

How plague-causing bacteria disarm host defense

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Effector proteins are the bad guys that help bacterial pathogens do their job of infecting the host by crippling the body's immune system. In essence, they knock down the front door of resistance and disarm the cell's alarm system.

Now, researchers at the University of California, San Diego (UCSD) School of Medicine have identified a novel molecular target for an effector protein called YpkA, one of several effectors of the bacteria *Yersinia* – the pathogen responsible for the Middle Ages' "Black Death" and a virulent form of food poisoning today. Their study will be published online in the May 25 issue of *Molecular Cell*.

YpkA targets a host protein called Gaq, the messenger that transmits extracellular signals ("we are under attack!") into the host cell, so that it can mount a defense.

"The alarm signal sent by Gaq is intercepted by YpkA, which sets up a roadblock along several cellular pathways that Gaq uses to deliver the alarm," said lead author Lorena Navarro, Ph.D., post-doctoral researcher in the lab of the study's principle investigator, Jack E. Dixon, Ph.D., professor of Pharmacology and Cellular and Molecular Medicine at the UCSD School of Medicine.

Identifying this new target is the first step to developing effective strategies for preventing disease, including means to fight antibiotic-resistant strains of *Yersinia* that could be used in biological warfare,

according to Navarro.

The genus *Yersinia* includes three species of bacteria that are pathogenic to humans: *Y. pestis* is perhaps the most infamous, being responsible for the bubonic plague (also known as the Black Death), which killed more than 200 million people in the Middle Ages.

"This bacterial species could still be a threat today," said Navarro, adding that scientists had isolated an antibiotic-resistant strain of this species. In addition *Y. pseudotuberculosis* and *Y. enterocolitica* are big words for nasty, little bugs that cause what's commonly known as food poisoning. All three bacteria species find their way past the body's immune system through a sophisticated invasion system that injects the effector proteins directly into the host cell's cytoplasm.

"More than a decade after its discovery, our understanding of YpkA is still incomplete," Navarro said. "But *Yersinia* has maintained YpkA over millions of years, so it must be doing something important." The researchers speculate that YpkA plays an important role in disabling the body's immune system beyond its previously known role of disrupting the host cell's normal structure, which interferes with the cell's innate ability to engulf and destroy invading bacteria. "The question now becomes, why is Gaq targeted by YpkA?"

Source: University of California - San Diego

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