# The chaperone-usher pathway of pilus biogenesis: structural basis of the assembly process and of host recognition

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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 $7^{th}$ 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 zippering 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.

**References**

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