UT SOUTHWESTERN MEDICAL CENTER NEWS

Media Contact: Kristen Holland Shear
214-648-3404
kristen.hollandshear@utsouthwestern.edu

UT Southwestern immunologists identify biochemical signals that help immune cells remember how to fight infection

DALLAS – May 28, 2009 – Immunology researchers at UT Southwestern Medical Center have discovered how two biochemical signals play unique roles in promoting the development of a group of immune cells employed as tactical assassins.

In their initial response, these immune cells, known as cytotoxic T lymphocytes, or CTLs, kill cells infected with pathogens. They also provide long-term protection against pathogens by "remembering" which proteins the pathogen makes. Targeting the ability of these CTLs to remember the pathogen is one way vaccines protect against infection.

"Until now, no innate signals have been identified that regulate the development of memory cells," said Dr. David Farrar, assistant professor of immunology at UT Southwestern and senior author of the study appearing online and in a future edition of *Blood*. "Our study is the first to identify the signals that promote the development of these memory cells when you first get infected."

The researchers previously showed that two molecules – interferon alpha and another signaling protein, cytokine, or IL-12 – are needed to induce the creation of memory cells. They also found that interferon plays a key role in "teaching" the immune system how to fight off repeated infections of the same virus.

Dr. Farrar said the findings suggest that in order to be most effective, a vaccine should induce the secretion of both of these innate cytokines.

The immune system consists of two components – the innate system, which provides immediate defense against infection, and the adaptive system, whose memory cells are called into action to fight off subsequent infections. The human immune system churns out both IL-12 and interferon alpha in large quantities in response to a viral infection.

"The concept in the field has been that these cytokines perform the same function, but our new findings suggest that they actually have very distinct roles," said Hilario Ramos, student research assistant in immunology and the study's lead author. "It turns out that the IL-12 signal is really important in driving that immediate, or effector, immune response while interferon drives the development of long-term memory."

(MORE)

Immune cell memory – 2

Past UT Southwestern studies have shown that the two cytokines work together in CD4+ T-cells to generate memory cells; the new research suggests that these molecules perform distinct roles in another type of immune cell called CD8+ T lymphocytes.

For these cells, whether they become killers or long-term memory cells depends upon which cytokine they respond to. Those that receive the IL-12 become killers while those that receive interferon alpha turn into long-term memory cells.

"Regardless of the precise mechanism, what we know now is that you can develop both long-term and immediate memory cells at the same time," Dr. Farrar said.

The next step, he said, is to identify pools of memory cells that "remember" specific pathogens in humans.

"There are some vaccines that are extremely effective, while others are only moderately effective," Dr. Farrar said. "If we can isolate pools of antigen-specific memory cells, we should be able to determine what it is about those pools of memory cells that is different between an extremely effective vaccine and one that's not so effective.

"If we can figure that out, then we can start to think about altering our approach to vaccinating based on the different type of microorganism that we're trying to vaccinate against," he said.

Other UT Southwestern researchers involved in the study were Ann Davis, former student research assistant in immunology; Alexander Cole, undergraduate research fellow; Dr. John Schatzle, associate professor of pathology; and Dr. James Forman, professor of immunology.

The National Institutes of Health supported the research.

###