Cholera discovery could revolutionize antibiotic delivery

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(Phys.org)—Three Simon Fraser University scientists are among six researchers who've made a discovery that could help revolutionize antibiotic treatment of deadly bacteria.

Lisa Craig, Christopher Ford and Subramaniapillai Kolappan, SFU researchers in molecular biology and biochemistry, have explained how *Vibrio cholerae* became a deadly pathogen thousands of years ago.

V. cholerae causes the diarrheal disease cholera, which is endemic in many developing countries and can emerge in regions devastated by war and natural disasters. An outbreak following the 2010 earthquake in Haiti has killed at least 7,500 people.

Two genes within *V. cholerae*'s genome make it toxic and deadly. The bacterium acquired these genes when a bacterial virus or bacteriophage called CTX-phi infected it.

The SFU researchers and their colleagues at the University of Oslo and Harvard Medical School propose that a Trojan horse-like mechanism within *V. cholerae* enabled CTX-phi to invade it.

The CTX-phi latches onto a long, hair-like pilus filament floating on the surface of *V. cholerae*. The filament then retracts, pulling the toxin-gene-carrying CTX-phi inside the bacterium where it binds to TolA, a protein in the bacterial wall.

The process transforms *V. cholerae* into a deadly human pathogen.

The Journal of Biological Chemistry has just published a paper written by the researchers describing the atomic structures of the CTX-phi protein pIII alone and bound to *V. cholera* TolA.

The authors recommend that pilus filaments be explored further as a transport mechanism to deliver antibiotics into a bacterium.

"We'd be exploiting the pilus retraction mechanism to introduce antibiotics directly into a cell, bypassing its outer membrane barrier," explains Craig. The SFU associate professor is an expert on the role that pili play in bacterial infections.

"We do have antibiotics for *V. cholerae*, but these antibiotics also kill beneficial bacteria in the gut. The idea of using pili as a Trojan horse for antibiotic delivery is new and allows us to specifically and effectively target a given bacterial pathogen."

Craig says her team's discovery of *V. cholerae*'s retractable pili is made all the more exciting by the simplicity of its workings. "We know that other deadly bacteria have retractable pili but it'll be much easier to isolate how the mechanism can be used to uptake antibiotics in *Vibrio cholerae*."

Craig says using pili as an antibiotic delivery mechanism to treat Pseudomonas aeruginosa, a deadly bacterial respiratory infection that hits mainly people with Cystic Fibrosis, could save many lives.

Christopher Ford is a research associate in Craig's lab. Subramaniapillai Kolappan, one of Craig's master's students, recently graduated from SFU.