STRUCTURAL BIOLOGY

POTRA domains close up

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In recent years, researchers have begun to make great progress in understanding how proteins cross or are inserted into the outer membrane of Gram-negative bacteria. Two papers in *Science* now provide structural insights into these processes, and also give a first glimpse of the structure of the conserved polypeptide-transport-associated (POTRA) domain.

Seokhee Kim and colleagues report the structure of a periplasmic fragment of the *Escherichia coli* integral outer-membrane protein YaeT (Omp85), which, along with four lipoproteins, makes up the *E. coli* outer-membrane protein-assembly complex. The periplasmic domain of YaeT comprises five POTRA domains, and in the crystallized fragment four of the domains were intact, and part of the fifth was also present. The primary-sequence similarity of the POTRA domains is low, but the structure revealed that the folds in each domain are similar, comprising a three-stranded β-sheet and two α-helices.

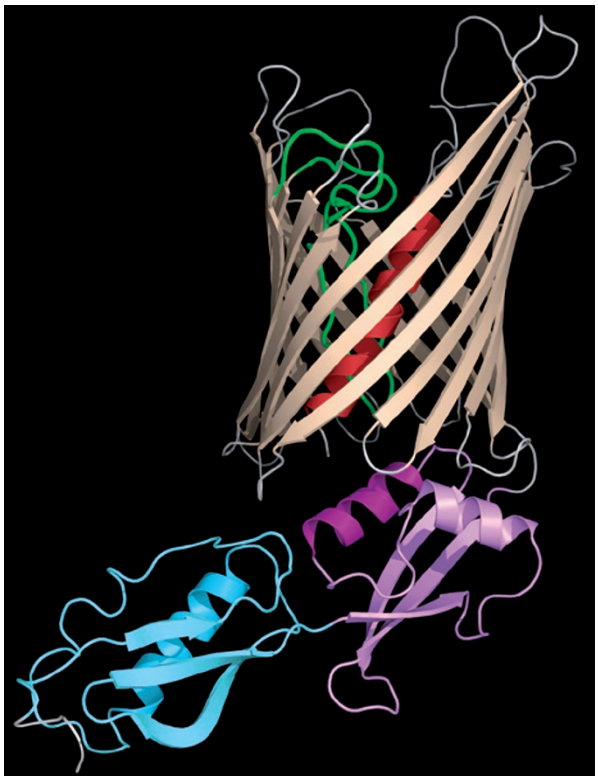

Image of FhaC kindly provided by Francoise Jacob-Dubuisson

YaeT is the only essential component of the outer-membrane protein-assembly complex and it had previously been suggested that YaeT could act as a scaffold for the other components. Histidine-tagged deletion constructs, each lacking a single POTRA domain, and complementation studies of an *E. coli* Δ*yaeT* strain using non-tagged deletion mutants, revealed that the POTRA domains allow YaeT to fulfil this scaffolding role; information on the functional importance of each POTRA domain was also obtained. Finally, although the fragment crystallized as a dimer, the authors do not think the dimer is physiologically relevant, but they do suggest that the β-augmentation that is observed at the dimer interface could be a mechanism by which the POTRA domains can capture target polypeptides.

Clantin and colleagues report the 3.15 Å structure of FhaC, the outer-membrane transporter that secretes the *Bordetella pertussis* adhesin filamentous haemagglutinin (FHA). FhaC is a monomer that comprises a β-barrel channel that contains 16 anti-parallel β-strands and an amino-terminal extension that contains an α-helix and two POTRA domains. The structure of the POTRA domains resembles that found by Kim and colleagues, and both POTRA domains were required for FHA secretion.

In the structure, the channel in FhaC appears to be occluded by an α-helix and an extracellular loop, and it has a diameter of only 3 Å, which would be too narrow to accommodate FHA. Based on planar lipid-bilayer conductance assays, however, the authors predict that the diameter of the channel when functional is 8–10 Å, which could accommodate FHA. The authors propose a model in which binding of the amino-terminal domain of FHA to the first POTRA domain of FhaC in the periplasm opens the β-barrel channel in the outer membrane through a conformational change that removes the occluding elements. FHA is then translocated through the channel in an extended conformation, and it acquires its final folded structure at the cell surface. FhaC is also a member of the Omp85 protein superfamily, and Clantin *et al.* suggest that this could be a general model for this type of secretion by such proteins.

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ORIGINAL RESEARCH PAPERS Clantin, B. *et al.* Structure of the membrane protein FhaC: a member of the Omp85–TpsB transporter superfamily. *Science* **317**, 957–961 (2007) | Kim, S. *et al.* Structure and function of an essential component of the outer membrane protein assembly machine. *Science* **317**, 961–964 (2007)