MedicalXpress

Early immune response needed for hit-and-hide cancer viruses

January 14 2010

Retroviruses such as HIV and HTLV-1 don't hit-and-run, they hit-and-hide. They slip into host cells and insert their own DNA into the cell's DNA, and from this refuge they establish an infection that lasts a lifetime.

But that infection might be much less troublesome and much more manageable if the immune system could mount a strong response to the virus during its first few days in the body, according to a new study by cancer researchers at the Ohio State University Comprehensive Cancer Center-Arthur G. James Cancer Hospital and Richard J. Solove Research Institute (OSUCCC-James).

The animal study, published online in the journal *Blood*, examined the human T-lymphotropic virus type 1 (HTLV-1), which causes adult T-cell leukemia and several inflammatory diseases in some people.

"Our findings indicate that if the immune system could respond strongly to HTLV-1 and kill infected target cells early, it may inhibit the virus's ability to establish reservoirs of infected cells and make the infection more manageable later," says principal investigator Michael Lairmore, a professor and chair of veterinary biosciences and a cancer researcher at OSUCCC-James.

"This study tells us that the more we know about the earliest events of infection, the more it will help us develop vaccines and might block those events."

Lairmore and his colleagues examined HTLV-I infection in rabbits that were treated with the drug cyclosporin A, which is commonly used to suppress the immune system in people following organ transplantation. The researchers compared animals treated with this drug prior to viral infection with those given the drug one week after infection.

This study builds on earlier work by Lairmore and his colleagues showing that HTLV-I produces proteins that activate infected immune cells and causes them to divide, thereby increasing the number of infected cells in the body. The researchers found that cyclosporin A blocked that activation.

In this new study, the researchers used cyclosporin A to learn whether modifying the immune response - by providing fewer immune cells for the virus to attack - at a critical time, after the first week of infection when the virus needs to spread, would influence the extent of the infection weeks later.

In animals given the immune-suppressing drug first, the virus flourished. The number of virus copies jumped to 200 per 10,000 immune cells (lymphocytes), compared with 40 per 10,000 immune cells in control animals (these were infected with the virus but not given the drug). After a week or two, the number of virus copies fell, ranging from 113 to 160 for remainder of the 10-week experiment.

In the animals that were given the virus first and then the immune-suppressing drug a week later, on the other hand, the virus languished. The number of virus copies in these animals was lower than the controls, and it remained that way throughout the 10-week experiment. At week four after infection, for example, the immune-suppressed animals had on average nine virus copies per 10,000 immune cells, compared with 40 copies in control samples. At week 10, they had 10 virus copies compared with 30 in controls.

"The first experiment told us that if the immune system is suppressed, the viral load goes up - and we expected that," says Lairmore. "The second group was the surprise. Their viral load was low from the start, and it stayed that way. We didn't expect that. We thought the virus would recover and come back up.

"Collectively, our findings indicate that the immune system plays a key role in controlling HTLV-1 spread during early infection, which has important implications for a vaccine against this virus and for therapy for HTLV-1-associated diseases," says Lairmore.

Provided by The Ohio State University