# New target for HIV/AIDS drugs and vaccine discovered

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Researchers from Rome, Italy, describe a finding in the August 2007 print issue of The FASEB Journal that could lead to new drugs to fight the HIV/AIDS virus, as well as new vaccines to prevent infection.

It has been known that HIV proteins disable the antibody-forming part of the immune system (the "homeland defense" or acquired immune system). In this report, researchers demonstrate for the first time how the HIV-1 Nef viral protein delivers a one-two punch to the body's innate immune system (our "early warning system" composed of dendritic and natural killer cells). First, Nef hijacks dendritic cells (DCs) to upset the function of natural killer (NK) cells. Second, after blocking this first line of defense against the immune system, Nef uses DCs and NK cells to create a microenvironment that actually makes it easier for HIV/AIDS to replicate.

According to Maria Giovanna Quaranta of Instituto Superiore de Sanità and first author of the article, "The findings described in this work may have several implications for AIDS treatment: the understanding of Nef function, mechanism of action, and cellular partners might aid the discovery of suitable drugs able to block the activity of this smart protein." Quaranta added, "An exciting possibility is the design of a vaccine including a mutated Nef protein unable to assist the virus in the control of its host."

The research findings also raise another intriguing possibility: Nef proteins may be able to boost or suppress DC and NK cell activity. If so,

it may prove to be a valuable new therapeutic approach for people with diseases and disorders that involve overactive or underactive immune responses. DCs and NK cells play critical roles in the body's initial defense against infection. DCs are instrumental in identifying foreign invaders to the body and then orchestrating an immune response that ultimately removes them. NK cells are among the first cells summoned by DCs to help isolate and contain the infection until more potent reinforcements can be manufactured to eradicate the virus or bacteria. When DC cells can no longer adequately "manage" the immune response and when NK cells can no longer contain infections, the likelihood of survival without medical intervention is relatively low.

"HIV's relatively rapid evolution has given it an ability to handle all our bodies can throw at it and more," said Gerald Weissmann, MD, Editor-in-Chief of The FASEB Journal. "Now that we know how the viral protein disables the innate as well as the acquired arm of our immune system, we can begin to design decoy proteins or to devise new vaccines. Millions of lives depend on our finding a way to restore both aspects of our immune defense against HIV/AIDS—this study should go a long way toward that goal."

Source: Federation of American Societies for Experimental Biology