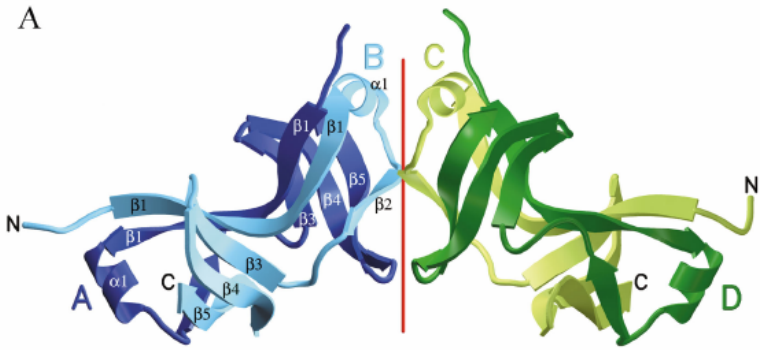
Structural studies of proteins from the type III secretion system, a bacterial device for the combat with eukaryotic host cells

Kokkinidis M., Fadouloglou V., Gazi A. and Panopoulos N.
Institute of Molecular Biology and Biotechnology, PO Box 1527, GR-71110 Heraklion, Crete, Greece & University of Crete, Department of Biology, PO Box 2208, GR-71409 Heraklion, Crete, Greece

Type III secretion systems (TTSS) are essential mediators of the interaction of many Gram-negative bacteria with human, animal or plant hosts. They are associated with a broad spectrum of diseases including bacteremia, septicemia, typhoid fever and bubonic plague in mammals and localized lesions, systemic wilting and blights in plants. In addition, type III secretion systems are also required for biogenesis of the bacterial flagellum. Extensive sequence and functional similarities exist between components of TTSS from bacteria as diverse as animal and plant pathogens. Recent crystal structure determinations of TTSS proteins reveal extensive structural homologies and novel structural motifs and provide a basis on which protein interaction networks start to be drawn within the TTSS systems, that are consistent with and help rationalize genetic and biochemical data. Such studies, along with electron microscopy, also established common architectural design and function among the TTSS systems of plant and mammalian pathogens, as well as between the TTSS injectisome and the flagellum. Based on advances in TTSS biology, new diagnostics, crop protection and drug development applications, and new cell biology research tools are beginning to emerge.

The HrcQB protein, is an example of a TTSS component of Pseudomonas syringae with homologues in all type III systems. HrcQB has a variable amino-terminal and a conserved carboxy-terminal domain (HrcQB-C). The crystal structure of HrcQB-C will be presented. HrcQB-C retains the ability of the full-length protein to interact with other type III components. A 3D-analysis of sequence conservation patterns reveals two clusters of residues potentially involved in protein-protein interactions. Based on the analogies between HrcQB and its flagellum homologues, we propose that HrcQB-C participates with the HrcQA protein in the formation of a C-ring-like assembly. Molecular dynamics simulations have been used to explore the association of HrcQB molecules. The complex of HrcQB with HrcQA has been recently isolated and preliminary characterization is in progress. Efficient secretion and translocation of TTSS substrates (i.e. effectors and translocators) frequently requires specific chaperones. Structural studies of TTSS chaperones or chaperone-like proteins using small angle X-ray scattering (SAXS) will be reported.



Schematic representation of the $HrcQ_B$-C structure. Each chain of the tetrameric protein is individually coloured and labelled