruption to cell signalling produced when bovine pulmonary endothelial cells are challenged by alpha-toxin.

We have also taken an important step forward in understanding another of the major toxins produced by *C. perfringens*. Epsilon-toxin is a pore-forming toxin produced by strains of the bacterium that inhabit the gut of sheep and lambs. Intoxication results in enterotoxaemia and neurological disorders and is usually fatal. We have solved the structure of the prototoxin by X-ray analysis and have prepared a heptameric form of the protein that is probably involved in pore formation. We have also obtained crystals of the *C. perfringens* enterotoxin, the causative agent of 20% of cases of food poisoning.

Date: 12 Mar 2004, Fri
Time: 4 pm
Venue: LT 20
Host: Dr J Sivaraman

All are welcome

Structural Biology & Functional Genomics Lecture Series

Seminar Announcement

(Department of Biological Sciences & Office of Life Sciences, NUS)

