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Structural relationships between *Clostridium perfringens* Beta-Pore-forming toxins

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Abstract

The bacterium *Clostridium perfringens* secretes a large panel of toxins and is associated with a wide range of diseases in human and animals. A number of the secreted toxins are pore-forming toxins (PFTs) that are secreted as soluble monomers, bind to target cells via specific receptors and undergo a conformational change leading to pore formation. We have studied several of *C. perfringens*' PFTs by X-ray crystallography, electron microscopy and other biophysical analyses, and our work has uncovered interesting, sometimes unexpected, relationships between these PFTs and those from other organisms.

C. perfringens PFTs fall into two categories: (i) aerolysin-like and (ii) alpha-haemolysin-like PFTs. Our 3D-structure of epsilon-toxin confirmed that it is an aerolysin-like PFT, as is our recently published enterotoxin (CPE) structure. This is unexpected as neither toxin has sequence homology to other members of this group. CPE is a causative agent of type-A food poisoning and hospital- and community-acquired antibiotic-associated and sporadic diarrhoea, and is a target for cancer therapeutic design. CPE's membership of aerolysin-like PFT family and its implications for pore-formation and mechanism of action will be discussed.

We have also recently determined 3D-structures of soluble monomeric delta-toxin (implicated in animal cell haemolysis) at 2.4 Å and NetB, which is implicated in necrotic enteritis in industrial poultry, heptameric pore-form to 3.9 Å. These toxins are both members of the alpha-haemolysin-like PFT family. NetB is highly related to the delta-toxin and the complementary results have allowed us to draw conclusions about receptor interaction and membrane insertion in these toxins.

Biography

Ajit K. Basak has completed his Ph.D. from 'Saha Institute of Nuclear Physics', Calcutta University, India in 1987. In 1988, he moved to the Laboratory of Molecular Biophysics, Oxford and until April 1995, worked simultaneously both in LMB and NERC Institute of Virology. He moved to Birkbeck College in 1995, where he is now a senior research fellow. His research, more than 50 peer reviewed papers, have been extensively published in wide variety of journals, holding research grants, two vaccine patents and in the editorial board of few journals.