

Wave of interest in new cancer therapy

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Using viruses and bacteria that normally cause disease to cure disease is an apparent contradiction, but it's fundamental to the work being carried out by Dr. David Ackerley.

The Director of Biotechnology at Victoria University is part of a multidisciplinary team that aims to use [viruses and bacteria](#), or microbes, that cause diseases, such as measles, botulism, gangrene and the common cold, as the basis of new forms of [cancer](#) treatment.

These microbes will be engineered to make an enzyme that can activate cancer prodrugs—a new generation of therapies that remain inert in the body until activated by the enzymes that Dr Ackerley's group at Victoria are developing.

There is growing international interest in prodrugs as an alternative to chemotherapy, because of their ability to kill [cancer cells](#) while leaving healthy cells unharmed.

Dr. Ackerley's area of expertise is directed evolution, where scientists use a form of selective breeding to make enzymes with new or improved functions.

It involves introducing a range of mutations into an enzyme encoded by a bacterial gene, essentially mimicking what would have happened through evolution but at an accelerated pace.

"It's very hard to predict what you'll get when you put in random

mutations. We screen millions at a time and well over 99 per cent are unhelpful, but occasionally you find one that improves the function of your enzyme."

Dr. Ackerley started working in the field during postdoctoral study at Stanford University in the United States, when he was involved in projects aiming to use naturally occurring bacteria for decontaminating polluted areas, a process known as bioremediation.

One of his projects focused on an enzyme able to convert the toxic nasty in the famous Erin Brokovich case—chromium(VI)—into its natural form, chromium(III), to speed up the environmental cleanup.

Since coming to Victoria in 2006, Dr. Ackerley has continued to work with enzymes very similar to those developed on the chromium case but for a very different purpose.

"The fundamental idea behind our cancer therapy is that certain viruses and bacteria can more easily infect a cell in a cancerous tumour than a healthy, human cell. The latter have defences against infection that tumour cells have lost."

Dr Ackerley and his group (currently nine students and one postdoctoral fellow) are using directed evolution to make enzymes that are more efficient at activating prodrugs.

The idea is that patients will be given the enzyme via a microbe that will deliver it only to cancer cells. The enzyme will then activate the prodrug, killing only the cancer cells. But it does not stop there.

Dr. Ackerley says the enzyme developed at Victoria has another property which makes it unique.

"Once you let a potentially dangerous microbe loose inside a patient you want to know exactly where it is and what cells it is affecting. Ours is also able to activate molecules used in PET scans, a form of whole-body imaging that will enable clinicians to track its progress and ensure that it is only infecting cancer cells."

The team has applied for a patent on its discovery, a move that Dr Ackerley says is usually essential in drug development.

"It costs huge amounts of money—literally hundreds of millions of dollars—to develop a therapeutic agent and take it through cancer clinical trials. You need to raise venture capital and you need patent protection to do that as it provides reassurance to investors that their investment can be recouped."

Dr. Ackerley's main collaborators are Dr. Adam Patterson and Dr. Jeff Smaill at the Auckland Cancer Society Research Center, who have played key roles in development and testing of next-generation prodrugs and imaging molecules.

The team anticipates that its first [cancer therapy](#) package will be ready for clinical trials within two years—in time to ride a growing wave of interest in cancer-targeting microbes. The team's core inventions are being actively developed through a commercial partnership between Viclink and Auckland UniServices, the commercialization companies at Victoria and Auckland universities.

"This area has been seen as promising for a very long time but it's moving to a new level," says Dr. Ackerley.

"Earlier this year, biotechnology company Amgen paid \$425 million upfront in a deal worth nearly \$1 billion in total to buy BioVex, which has a drug development platform based on a genetically altered herpes

simplex virus that is engineered to enter tumour cells and promote their death. That signals a shift in perceptions about the value of this area of research."

Provided by Victoria University

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