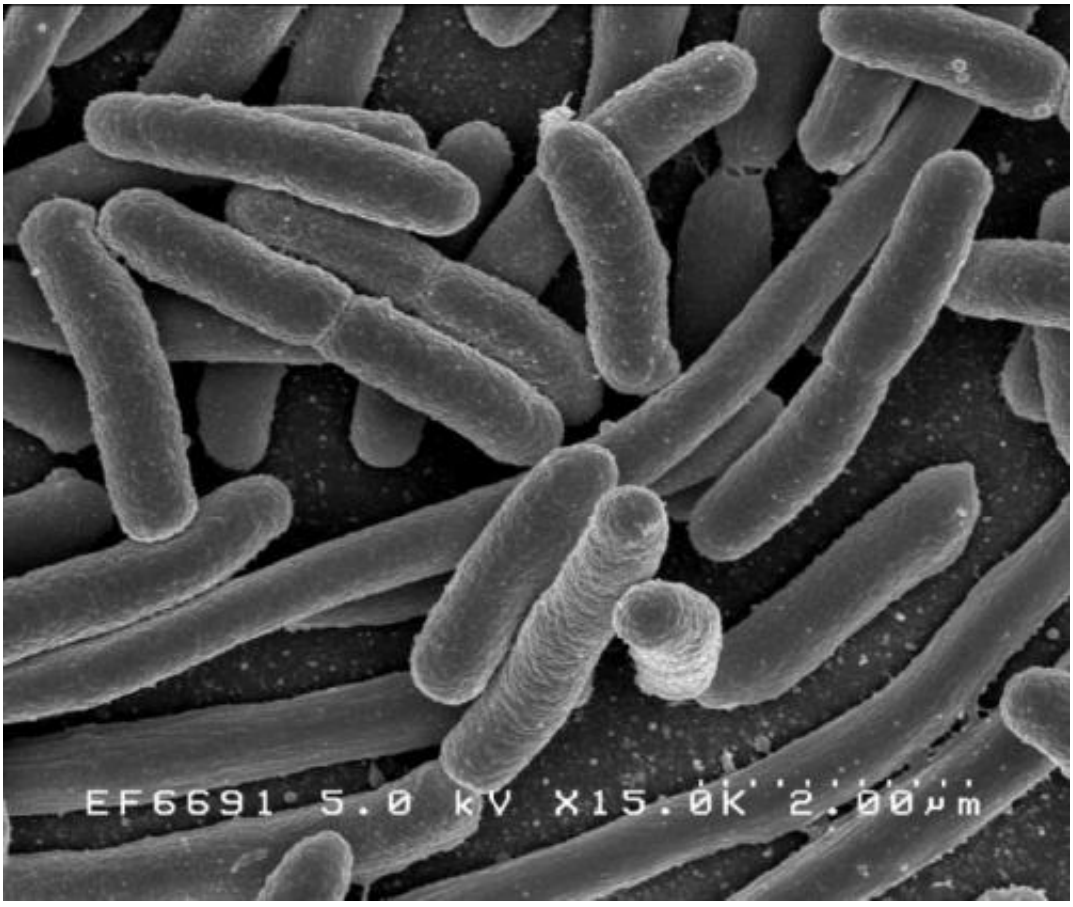
E.coli 'anchors' provide novel way to hijack superbugs

May 16 2016



Escherichia coli. Credit: Rocky Mountain Laboratories, NIAID, NIH

Australian scientists may have found a way to stop deadly bacteria from infecting patients. The discovery could lead to a whole new way of treating antibiotic-resistant "superbugs". The researchers have uncovered

what may be an Achilles heel on the bacteria cell membrane that could act as a potential novel drug target.

Almost every second woman suffers from a urinary tract infection during her lifetime, mostly caused by the intestinal bacterium *E. coli*. It travels along the urethra to the bladder where it triggers painful infections.

In order to infect the bladder (which is constantly being flushed out with urine), the bacteria have developed nanofilaments which effectively anchor the bacteria to the walls of the urinary tract.

A team headed by Professor Trevor Lithgow, from the Biomedicine Discovery Institute at Monash University, has found a protein—called the TAM—that is crucial to the assembly of these anchoring filaments.

In a paper, published today in *Nature Microbiology*, the researchers describe how they developed an assay to measure the assembly of the filament forming protein, called usher.

"Using our assay we tested whether blocking TAM had any effect on usher. What we found was that TAM is required for the assembly of usher and therefore for production of the filaments needed to anchor the bacteria to the urinary tract surface," he said.

The assay revealed that, under normal circumstances, E. coli can create filaments within two minutes of sensing the urinary tract environment. However, when TAM is blocked, it can take up to four hours for the same anchoring process to happen.

According to Professor Lithgow the discovery of how TAM impacts on the *E. coli*'s ability to latch onto the wall of the urinary tract could be a very important target for drug therapy. "Most antibiotics against *E. coli*

have to get across the bacterial cell membranes in order to kill the invader," he said.

"The TAM is on the bacterial surface, so it is directly accessible to the sorts of drugs that would inhibit its function, and thereby halt the rapid production of these nanofilaments."

Importantly, other potentially lethal bacteria also use filaments which are controlled through TAM, according to Professor Lithgow. These include *Klebsiella pneumoniae carbapenemase-producing bacteria* (KPC) which caused a scare in Victoria last year when Victorian authorities issued an alert that the antibiotic resistant superbug may have contributed to up to 18 deaths over the previous three years.

More information: Effective assembly of fimbriae in Escherichia coli depends on the translocation assembly module nanomachine, *Nature Microbiology*, DOI: 10.1038/nmicrobiol.2016.64

Provided by Monash University