

The Chaperone-usher Pathway of Pilus Biogenesis: Structural Basis of the Assembly Process and of Host Recognition

Gabriel Waksman, *Institute of Structural Molecular Biology, UCL/Birkbeck, Malet Street, London WC1 7HX, UK.* E-mail: g.waksman@mail.cryst.bbk.ac.uk

Pili are cell surface organelles and essential virulence factors responsible for host recognition by gram-negative bacterial pathogens. Type P and 1 pili of uropathogenic *Escherichia coli* target bacteria to the kidney and bladder, respectively, through their specific interaction with host surface receptors. They are assembled by the chaperone-usher pathway of pilus biogenesis, which involves a chaperone which ferries pilus subunits through the periplasm and an usher which forms the site of assembly at the outer-membrane. Structural biology work in my lab has characterized the interactions between chaperone and subunits and shown that pilus subunits have truncated Ig fold where the 7th strand is entirely missing. The chaperone “donates” one of its strands to complement the truncated Ig fold of the subunits. At the usher, the donated strand is substituted with the N-terminus extension of the subunit coming next in the assembly process. This substitution process is termed “donor-strand exchange”. Recent biochemical work has provided details of the donor-strand exchange reaction and shown that it proceeds via a zipper mechanism. Finally, the interactions of the pilus with the host receptor have been characterized. This work provides fundamental insight into the first event in a bacterial infection i.e. host recognition/attachment and provides the basis for designing novel antibiotics targeting specifically virulence factors.

Keywords: pilus biogenesis, host recognition, bacterial infection