Decoding the molecular machine behind E. coli and cholera

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Scientists from Queen Mary, University of London have discovered the workings behind some of the bacteria that kill hundreds of thousands every year, possibly paving the way for new antibiotics that could treat infections more effectively.

With antibiotic resistance on the rise in strains of pathogenic bacteria, innovative strategies are needed to discover ways of treating bacterial infections in both humans and in agriculture.

Writing in the journal PLoS Pathogens, the team from Queen Mary's School of Biological and Chemical Sciences show how they studied the molecular machine known as the 'type II bacterial secretion system', which is responsible for delivering potent toxins from bacteria such as enterotoxigenic *E. coli* and *Vibrio cholerae* into an infected individual.

Professor Richard Pickersgill, who led the research, said: "Bacterial secretion systems deliver disease causing toxins into host tissue. If we can understand how these machines work, then we can work out how it they might be stopped."

In order to infect, Gram negative bacteria have to export their toxins into their host across both an inner and outer membrane. Professor Pickersgill explains: "The pore in the outer membrane which the toxins pass through is formed from protein subunits which are guided into place by a protein pilot. The protein pilot interacts with the subunits that form the pore in the outer membrane; if the protein pilot is missing, then

the pore forms in the inner membrane and not the outer membrane and secretion is stopped."

Professor Pickersgill adds: "If we can successfully interfere with this or with other interactions we are discovering then we might be able to halt the secretion system and prevent these harmful diseases."

The same type II secretion system that enables *E. coli* and cholera is also used by bacteria that cause substantial food spoilage, such as *Dickeya dadantii*. Crop spoilage by plant infecting bacteria is becoming an increasing problem in the UK due to the warmer and wetter summers caused by global climate change, and the team hope that the results of this study will be of interest to both agrichemical scientists seeking ways of preventing crop damage and pharmaceutical companies seeking new antibiotics.

More information: 'Structural and functional insights into the pilotin-secretin complex of the type II secretion system' will be published in the online edition of *PLoS Pathogens* on Thursday 9 February 2012.

Provided by Queen Mary, University of London