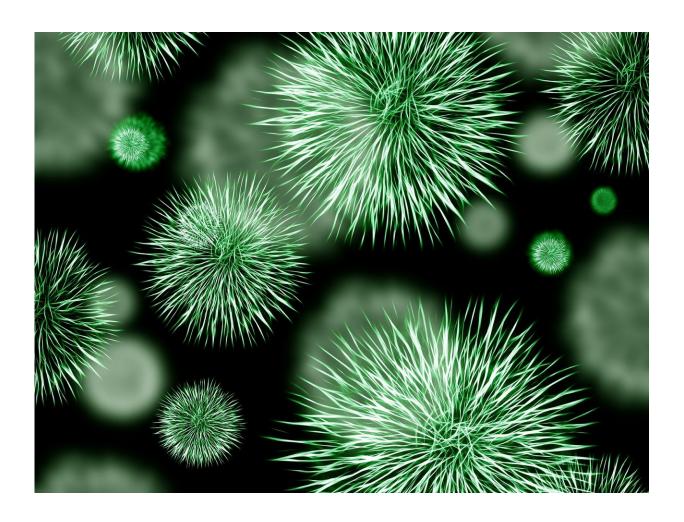


New breakthrough in the war against antibiotic resistance

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Scientists at The University of Western Australia, in collaboration with



researchers in Canada, have developed a new compound that can combat antibiotic-resistant bacteria.

B-lactam <u>antibiotics</u>, better known as penicillins, are widely used to treat everything from skin infections and throat infections to diseases in humans such as pneumonia, tuberculosis and gonorrhoea. However the rise of drug-resistant bacteria in the past decade is threatening their effectiveness.

Lead author and chemical biologist Associate Professor Keith Stubbs, from UWA's School of Molecular Sciences said one method bacteria use to resist antibiotics is to produce an enzyme, called AmpC b-lactamase, to destroy the antibiotic.

"Many bacteria produce AmpC b-lactamase only when b-lactam antibiotics are present, and this is controlled by a sensory 'on switch' molecule found inside the bacteria," Associate Professor Stubbs said.

"Previous ways to overcome AmpC b-lactamase was to provide patients with an inhibitor of the AmpCenzyme as well as prescribing them the b-lactam antibiotic, but this approach is quickly becoming much less effective, with bacteria developing stronger and stronger resistance in recent years."

The UWA-led research team has developed a compound that can stop the 'switching on' of the AmpC enzyme.

"If the 'switch' is not activated, AmpC b-lactamase can't be made and then the antibiotic can work to treat the bacterial infection successfully," Associate Professor Stubbs said.

The researchers tested the compound on a bacterial strain of Pseudomonas aeruginosa, which affects patients suffering with Cystic



Fibrosis, and found the new compound makes the <u>bacteria</u> much more susceptible to the effects of b-lactam antibiotics.

UWA Research Associate Louisa Ho from the UWA School of Molecular Sciences said because the new method could be applied to many b-lactams, older ones no longer on the market were potentially back in the game.

"More work is needed but this sets the foundation for a new chemical approach to stop b-lactam resistance," she said.

The study was supported by funding from the Australian Research Council, the Canada Research Chairs Program, Cystic Fibrosis Canada and the Canadian Institutes of Health Research.

It has been published in the Society of Chemistry journal *Chemical Communications*.

More information: Louisa A. Ho et al. A mechanism-based GlcNAc-inspired cyclophellitol inactivator of the peptidoglycan recycling enzyme NagZ reverses resistance to β-lactams in Pseudomonas aeruginosa, *Chemical Communications* (2018). DOI: 10.1039/C8CC05281F

Provided by University of Western Australia

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