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Researchers use chemical from medicinal plants to fight HIV

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Like other kinds of cells, immune cells lose the ability to divide as they age because a part of their chromosomes known as a telomere becomes progressively shorter with cell division. As a result, the cell changes in many ways, and its disease fighting ability is compromised.

But a new UCLA AIDS Institute study has found that a chemical from the Astragalus root, frequently used in Chinese herbal therapy, can prevent or slow this progressive telomere shortening, which could make it a key weapon in the fight against HIV.

"This has the potential to be either added to or possibly even replace the HAART (highly active antiretroviral therapy), which is not tolerated well by some patients and is also costly," said study co-author Rita Effros, a professor of pathology and laboratory medicine at the David Geffen School of Medicine at UCLA and member of the UCLA AIDS Institute.

The study, to be published in the Nov. 15 print edition of the *Journal of Immunology*, is available online at http://www.jimmunol.org/cgi/content/full/181/10/7400.

A telomere is a region at the end of every cell chromosome that contains repeated DNA sequences but no genes; telomeres act to protect the ends of the chromosomes and prevent them from fusing together — rather like the plastic tips that keep shoelaces from unraveling. Each time a cell divides, the telomeres get shorter, eventually causing the cell to reach a stage called replicative senescence, when it can no longer divide. This

seems to indicate that the cell has reached an end stage, but, in fact, the cell has changed into one with new genetic and functional characteristics.

A great deal of cell division must take place within the immune system for the system to function properly. For example, the so-called "killer" CD8 T-cells that help fight infection have unique receptors for particular antigens. When a virus enters the body, the killer T-cells whose receptors recognize that virus create, through division, versions of themselves that fight the invader.

Generally, the telomeres in cells are sufficiently long that they can divide many times without a problem. Moreover, when fighting infections, T-cells can turn on an enzyme called telomerase, which can prevent the telomeres from shortening.

"The problem is that when we're dealing with a virus that can't be totally eliminated from the body, such as HIV, the T-cells fighting that virus can't keep their telomerase turned on forever," Effros said. "They turn off, and telomeres get shorter and they enter this stage of replicative senescence."

Previous studies have shown that injecting the telomerase gene into T-cells can keep the telomeres from shortening, enabling them to maintain their HIV-fighting function for much longer. This gene-therapy approach, however, is not a practical way to treat the millions of people living with HIV.

For the present study, rather than utilizing gene therapy, the researchers used a chemical called TAT2, which was originally identified from plants used in traditional Chinese therapy and which enhances telomerase activity in other cell types.

They tested TAT2 in several ways. First, they exposed the CD8 T-cells from HIV-infected persons to TAT2 to see if the chemical not only slowed the shortening of the telomeres but improved the cells' production of soluble factors called chemokines and cytokines, which had been previously shown to inhibit HIV replication. It did.

They then took blood samples from HIV-infected individuals and separated out the CD8 T-cells and the CD4 T-cells — those infected with HIV. They treated the CD8 T-cells with TAT2 and combined them with the CD4 T-cells in the dish-and found that the treated CD8 cells inhibited production of HIV by the CD4 cells.

"The ability to enhance telomerase activity and antiviral functions of CD8 T-lymphocytes suggests that this strategy could be useful in treating HIV disease, as well as immunodeficiency and increased susceptibility to other viral infections associated with chronic diseases or aging," the researchers write.

Source: University of California - Los Angeles