New HIV vaccine target could solve mutation problem

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Researchers at UCSF and the University of Toronto have identified a potential new way of fighting against HIV infection that relies on the remnants of ancient viruses, human endogenous retroviruses (HERV), which have become part of the genome of every human cell.

Mounting evidence suggests that HIV infection could enable HERV expression by disrupting the normal controls that keep HERV in check.

In some HIV-infected individuals, infection fighting T cells are able to target HERV expressing cells.

Researchers believe that their findings, published in the November 9, 2007 issue of the journal "PLoS Pathogens," could lead to a vaccine targeting HERV that kills HIV infected cells.

"One important limitation to a T-cell vaccine targeting HIV itself is that HIV exists in so many variations and is constantly mutating. If we can find other ways for the immune system to target HIV-infected cells, we can overcome this problem in making an HIV vaccine. HERV may provide us with a good target to test," said study co-first author, Keith E. Garrison, PhD., post-doctoral fellow in UCSF's Division of Experimental Medicine.

HERV, human endogenous retroviruses, are the genomic fossils left behind from ancient viral infections that exist largely dormant within every cell. While HERV are present in every cell, HIV may disrupt the

normal constraints on HERV activity as it alters the cell to produce more HIV. This led the authors of the study to look for T cell responses to HERV in HIV-positive people.

They found T cell responses to HERV in HIV-positive people that were not present in HIV-negative people.

The researchers also compared the T cells that recognize HERV to other types of T cells, including those that recognize HIV. They found that T cells recognizing HERV were different from T cells that recognize HIV.

"HIV is poorly contained by the immune system, resulting in disease progression in most people. In contrast, infection with cytomegalovirus (CMV) is generally controlled for life. HERV specific T cells have more features in common with T cells that kill CMV, than with T cells that kill HIV. This is an encouraging finding which suggests that HERV specific T cells may be more effective than HIV specific T cells in controlling virus," said study co-first author, Brad Jones, BSc, a graduate student in the Department of Immunology at the University of Toronto.

The researchers looked at 29 individuals recently infected with HIV from the UCSF OPTIONS Project and 13 HIV-negative individuals and 3 hepatitis C infected, HIV-negative individuals from Toronto. In the group recently infected with HIV, researchers found a relationship between the degrees of T-cell response to HERV and the levels of HIV virus present in their blood.

“Although these results are preliminary, they encourage new ways to make the immune system potentially target HIV infected cells,” said study co-senior author, Mario A. Ostrowski, MD, associate professor in the Department of Immunology, University of Toronto.

Researchers believe that a vaccine could be created containing HERV

antigens that would stimulate T-cells targeting cells expressing HERV. Although the vaccine would not produce T cells capable of recognizing HIV itself, it would evoke a cellular immune response that could still protect people from becoming infected or limit the extent of damage caused by HIV.

“These findings may lead to new lines of attack against HIV, and the clue came from the study of the viruses within us,” said study co-senior author, Douglas F. Nixon, MD, PhD, professor of medicine in the UCSF Division of Experimental Medicine.

Source: University of California - San Francisco