

## Research Update

### A Starfish that stops deadly toxins

A simple injection to treat often-deadly cholera and hamburger disease may be developed in the future, thanks to a research team at the University of Alberta that has designed a molecule to treat enterotoxins (*Nature* 2000;403:669–72).

Shiga and cholera toxins, caused by gastrointestinal pathogens, are responsible for millions of deaths annually. Once the toxins enter the circulatory system, they cause cramps, bloody diarrhea, vomiting and fever. Many patients eventually suffer severe kidney damage because there is no effective cure.

But the newly developed “Starfish” molecule holds tremendous promise, standing out during in vitro tests as 1 million to 10 million times more effective than any other inhibitor of these toxins. That is no small feat. Shiga and shiga-like toxins are armed with 15 binding sites in 3 groups of 5 that lock onto cell surfaces. The Starfish mole-

cule designed by Dr. David Bundle’s team mimics receptors on healthy cells that the toxins seek out, acting as a decoy to lure the toxins away from the body. And, because of its shape, the Starfish molecule can lock onto 2 toxin molecules simultaneously.

“We have embraced the whole surface so, if you like, we have taken 2 donuts and stuck them together,” says Bundle. “These 2 surfaces are now facing each other with the inhibitor [Starfish molecule] in the middle. The toxins are facing each other so they are totally prohibited from binding to another cell.”

The molecule’s ability to take on 2 toxin molecules at once was a pleasant

surprise. “It was better than we envisaged. It was an accident, but it worked in our favour.”

Currently, clinical trials are under way to test an insoluble absorbent called Synsorb Pk that could attack the toxins in the gut. But because the Starfish molecule is soluble, it could be used as an injectable treatment to clean up toxins in the bloodstream, where they cause the most damage.

“The real problem is for patients who have toxins that have exited the gut and entered the circulation. Our molecule could be used as an injectable that could neutralize the toxin in the circulation system,” says Bundle. — *Richard Cairney*, Edmonton

