# Researchers find cell protein that literally nips HIV in the bud

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UCLA researchers have found that a key protein in the body's dendritic cells can stop the virus that causes AIDS from "budding" — part of the virus' life cycle that is crucial to its ability to replicate and infect other cells.

The study, scheduled for publication in the April issue of the Federation of American Societies for Experimental Biology's FASEB Journal, is currently available online at www.fasebj.org/cgi/rapidpdf/fj.07-9443comv3.pdf.

"If we can block virus generation, then we can control the disease," said lead author Shen Pang, associate professor in the division of oral biology and medicine at the UCLA School of Dentistry and a member of the UCLA AIDS Institute.

Dendritic cells are specialized white blood cells in the skin, mucosa and lymph nodes that kick-start a primary immune response to foreign invaders by activating lymphocytes, including the T cells that HIV targets. Though dendritic cells can be infected with HIV — and indeed play a crucial role in transmitting the virus to T cells — studies have shown that viral generation from these cells is nearly a hundred times lower than from infected T cells, indicating that the cells may possess some inhibiting property.

Pang hypothesized that DC-SIGN, a protein expressed in dendritic cells, may be responsible for such inhibition. He and his colleagues found that

DC-SIGN and a related protein, DC-SIGNR, both demonstrated 95 percent to 99.5 percent inhibition of viral production from host cells.

Very few cells are infected when HIV first enters the human body, but the virus rapidly creates new copies of itself, which in turn infect more cells. To achieve this, the virus, after infecting a cell, sends envelopes of protein to the cell's membrane. The viral genomes then combine with viral structural proteins and move into these envelopes. The envelopes bubble, or bud, outward, releasing viral particles that will infect more cells and start new viral life cycles.

According to the researchers, DC-SIGN appears to block HIV generation by efficiently neutralizing an HIV glycoprotein on the surface of the HIV envelope known as gp120, a key to viral infection. In such cases, while some viral particles may still be released from the infected dendritic cells, the lack of gp120 in their envelopes means they are not infectious to CD4-positive T-lymphocytes and macrophages. In other words, these viral particles have been rendered uninfectious.

Current methods to interrupt the life cycle of the virus are limited because they generally target HIV at the stages of viral entry, reverse transcription and post-translational protein cleavages. Once the virus passes through these stages, treatment fails. The UCLA researchers, therefore, focused on halting the virus' generation at different stages in its life cycle.

"The strong inhibition of viral production by DC-SIGN suggests the possibility of using this protein for treatment of HIV-infected patients," the researchers write. "Expression of this protein in various CD4-positive cells should inhibit viral production from infected cells. Because it can also enhance the immune response, DC-SIGN is expected to be useful for in vivo studies for developing an HIV vaccine."

Source: University of California - Los Angeles