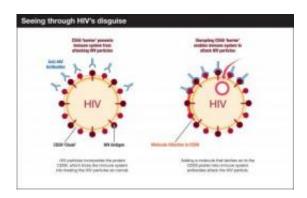


Scientists work to detach protein that HIV uses as protective shield

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Andy Qigui Yu, M.D., Ph.D., assistant professor of microbiology and immunology at Indiana University School of Medicine, is researching a compound that could help the immune system, more effectively fight HIV. Credit: Indiana University

One of the frustrations for scientists working on HIV/AIDS treatments has been the human immunodeficiency virus' ability to evade the body's immune system. Now an Indiana University researcher has discovered a compound that could help put the immune system back in the hunt.

It's not that the human <u>immune system</u> doesn't recognize HIV. Indeed, an infection causes the body to unleash antibodies that attack the virus, and initially some HIV is destroyed.

But HIV is able to quickly defend itself by co-opting a part of the innate



human immune system — the immune system people are born with, called the complement. The complement includes a vital mechanism that prevents immune system cells from attacking the body's own cells. HIV is able to incorporate a key protein in that self-protection mechanism, CD59, and by doing so makes itself appear to be one of the body's normal cells, not an infective agent.

In laboratories at the Indiana University School of Medicine, Andy Qigui Yu, M.D., Ph.D., assistant professor of microbiology and immunology, is testing a promising compound that may counteract HIV's ability to hijack the immune system's protection mechanism.

"HIV is very clever. As it replicates inside cells, it takes on the CD59. The virus is covered with CD59, so the immune system treats the virus like your own normal cells," Dr. Yu said.

In November, the Bill & Melinda Gates Foundation announced it had awarded nine new Grand Challenges Explorations Phase II grants, one of them to Dr. Yu. The Phase II grants were awarded to researchers who had received initial \$100,000 awards and had shown promising results.

The new grant will support not only Dr. Yu's research into compounds that may block the ability of HIV to hide behind the CD59 "cloak," but also his work to identify the mechanism the virus uses to incorporate CD59.

"If we find that mechanism, then we can develop something to block that incorporation, and HIV may lose that protection from the immune system," Dr. Yu said.

Researchers have been able in the past to generate antibodies that successfully attacked HIV in the laboratory. But these antibodies have failed in human testing because the virus in the body escapes from



immune system attacks, Dr. Yu said.

In an attempt to disrupt HIV's hijacking of CD59, Yu and colleagues at IU and Harvard University crafted a molecule from a bacterial toxin that is known to bind to the CD59 protein. In laboratory tests, they administered the molecule to blood samples taken from patients with HIV. The bacteria toxin molecule latched on to the CD59 proteins, revealing the viral particles to be invaders and enabling the <u>antibodies</u> to attack the virus.

Reporting their findings in the Journal of Immunology in December 2010, the researchers suggested that the molecule could potentially be developed into a new therapy to fight <u>HIV/AIDS</u>.

More recent experiments have indicated that the administration of the molecule enabled the antibody-complement to attack infected cells and not just the <u>virus</u> particles found in the blood samples. The next steps will include more extensive testing of the molecule in a broader range of patient samples, Dr. Yu said.

Provided by Indiana University School of Medicine

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