Researchers work towards pharmacological targets for cholera

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Just over a year after the earthquake in Haiti killed 222,000 people there's a new problem that is killing Haitians. A cholera outbreak has doctors in the area scrambling and the water-borne illness has already claimed 3600 lives according to officials with Médicin Sans Frontières (Doctors without Borders).

Stefan Pukatzki, a bacteriologist in the Faculty of Medicine & Dentistry at the University of Alberta, is hoping that down the road he can help prevent deadly cholera outbreaks.

His lab studies *Vibrio cholerae*, the bacteria that makes up the disease, and he has discovered how it infects and kills other bacteria and host cells. This discovery, published in November's *Proceedings of the National Academy of Sciences*, could explain how this organism survives between epidemics. Pukatzki says Vibrio cholerae lives in fresh water mix between epidemics and no one has known how it competed and survived with other bacteria in the water.

A better understanding of how this organism infects cells means Pukatzki may be able to devise novel strategies to block the function.

Pukatzki discovered that Vibrio cholerae uses molecular nano-syringes to puncture host cells and secrete toxins straight in to the other organism; this is called the type six secretion system.

"Vibrio cholerae uses these syringes so when it comes in contact with another bacteria, like *E. coli*, which is a gut bacterium, it kills it," said Pukatzki. "That's a novel phenomenon. We knew it [*Vibrio cholerae*] competed with cells of the immune system but we didn't know it was able to kill other bacteria.

"Keep in mind these syringes are sitting on the outside of the bacterium so they make good vaccine targets," said Pukatzki. "That's actually better because you could either inhibit the type six function or you could induce an immune response with these components that are sitting on the outside."

Pukatzki is excited because the type six secretion system isn't unique to *Vibrio* cholera; it is found in most major pathogens.

"We really think that even though this pathway is important for cholera, I think that whatever we find we can apply to other diseases as well because they're so highly conserved," said Pukatzki.

Pukatzki's lab is now looking to get a better understanding of this mechanism and continue working towards a potential pharmaceutical target.

Provided by University of Alberta