UT SOUTHWESTERN MEDICAL CENTER NEWS

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UT Southwestern scientists unmask mysterious cells as key 'border patrol agents' in the intestine

DALLAS – May 9, 2011 – Researchers at UT Southwestern Medical Center have uncovered new clues about how the intestine maintains friendly relations with the 100 trillion symbiotic bacteria that normally live in the digestive tract.

Their latest findings, available online today and in a future edition of the *Proceedings of the National Academy of Sciences*, suggest that a once enigmatic cell population which lurks in the intestinal lining is essential for preventing friendly bacteria from invading into deeper tissue where they can cause debilitating conditions like inflammatory bowel disease (IBD).

"Possible new therapies for IBD could be devised by learning how to boost the antibacterial functions of this particular group of cells," said Dr. Lora Hooper, associate professor of immunology and senior author of the study. "The findings also might help researchers better understand how probiotics – mixtures of beneficial bacteria that are added to food products – boost the immune system."

The human intestine is home to a staggering number of bacteria. These microorganisms are put to good use as metabolic workhorses that help to liberate nutrients from the diet for our uptake and use.

While most healthy people have a friendly relationship with their gut microbes, this relationship turns sour in patients battling IBD. People suffering from the disease frequently have more bacteria that adhere to or invade their gut lining. When their immune system mounts an attack on these microbial invaders, they can develop painful ulcers and bloody diarrhea.

For this study, researchers studied mice genetically engineered to lack a mysterious immune cell called a gamma deltaintraepithelial lymphocyte (γδ IEL). This specialized T cell is found at body surfaces such as the skin and the gastrointestinal tract, where it insinuates itself between the epithelial cells that line these surfaces. These cells make up a large proportion of the body's T cells, but their exact function had been unclear.

"Our findings suggest that a major function of these T cells is to patrol intestinal borders, sensing when microorganisms have invaded the epithelial cells lining the intestine," said Dr. Hooper,

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who is also an investigator for the Howard Hughes Medical Institute at UT Southwestern. "When this happens, these T cells swing into action, making antibiotic proteins that kill the rogue bacteria and prevent their entry into deeper tissue."

The researchers also found γδ IEL cells play an important role in preventing intestinal pathogens such as *Salmonella* bacteria from spreading to deeper tissues.

"These T cells manifest their importance in the first three to four hours after the pathogen is encountered. This suggests that their primary responsibility may be to 'hold down the fort' until other immune cells can be recruited as backup," Dr. Hooper said.

Other UT Southwestern researchers involved in the investigation were Dr. Anisa Ismail, lead author and former graduate student and postdoctoral fellow in immunology; Cassie Behrendt and Kelly Ruhn, HHMI research technicians; Dr. Kari Severson, HHMI postdoctoral researcher; Dr. Shipra Vaishnava, instructor of immunology; Xiaofei Yu, graduate student in immunology; Jamaal Benjamin, Medical Scientist Training Program student; and Dr. Felix Yarovinsky, assistant professor of immunology. Researchers from the University of California, San Francisco, also participated. Dr. Ismail is now a postdoctoral fellow at Princeton University.

The work was funded by the National Institutes of Health, Crohn's & Colitis Foundation of America, Burroughs Wellcome Fund and the HHMI.

Visit http://www.utsouthwestern.org/digestive to learn more about UT Southwestern's clinical services for digestive disorders, including IBD.

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