



# GLADSTONE INSTITUTE OF VIROLOGY AND IMMUNOLOGY

## NEWS

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**FOR YOUR INFORMATION**  
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### **HIV PROTEIN STOPS CELL DIVISION, LEADING TO MORE VIRUS AND SICKER PATIENTS, GLADSTONE RESEARCHERS FIND**

**SEATTLE** --T cells are supposed to be one of the body's best defenses against the invading intracellular foes like viruses and some bacteria. But when they encounter HIV, some of these immune system cells become targets for infection. Once infected, T cells begin producing HIV. New research at the Gladstone Institute of Virology and Immunology is showing how the virus coerces T cells into becoming very efficient virus factories.

At the center of it is the HIV protein Vpr, which stops infected T cells from dividing. In doing so, Vpr helps HIV to harness the infected cell's resources to create more HIV. The process goes on, creating more virus, which then go on to kill more T cells. The outcome is a sicker patient.

Michael P. Sherman, MD, PhD, Gladstone research scientist and UCSF assistant clinical professor of medicine, presented his research on Feb. 26 at the Ninth Annual Conference on Retroviruses and Opportunistic Infections.

Scientists already knew that laboratory cultured cells stopped dividing when large amounts of Vpr were artificially introduced into cells. Sherman and his research team showed that the cells also stopped dividing when natural amounts of Vpr were produced under the control of HIV.

What they didn't know was whether Vpr was also halting cell division in the cells of HIV-infected patients. The new research shows cell division is halted in HIV-infected cells taken from patient blood samples. The finding helps explain how HIV is able to reproduce so efficiently in the human body.

As cells normally move through the cell cycle, they arrive at S phase during which DNA is synthesized to duplicate the chromosomes in preparation for cell division. Prior to cell division, the cells will enter the G2 phase when the cell checks its internal systems to see if it is ready to divide. The recent studies reveal that infected activated cells do not divide but instead are paused in the G2 phase, a state more favorable for HIV replication.

The researchers verified that Vpr is indeed a major player in G2 cell cycle arrest by infecting cultured peripheral blood cells taken from HIV-free donors. Some of the cells were

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infected with normal HIV while other cells were infected with HIV lacking Vpr. Cells infected with normal HIV were found to be in G2 cell cycle arrest. Cells infected in the absence of Vpr divided normally.

“If we can show that this arrest is responsible for a large proportion of virus replication, then it might in the future lead to another target to hamper HIV replication in patients,” Sherman said.

The research was possible because of a laboratory technique that can detect infected cells. Fine-tuned at Gladstone, the new technique uses a fluorescent antibody to tag cells containing p24, a protein present in all HIV-producing cells. While the technique was introduced a decade ago, the results were unreliable, Sherman said. But technical advances and the recent availability of the fluorescently-labeled p24 antibody allowed Sherman and his team of researchers to obtain reliable results.

“The standard method of detecting infected cells can take weeks and use laboratory cultured cells. It doesn’t really tell you what’s going on in the patient,” Sherman said. “The technique utilized here is called intracellular p24 staining and churns out results in a matter of days, using the patient’s own blood cells. This gives physicians a window into the world of the infected cell.”

“The ability to identify infected cells directly from the human host will allow a myriad of future analyses on the characteristics of the cells,” Sherman said.

With further study, physicians may be able to use p24 staining as an indicator of how patients are faring. Current measures of clinical status, such as viral load and CD4 counts, sometimes don’t give physicians enough information to tailor drug treatments for individual patients, Sherman said. Knowing how many cells are infected in the patient might be valuable and improve treatment.

Warner Greene, MD, PhD, one of the lead researchers in the Vpr study, said that the research contributes to the arsenal of knowledge about HIV, which can be used to combat the virus.

“Understanding more about how this virus ticks and what it wants to do will put us in a better position to prevent those events from occurring,” said Greene, director of the Gladstone Institute of Virology and Immunology and UCSF professor of medicine, microbiology and immunology.

The Gladstone Institute of Virology and Immunology is one of three research institutes that comprise The J. David Gladstone Institutes, a private nonprofit biomedical research institution affiliated with UCSF. The institute is named for a prominent real estate developer who died in 1971. His will created a testamentary trust that reflects his long-standing personal interest in medical education and research.

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