SOUTHWESTERN NEWS

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THYMUS MAY HOLD CLUE TO REBUILDING IMMUNE SYSTEM AFTER HIV

DALLAS – December 17, 1998 – Discovery of a marker that allows tracking of thymus function also shows how the adult immune system might repair itself after being damaged by human immunodeficiency virus (HIV), UT Southwestern Medical Center at Dallas scientists reported in today's issue of *Nature.*

The research shows that the thymus makes new T-cells throughout adulthood and that HIV may block their production, said Dr. Richard Koup, chief of infectious diseases. The study, a collaboration including Koup, Dr. Daniel Douek, a postdoctoral fellow in infectious diseases, and Dr. Louis Picker, associate professor of pathology, also has important implications for people whose immune system has been damaged by cancer treatment.

The thymus produces T-cells, the body's main defense against infections. HIV infection destroys these cells, leading to the complications from AIDS.

For many years it was believed that the thymus only produced T-cells in people until about age 30 by which time it had slowly disappeared, replaced by fat. But the investigators found that patients in their 30s whose HIV infection was treated with highly active antiretroviral therapy (HAART) produced new T-cells.

This is important because HIV patients have lower than normal numbers of T-cells. This makes them highly vulnerable to other infections, as are cancer patients whose treatment has destroyed many of their T-cells.

"T-cells can be increased by expanding the few old ones remaining after HIV infection or cancer treatment, or through production of new T-cells," said Koup, who holds the Jay P. Sanford Professorship in Infectious Diseases. "If you expand the few surviving T-cells, you may not recover broad immunity to all infections. If T-cells programmed to fight certain infections

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have been destroyed, they can only be replaced by new T-cells produced by the thymus."

Using a marker for TCR-rearrangement excision circles, which are pieces of DNA produced during normal T-cell development in the thymus, the scientists were able to estimate the number of new T-cells produced by the thymus. The number of these cells in the blood indicates the level at which the thymus is functioning. The research showed that as HAART reduced the level of HIV, the number of these cells increased.

"The data suggests that HIV specifically inhibits the thymus either by infecting the cells within the organ, or affecting the ability of the thymus to produce T-cells by an unknown mechanism," Koup said.

The investigators now will look for ways to stimulate the thymus, thereby speeding recovery of the immune system after HAART or cancer treatment.

"Now that we have a way to measure thymus output, we will be able to test therapies that will increase T-cell production," Koup said.

The other researchers involved in the study are: Dr. Philip Keiser, internal medicine assistant professor; Dr. Richard McFarland, pathology technical staff associate; Earl Gage, UT Southwestern medical student; and researchers from Duke University Medical Center, National Institute of Allergy and Infectious Diseases, University of Minnesota Medical School, Emory University School of Medicine, the University of Massachusetts Medical Center, University of California, Los Angeles, School of Medicine and UCLA Institute.

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