Salmonella: Trickier than we imagined

June 13 2008

Salmonella is serving up a surprise not only for tomato lovers around the country but also for scientists who study the rod-shaped bacterium that causes misery for millions of people.

In research published June 4 in the online journal *PloS One*, researchers say they've identified a molecular trick that may explain part of the bacteria's fierceness. A team from the University of Rochester Medical Center has identified a protein that allows the bacteria to maintain a low profile in the body, giving the bacteria crucial time to quietly gain a foothold in an organism before the immune system is roused to fight the invader.

"Inflammation immediately after a bacterial infection occurs helps the body fight off bugs like Salmonella quickly," said Jun Sun, Ph.D., the leader of the team and assistant professor of Gastroenterology and Hepatology. "But it may be that Salmonella is especially equipped with tools to allow it to evade the immune system early on, growing quietly and then really making the host quite ill. Salmonella is trickier than we imagined."

Sun's team found that a virulence protein known as AvrA dampens the inflammatory response. That helps the bacteria avoid the wrath of the immune system and gives the infection crucial time to grow and develop before it needs to expend energy to fight off immune cells like neutrophils, which would attack the intruder more quickly if the bacteria attacked the body in a more clear-cut fashion.

"AvrA allows Salmonella to make peace with you, buying the bacteria a little time to survive in the body," said Sun. "That's bad news for the body, because then the bacteria spreads. AvrA allows the bacteria to do harm in the body without the body realizing it. Bacteria have been evolving for millions of years. That gives them some tricks that perhaps we don't understand yet."

AvrA is one of several proteins in Salmonella that affect cells in the wall of the intestines and stomach known as epithelial cells. These cells link up tightly together thanks to molecules known as tight junction proteins, which form an elaborate barrier to keep molecules and substances in or out of the colon. The bacterium employs several proteins enabling it to loosen these junctions, effectively breaking up the barrier and making the body vulnerable to the infection.

While several of Salmonella's proteins allow it to loosen up and punch through this latticework, Sun's team unexpectedly found that AvrA allows the bacteria to maintain these tight junctions. This ability reduces the body's inflammatory response and allows the bacteria to avoid detection by the immune system for some time, enabling the bacteria to survive in the host. The severe symptoms of infection, including nausea, vomiting, diarrhea, and abdominal cramps, typically hit anywhere from 8 to 72 hours after initial exposure to the bug.

"It's a surprising finding, which is why we've repeated our studies many times and done tests in different experimental models," said Sun, whose team studied the phenomenon in the laboratory, in mice, and in cultured human cells.

AvrA is one of several virulence proteins that Salmonella has at its disposal, using syringe-like molecular machinery to shoot toxins and proteins into cells just seconds after its first encounter with a cell in the small or large intestine. The protein is especially adept at functioning in

low-acid locales like the gut and bears close resemblance to a virulence protein known as YopJ that is active in Yersinia – the bug that caused the Black Plague.

Sun is one of several scientists who have shown that AvrA reduces inflammation in the body, acting to some degree like new arthritis medications by reducing the activity of an inflammatory molecule known as NF-Kappa B.

There are thousands of types of the bug. Sun studied Salmonella Typhimurium, one of the two most common types; that bacterium and Salmonella enteritidis together cause more than half the Salmonella illnesses seen in people. While the current outbreak in tomato involves a much more rare form, Salmonella saintpaul, Sun says that the AvrA gene is in more than 80 percent of Salmonella types overall, including the "saintpaul" variety.

Source: University of Rochester