Bacteria research opens way for new antibiotics

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University of Adelaide researchers have discovered a target for the development of completely new antibiotics against disease-causing bacteria.

Published online ahead of print in the leading microbiology journal *Molecular Microbiology*, the researchers have identified a building block common to many types of bacterial 'virulence factors' (the bacterial proteins which act as weapons to cause disease, such as toxins or degrading enzymes).

The building block, called the Passenger-associated Transport Repeat (PATR), has been found in virulence factors of many major harmful bacteria including Salmonella, Shigella, and Meningococcus as well as bacteria that cause infections in cystic fibrosis and burns patients. It has been found in many of the major so-called 'Gram negative bacteria', including those that have developed resistance to a broad range of antibiotics.

The PATR was shown to be integral in the transport of the virulence factors to the surface of the bacterial cell, where they need to be to function as disease-causing agents.

"Bacteria can only cause disease when virulence factors are appropriately produced by the bacteria and transported (or secreted) onto the cell surface where they become harmful," says first author Matthew Doyle, PhD candidate in the School of Biological Sciences.

"Our results are very exciting — we are not just talking about one molecule in one particular pathogen but rather a building block which is shared by thousands of common virulence factors produced by many major pathogenic bacteria. The PATR is crucial for those virulence factors to mature appropriately.

"It opens up the possibility for development of a completely new class of broad-spectrum bacterial virulence inhibitors. If we can inhibit this building block, we are really onto something."

The discovery will also be useful in the biotechnology field for the development of a variety of marketable products and processes which rely on coupling biological molecules to cell surfaces.

The latest findings follow more than a decade of work led by Associate Professor Renato Morona looking at how bacteria cause disease. The research is expected to gain a lot of attention from the many groups around the world working in the field.

"We initially could not believe that this building block has been overlooked," says Associate Professor Morona. "We've discovered something that's been hidden in plain sight. It may shift the way research in this field is conducted."

More information: "The passenger-associated transport repeat promotes virulence factor secretion efficiency and delineates a distinct autotransporter subtype." *Mol Microbiol*. 2015 Apr 13. DOI: 10.1111/mmi.13027

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