Bacteria in urinary tract infections caught making burglar's tools

February 20 2009

Differences in the way they use their genes cause different strains of the E. coli bacterium to take on different hues. The beaker in the foreground contains strains of bacteria linked to urinary tract infections, while the background beaker holds more benign strains of bacteria isolated from the gut. Scientists are hoping to develop drugs that specifically target infection-causing strains of bacteria like those in the foreground beaker. Credit: Michael Purdy/Washington University School of Medicine in St. Louis

Bacteria that cause urinary tract infections (UTIs) make more tools for stealing from their host than friendly versions of the same bacteria found in the gut, researchers at Washington University School of Medicine in St. Louis and the University of Washington have found.

The tools, compounds called siderophores, allow the bad bacteria to steal iron from their hosts, making it easier for the bacteria to survive and reproduce. But they also provide a potential way to target the bad strains

of bacteria for eradication without adversely affecting the good strains, researchers report in a study published online Feb. 20 by *PLoS Pathogens*.

"When we treat an infection with antibiotics, it's like dropping a bomb—nearly everything gets wiped out, regardless of whether it's helpful or harmful," says lead author Jeff Henderson, M.D., Ph.D., a Washington University infectious disease specialist who treats patients with UTIs at Barnes-Jewish Hospital. "We'd like to find ways to target the bad bacteria and leave the good bacteria alone, and these siderophores are a great lead in that direction."

UTIs are one of the most common infections, causing around $1.6 billion in medical expenses every year in the United States. Half of all women will experience a UTI at some point in their lives, and recurrent UTIs affect 20 to 40 percent of these patients. Scientists believe 90 percent of all UTIs are caused by the bacterium *Escherichia coli* (*E. coli*).

The *E. coli* that cause UTIs may come from the human gut, where several strains of the bacteria reside. Scientists think some of those strains help their human hosts by aiding digestion and blocking other infectious organisms. To study how friendly and infection-causing *E. coli* strains differ, Henderson and colleagues at the Center for Women's Infectious Disease Research at Washington University used a new approach called metabolomics. Instead of examining genes, metabolomics analyzes all the chemicals produced by a cell, which includes bacterial growth signals, toxins and waste products.

"This allows us to look at the end products of many genes working together," says senior author Scott Hultgren, Ph.D., the Helen L. Stoever Professor of Molecular Microbiology. "We assess what all the various assembly lines are producing and which products disease-causing bacteria prefer to make, such as certain siderophores."

Bacteria studied in the experiment came from recurrent UTI patients treated at the University of Washington. Researchers cultured both *E. coli* from stool samples and urine samples. They found that the strains from urine made more yersiniabactin and salmochelin, two siderophores that help bacteria scavenge iron to support their own survival.

Iron is an important nutrient typically kept under tight control by the host, and there's evidence that a back-and-forth contest centered on iron has been raging for millennia between disease-causing microbes and the hosts they exploit. For example, studies suggest that humans may make a protein that specifically blocks particular bacterial siderophores.

There may be multiple ways to take advantage of the infectious bacterial strains' reliance on siderophores. Researchers will try to block or disrupt the activity of the proteins that make siderophores, but they also may use what Henderson calls a "Trojan horse" strategy.

"To steal iron, siderophores have to be sent out from the cell, bind to the iron, and then be taken back into the cell," he explains. "If we can design an antibiotic that looks like a siderophore, we might be able to trick only disease-causing bacteria into taking up the drug while leaving other bacteria alone."

More information: Henderson JP, Crowley JR, Pinkner JS, Walker JN, Tsukayama P, Stamm WE, Hooton TM, Hultgren SJ. Quantitative metabolomics reveals an epigenetic blueprint for iron acquisition in uropathogenic Escherichia coli. *PLoS Pathogens* 5(2): e1000305. doi:10.1371/journal.ppat.1000305

Source: Washington University School of Medicine