

Combating Diarrheal Diseases

SCHOOL OF MEDICINE RESEARCHERS HELP ID STRUCTURE OF BACTERIUM THAT CAUSES TRAVELER'S DIARRHEA

— ANYONE WHO'S HAD traveler's diarrhea knows that one small bug can spoil many big plans. That same bug, a strain of bacteria called enterotoxigenic *Escherichia coli* (ETEC), is capable of wreaking more serious havoc: it's the leading cause of community-acquired childhood diarrhea in the developing world, according to the World Health Organization. All told, ETEC sickens hundreds of millions of people each year.

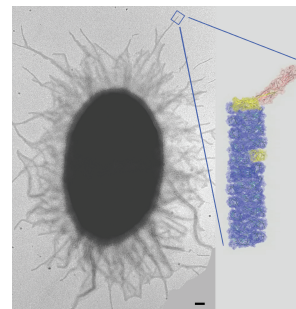
Researchers at the School of Medicine, the Naval Medical Research Center, and the National Institutes of Health have now figured out how the bacteria stick around long enough to cause diarrheal diseases, a discovery that has important implications for creating better therapeutics. The researchers have mapped the structure of the thin, hairlike fibers, called pili or

fimbriae, that extend from the surface of bacteria and attach the bug to epithelial cells lining the intestine.

"Each fiber is made of proteins, including a specialized protein at the tip that does the binding, and about a thousand copies of another protein that forms a springlike fiber that can unwind and rewind during the churning motion bacteria must endure to remain bound in the gut long enough to cause disease," says Esther Bullitt, a MED associate professor of physiology and biophysics and the study's senior author.

The researchers believe that their newfound knowledge of the proteins — particularly the specialized tip protein — will guide the development of a vaccine. The study appeared in the June issue of the *Proceedings of the National Academy of Sciences*.

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An electron micrograph of an enterotoxigenic *Escherichia coli* bacterium, which causes traveler's diarrhea. The bacterium has hundreds of surface fibers that attach to the intestine. Each fiber is made of proteins, including a specialized protein at the tip (shown in pink on the right) and about a thousand copies of another protein (two shown in yellow and the rest in blue) that form a springlike fiber.

Shutting Down Oral Cancer

BU TEAM LINKS OVEREXPRESSED GENE TO SPREADING TUMORS

— ORAL CANCER, WHICH affects the mouth and throat, can spread quickly and has a 50 percent survival rate beyond five years. But research at BU's Henry M. Goldman School of Dental Medicine offers new insight into how the disease might be treated.

Maria Kukuruzinska, an SDM professor of molecular and cell biology, has shown a direct relationship between the aberrant behavior of a gene known as DPAGT1 and the loss of adhesion between cells in oral cancer cell lines and oral tumor tissues. In healthy tissues, cells are held together with the help of an adhesion receptor called E-cadherin. In oral

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cancer, the DPAGT1 gene is overactive, and interferes with E-cadherin's adhesive properties. Tumors spread when cells can't stick to one another.

"Such discohesive cells peel off the tumor and establish new tumor islands," Kukuruzinska says. "The hallmark of malignancy is when cells break apart, migrate, and nest in

inappropriate organs."

When researchers suppressed DPAGT1, they enhanced the E-cadherin molecule's ability to form junctions between cells. The team's findings suggest that diminishing DPAGT1's activity could interrupt the growth of a tumor.

"You can't jump to the conclusion that you can stop cancer from developing," says Kukuruzinska, whose study appeared in the July 15 issue of *Cancer Research*. "But we can perhaps stop tumors from spreading."



Now researchers want to find the cause of the gene's overexpression. They hope to identify repressor molecules that regulate the gene. "We believe this is not going to be restricted to oral cancer," Kukuruzinska says, "but will be a feature common to subsets of

epithelial tumors in general."

"Oral cancer is very pernicious and deadly," she adds. "It's extremely painful and difficult to treat.

And it's damaging aesthetically. Once a piece of a tongue or a jaw is removed, it's very visible."

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