SOUTHWESTERN NEWS

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UT SOUTHWESTERN RESEARCHERS KILL LATENT HIV-INFECTED CELLS USING IMMUNOTOXIN

DALLAS –October 15, 1999 – UT Southwestern Medical Center at Dallas researchers linked an antibody to a toxin, killing more than 99 percent of the human cells carrying a latent form of the human immunodeficiency virus (HIV)-1 in a laboratory study.

The researchers targeted cells harboring latent HIV by using an immunotoxin formed by joining a monoclonal antibody – an antibody made up of a protein from a single clone of cells – and a subunit of a plant toxin, ricin. Antibodies are the molecules that fight infections in the body. HIV currently can be controlled by highly active antiretroviral therapy (HAART), but if that treatment is halted, the virus reappears. Similar immunotoxins directed against other molecules have been used in more than 200 cancer patients with encouraging results.

"This 'Trojan horse' phenomenon, where latent virus exists even though there is no evidence of HIV, has been a perplexing problem in efforts to cure the disease," said Dr. Octavio Ramilo, an associate professor of pediatrics and microbiology who participated in the study, reported in the latest issue of the *Proceedings of the National Academy of Sciences.*

The problem is multiplied because, although potentially deadly, there are few latent T cells in the body – possibly one in 10 million. In order to have enough of these cells to study, the investigators used blood from uninfected individuals then, in laboratory dishes, the scientists infected the cells with HIV-1. Next the researchers killed the cells' actively producing HIV, leaving the latent "Trojan horse" cells behind. An immunotoxin targeting a molecule called CD45RO, which is found on the surface of virtually all CD4 memory T cells, was then added. Once the antibody bound to the marker, the toxin killed the cells harboring latent HIV-1.

"In additional experiments we found that this immunotoxin could kill both latent cells and those actively cranking out the virus," said Dr. Ellen Vitetta, director of the Cancer

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Immunobiology Center and holder of the Scheryle Simmons Patigian Distinguished Chair in Cancer Immunobiology, who collaborated on the research. "This was both a surprise and additional bonus."

If this immunotoxin works in patients, the investigators predict that it will not knock out the normal immune system.

"This immunotoxin spares all the virgin T-cells so that an individual could be reimmunized with routine vaccines," Vitetta said. "It should also leave behind many CD8 T memory cells, which lack CD45RO, that are uninfected. They can continue to maintain the cytotoxic arm of the immune system (the part that is destructive to cells) to protect against future infection."

The scientists now are trying to develop optimal methods to easily find the latent cells in patients and determine whether those cells can also be killed by this immunotoxin. "This is really the $64,000 question," Vitetta said, "since the latent cells in patients could be different."

Other collaborators included Dr. Louis Picker, associate professor of pathology and a researcher in the Cancer Immunobiology Center; Dr. Chin-Sheng Chou, a former Cancer Immunobiology Center postdoctoral fellow; Dr. Cynthia McCoig, a postdoctoral fellow and instructor of pediatrics; and Gregory Van Dyke, a Medical Scientist Training Program fellow.

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