SOUTHWESTERN NEWS

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CROSS TALK BETWEEN BACTERIA, HOST LEADS TO *E. COLI* INFECTION

DALLAS – June 30, 2003 – A strain of *E. coli* that causes severe, sometimes deadly, intestinal problems relies on signals from beneficial human bacteria and a stress hormone to infect human cells, a researcher at UT Southwestern Medical Center at Dallas has discovered.

The finding, which will appear online today in *Proceedings of the National Academy of Sciences*, could lead to the development of beta blockers as a therapy to impede this cellular signaling system, causing the harmful bacteria to pass blindly through the digestive tract, said Dr. Vanessa Sperandio, lead author of the study.

"You're not really attacking the bacteria per se," said Dr. Sperandio, assistant professor of microbiology at UT Southwestern. "You are just rendering it blind. The bacteria won't activate the virulent genes unless it knows where it is. If it can't activate the things it needs to bind to the intestine, it will be washed away."

In the past, beta blockers have been used to treat migraines, high blood pressure, glaucoma and tremors but not to impede infection. Developing new therapies for infection with this strain of *E. coli* – known as enterohemorrhagic *Escherichia coli*, or EHEC – is important because treatment with conventional antibiotics can cause the release of more toxins and may worsen the disease outcome.

Dr. Sperandio found that when a person ingests EHEC, the bacteria travel blindly through the digestive tract until reaching the intestine, where friendly bacterial flora in the intestine and the human hormone epinephrine, or adrenaline, send cellular signals alerting the bacteria to its location. This cellular cross talk leads to a cascade of genetic activations in which the EHEC colonizes the intestine and translocates toxins into human cells, altering the makeup of the cells and robbing the body of nutrients.

"The bacteria gets what it wants – nourishment – and the person ends up getting diarrhea," Dr. Sperandio said.

(MORE)

EHEC is responsible for outbreaks throughout the world of bloody diarrhea and hemolytic uremic syndrome – a condition that can lead to renal failure and death. Severe symptoms are most common in children, the elderly and immune-suppressed people.

EHEC is commonly transmitted through contaminated food or water. Foods known to have caused human infections include raw meat and unwashed vegetables. The Centers for Disease Control and Prevention report 73,000 cases of EHEC infection annually in the United States, resulting in 61 deaths.

Bloody diarrhea typically lasts about a week after infection with *E. coli*. One week after the condition resolves, some patients may develop hemolytic uremic syndrome, which is characterized by gastrointestinal bleeding, reduced urine production and anemia.

Treating EHEC infection with conventional antibiotics has shown to increase the chances that a patient will develop hemolytic uremic syndrome, Dr. Sperandio said. In 2000, an EHEC outbreak in Scotland affected thousands of people. Half of those infected received antibiotics, and half received no therapy. Of those treated with antibiotics, 18 percent developed the syndrome; of those receiving no treatment, only 5 percent developed the syndrome.

Dr. Sperandio, a Brazilian native whose studies focus mainly on gene regulation, began this three-and-a-half-year study during a postdoctoral fellowship at the University of Maryland School of Medicine. Other authors of the study included University of Maryland researchers.

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