Bladder cells regurgitate bacteria to prevent urinary tract infections

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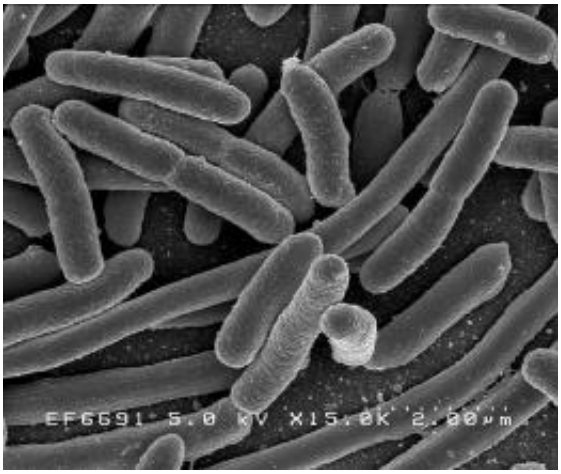

Scanning electron micrograph of Escherichia coli, grown in culture and adhered to a cover slip.

Duke Medicine researchers have found that bladder cells have a highly effective way to combat *E. coli* bacteria that cause urinary tract infections (UTIs).

In a study published online May 28, 2015, in the journal *Cell*, Duke researchers and their colleagues describe how bladder cells can physically eject the UTI-causing bacteria that manage to invade the host cell.

This response is analogous to having indigestion and vomiting to rid the

stomach of harmful substances.

The finding suggests there may be a potential way to capitalize on this natural tendency in bladder cells to help treat recurring UTIs.

UTIs are the second most common type of infection in the body, accounting for about 8.1 million doctor visits annually, the majority of which occur in women, according to the National Institutes of Health. Bacterial infections are the most common cause of UTIs, with 70 percent of infections arising from a particular type of *E. coli* bacteria.

"The cost for managing UTIs in the U.S. is close to $3 billion annually," said senior author Soman Abraham, Ph.D., professor in the departments of Pathology, Immunology, and Microbiology and Molecular Genetics at Duke University School of Medicine, and professor in the Program in Emerging Infectious Diseases, Duke-National University of Singapore.

"Because *E. coli* are able to hide inside of the bladder cells, it's especially difficult to treat UTIs with regular antibiotics," Abraham said. "So there is increased need to find new strategies for treatment, including co-opting any preexisting cellular tactics to combating infection."

When *E. coli* first attack bladder cells, the cell's surveillance machinery—known as autophagy—is the first line of defense against pathogens. The autophagy machinery encases the bacteria in a host membrane and shuttles them to the lysosome, a "capsular cauldron," that destroys harmful pathogens in its acidic environment. But upon entering the lysosome, some pathogens have the capacity to neutralize the acidic environment and avoid being degraded.

Using mouse models of UTIs and cultured human bladder cells, the authors found that the host cells can sense when lysosomes have been rendered neutral and are malfunctioning. The host cells then respond by

triggering the lysosome to eject its contents, including the bacteria.

"When the cells have trouble digesting the materials in the lysosomes, a logical way to get rid of this potential hazard is to throw it up," said first author Yuxuan Miao, a Ph.D. candidate in Duke's department of Molecular Genetics and Microbiology.

The bacteria that are expelled out of the bladder cells appear to be encased in a cell membrane, presumably ensuring their elimination in urine and avoiding any bacterial reattachment to the bladder wall.

"It was thought that lysosomes always degrade their contents," Miao said. "Here we are showing for the first time that when the contents cannot be degraded, the lysosome appears to have a back-up plan which is to expel the contents in capsules."

The researchers hope these findings will aid in finding chemical targets that can accelerate and amplify the bladder cell's ability to expel the bacteria.

"A lot of women tend to experience recurrent infections once they have an initial bout of UTI," Abraham said. "The reason for this is that there is bacterial persistence within the cells of the bladder. If we can eliminate these reservoirs using agents that promote expulsion, then we can potentially eradicate recurrent UTIs."

Provided by Duke University Medical Center