New insights in the fight against antibiotic resistance

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Credit: Victoria University

A looming antibiotic resistance crisis, which could turn even cuts and scrapes into life-threatening events, has put the pressure on scientists around the world to come up with solutions.

Some scientists—including researchers at Victoria University of Wellington—are focusing on discovering entirely new antibiotics. But

innovative work at Victoria is also exploring ways to stop the demise of current antibiotics in the first place.

Dr Scott Cameron is a chemist at Victoria's Ferrier Research Institute who is researching the process of antibiotic resistance, particularly the role of enzymes called lactamases.

"A lactamase effectively chews up penicillin and related antibiotics, which means the drug can no longer do its job of preventing bacteria from building their cell walls," explains Dr Cameron. "If there's a lactamase around, then penicillin isn't going to be much use to you at all."

He says bacteria are fairly efficient at finding ways of beating new threats, too. "Every time a new antibiotic is made and used, bacteria find a way of getting rid of it. Penicillin-like drugs have been met with lactamases—enzymes which degrade these antibiotics—thereby nullifying their effect," he says.

"Recently we've started seeing metal-based lactamases, which are unaffected by current lactamase inhibitors. The one I'm particularly interested is a di-zinc lactamase, which was only discovered in 2009," says Dr Cameron. "This metal-based lactamase is capable of destroying a broad range of different antibiotics, including penicillins, cephalosporins, and even carbapenems, which are usually a last resort antibiotic.

Using a technique called transition-state analysis, Dr Cameron hopes to investigate the precise nature of the process in which lactamase enzymes convert antibiotics to harmless by-products.

"I want to examine the fleeting moment—just a few quadrillionths of a second, in fact—in the enzymatic reaction when the antibiotic is most

tightly bound by the lactamase," he says.

The information gleaned from this technique can then be used as a kind of 'blueprint' for possible lactamase inhibitors.

"If we can figure out what that so-called transition state is, and make a stable mimic of that moment, then we would hopefully have a very potent inhibitor of that enzyme—for this study that would mean antibiotics such as penicillin can continue to be effective."

Using transition-state analogues as a way to inhibit enzymes is a technique that is already well established, including the recently approved drug Mundesine, which was first synthesised at the Ferrier Research Institute and is now used in the treatment of T-cell lymphomas. Dr Cameron's work would be the first time the technique has been applied to lactamases, and could be a promising solution to the threat of antibiotic resistance.

"There's an urgent need to be doing this work," explains Dr Cameron. "We are trending towards a post-antibiotic age where common infections could kill us or surgery could be dangerous—that's a pretty scary situation to be in."

Provided by Victoria University