Bacteria have their own immune system protecting against outside DNA

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Bacteria like Salmonella have a complicated immune system that helps them recognize and isolate foreign DNA trying to invade their cell membrane, according to a University of Washington-led study in the June 8 issue of *Science Express*.

The research, which also included scientists at the Sidney Kimmel Cancer Center in San Diego, could have major implications for understanding the evolution of disease-causing bacteria. The findings may also impact the biotech industry, where bacteria are used to produce recombinant human proteins for medical treatments and research.
A group of researchers led by Dr. Ferric Fang, professor of laboratory medicine and microbiology at the UW School of Medicine, were interested in learning how bacteria respond to genetic information coming from outside sources. Just as immune cells recognize and attack foreign invaders in the human body to protect against harmful infections, single-cell organisms have a protein called H-NS that recognizes foreign DNA and prevents it from becoming active, the researchers discovered.

But bacteria can also benefit from foreign DNA. When Salmonella is infecting an animal or person, for instance, many proteins the bacteria need to cause disease are encoded by DNA acquired from other bacteria. The researchers found that when the bacteria is infecting a host, other molecules can compete with the H-NS protein, allowing the disease-causing genes to be expressed. When the bacteria are in the environment, H-NS turns these genes off to avoid detrimental consequences if all the

disease-causing genes were to be expressed at once.

These findings give scientists new insight into how bacteria can protect themselves from an invasion by foreign DNA, yet still take in genetic information from diverse sources that makes them more virulent.

"By harnessing foreign DNA, bacteria that cause typhoid, dysentery, cholera and plague have evolved from harmless organisms into feared pathogens," explained Dr. William Navarre, a senior fellow at the UW and primary author of the study. "This research gives us an explanation of how pathogenic bacteria have evolved over millions of years."

The researchers also learned that the H-NS protein is able to recognize foreign DNA on the basis of its increased content of adenine and thymine, the building blocks of DNA.

"It has been a great mystery why disease-causing genes of bacteria usually contain more adenine and thymine," said Michael McClelland, professor and director of the Molecular Biology Program at the Kimmel Cancer Center. "Now we know this is because such sequences are easier to recruit and regulate than other DNA."

This research could also have major implications for the biotech industry, which uses bacteria for the production of recombinant proteins for medicine and research. These proteins, such as insulin or human growth hormone, are created when a piece of human DNA corresponding to that protein is introduced into bacteria. The bacteria then reproduce many times over, creating more of the protein each time they reproduce. The proteins are purified out from the bacteria, leaving behind only the useful protein. However, in that process, the yield of some human proteins produced in bacteria can be low. The new research indicates that the H-NS "immune system" may be responsible for interfering with the expression of human genes in bacteria.

"Having a better understanding of this system could help the biotech industry make recombinant proteins more efficiently," said Fang. "More foreign protein can be produced in bacteria that don't have the H-NS molecule."

Source: University of Washington