GHI Floor Seminars

Special seminar by

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Structure of a Chaperone-Usher Pilus Reveals the Molecular Basis of Rod Uncoiling

Chaperone-usher (CU) pili are ubiquitously displayed appendages on the surface of bacterial pathogens. These remarkable protein structures are crucial virulence factors that allow bacteria to attach and spread within the urinary tract. Type 1 and P pili are the most abundant CU pili produced by uropathogenic Escherichia coli (UPEC), which are responsible for ~80% of all urinary tract infections (UTIs). Due to their prevalence, UTIs contribute significantly to antibiotic use and the emergence of resistance. CU pili are organised into two subassemblies: the tip fibrillum and a 1-2 μm long rod, which is in turn composed of ~1000 copies of a single subunit.

Here, we present an atomic model of the P pilus rod generated from a 3.8 Å resolution cryo-electron microscopy reconstruction. The rod adopts a superhelical quaternary structure, which endows it with remarkable spring-like properties, allowing pili to reversibly uncoil when subjected to flow-induced shear forces in the urinary tract. Strikingly, each pilus subunit contacts ten other subunits forming an extensive interaction network, revealing the molecular basis for the rod’s mechanical properties. By targeting key residues in this interaction network by mutagenesis, we identified important sites of the pilus subunit essential for the integrity of the quaternary pilus rod structure, since mutation led to abrogation of rod polymerization in vitro.

In summary, this structure reveals the molecular basis for pilus rod uncoiling, a key adaptation of CU pili and the bacterial pathogens that display them. Moreover, it will allow us to address unanswered questions about CU pilus biogenesis in the future. Ultimately, detailed knowledge of the pilus rod structure, in conjunction with an understanding of its functional role in pilus translocation, will provide a unique opportunity to develop targeted drugs, critical in our fight against the emergence of widespread antibiotic resistance.

Host: Prof. Stewart Cole

Tuesday, July 18, 2017
12:15, SV 1717