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UT Southwestern researchers find mechanism that may stop *E coli* from developing in cattle

DALLAS – May 11, 2010 – Microbiologists at UT Southwestern Medical Center, working with the Department of Agriculture, have identified a potential target in cattle that could be exploited to help prevent outbreaks of food-borne illnesses caused by a nasty strain of *Escherichia coli*.

In the study, available online and in an upcoming issue of the *Proceedings of the National Academy of Sciences*, researchers interfered with a genetic sensing mechanism that allows the *E. coli* strain known as enterohemorrhagic O157:H7, or EHEC, to form colonies within cattle, causing the bacteria to die off before they could reach the animals' recto-anal junction, the primary site of colonization. Most other strains of *E coli* gather in the colon.

"We're diminishing colonization by not letting EHEC go where it needs to go efficiently," said Dr. Vanessa Sperandio, associate professor of microbiology and biochemistry at UT Southwestern and senior author of the study. "If we can find a way to prevent these bacteria from ever colonizing in cattle, it's possible that we can have a real impact on human disease.

"This could be something as simple as including some sort of antagonist in cattle feed, which would result in less shedding of the bacteria in fecal matter with less contamination down the road in food products."

Dr. Sperandio said the finding is important because an estimated 70 percent to 80 percent of the cattle herds in the U.S. carry EHEC.

Although EHEC can be a deadly pathogen to humans, the bacterium is part of cattle's normal gastrointestinal flora. EHEC harbors a gene called *sdiA*, which makes the SdiA protein. The SdiA protein senses a chemical made by microbes in the animal's rumen, the first of a cow's four stomachs, which serves as a large fermentation chamber. Detecting this signal allows EHEC to pass through the rumen and colonize the recto-anal junction.

For the study, the researchers injected two types of EHEC into the rumens of eight grain-fed adult cows. One mutant version lacked SdiA and could not detect the signal in the rumen. Another strain produced an enzyme that destroyed the chemicals in the rumen sensed by SdiA.

The researchers found that colonization diminished significantly when these EHEC strains were unable to sense the rumen chemicals. The process prevented the bacteria from moving on through the

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stomach and colonizing.

“If there’s no signal, then there’s no acid resistance, a requirement for the pathogen to make it to the recto-anal junction,” Dr. Sperandio said. “Everybody had thought that this type of signaling occurred naturally in the gastrointestinal tract of mammals. Our finding serves as a proof-of-principle that we might be able to target this system to prevent food contamination.”

EHEC, like other *E coli* strains, is usually transmitted through contaminated food. Recent outbreaks in the U.S. have been found in ground beef, spinach and raw sprouts. 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.

Cattle are the primary source for most *E coli* infections in the U.S. When cattle waste reaches water sources near food crops, contamination can occur. Unsanitary slaughtering of cattle also can lead to cross-contamination of the beef itself, and shipment of infected food speeds the rate at which the public can become ill.

Dr. Sperandio said the next step is to assess what happens to cows fed a grass-based, rather than grain-based, diet.

Other UT Southwestern researchers involved in the study were Dr. Darya Terekhova, postdoctoral researcher in microbiology; and Dr. David Hughes, lead author and former graduate student in microbiology. Dr. Hughes is now at the University of Miami.

Researchers from the University of Idaho, UT Dallas, the USDA Agricultural Research Service and the University of Maryland School of Medicine also contributed to the study.

The study was funded by the National Institutes of Health, Burroughs Wellcome Fund, and the National Cattlemen’s Beef Association.

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