Case Study

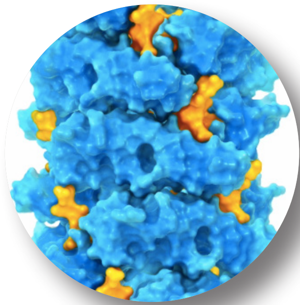
diamond

Mechanical Properties of Bacteria Revealed

The Problem

Antiobitic resistance is an increasingly serious threat to global public health that requires action across all government sectors and society. There are high proportions of antibiotic resistance in bacteria that cause common infections, for example urinary tract infections, and it is patients with these infections caused by drug-resistant bacteria that are generally at increased risk of worse clinical outcomes and death. These patients consume more health-care resources than patients infected with the same bacteria that are drug-resistant. Developing new treatments to tackle this worldwide problem is therefore of paramount importance.

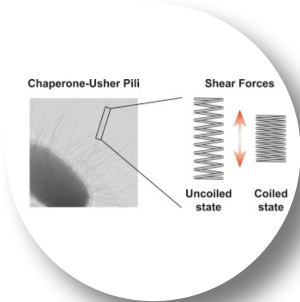
The Challenge



Bacteria, such as E.coli, naturally possess hair-like structures exposed at the cell surface, which are known as pili. Type P pili play an essential role in urinary tract infection as they are responsible for seeking out and latching onto specific host tissues. The shear forces exerted on the bacteria from the flow of urine would ordinarily dislodge them, so understanding how the pili are able to resist these forces is of great interest. The structure of the P pilus has to date remained unresolved, but by fully understanding the structure and function of these key structures, it is thought that new medicines could be developed to prevent tackle this common infection.

The Solution

A team of scientists from University College London (UCL), Birkbeck, University of London, and Universities in Washington and Virginia, USA used the cutting edge cryo-EM facility (eBIC - electron Bio-Imaging Centre) at Diamond to create an atomic model of the P pilus rod generated from a 3.8 Å resolution cryo-EM reconstruction. The data were collected on an FEI Krios electron microscope with Titan 2.2 software, equipped with an XFEG, and operated at 300 kV. The structure revealed that the pili were shaped like springs, which allowed the bacteria to cling on to host tissues even in adverse environments.



The Benefits

Solving the structure of the PapA helical rod using the cutting edge facilities available at eBIC provides unprecedented atomic detail of the interactions that play an essential role in E.coli pathogenesis. The studies show that the pili uncoil during urine flow and recoil when the forces recede and paves the way for the design of "coilicides", compounds and biologics that could interfere with rod formation and, thus, might greatly impair the ability of bacterial pathogens to maintain a foothold in the urinary tract.

"There is clearly a revolution in EM, which has been driven by improvements in three key areas: better microscopes, better detectors and better software, and all of this latest technology is available at eBIC."

Prof Gabriel Waksman, Institute of Structural and Molecular Biology, Birkbeck and UCL

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