



GLADSTONE INSTITUTE OF VIROLOGY AND IMMUNOLOGY

NEWS

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To coincide with presentation at the 14th International AIDS Conference

HIV PROTEIN STOPS CELL DIVISION, LEADING TO MORE VIRUS AND SICKER PATIENTS, GLADSTONE RESEARCHERS FIND

BARCELONA, SPAIN --T cells are supposed to be one of the body's best defenses against invading viral foes like HIV. But when CD4+ T cells encounter HIV, they themselves become targets for infection. Once infected, not only do they become impotent in protecting the body, but they also begin working for the enemy as HIV coerces the T cells to produce more virus.

New research at the Gladstone Institute of Virology and Immunology is showing how HIV transforms T cells into efficient virus factories. Gladstone director Warner Greene, MD, PhD, UCSF professor of medicine, microbiology and immunology presented the research on July 10 at the 14th International AIDS Conference here in Barcelona.

One culprit 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.

"Fewer CD4+ T cells almost always translates to sicker patients," Greene said. "Our research on Vpr is revealing how the virus alters the CD4 T cell in its favor but to the detriment of the normal function of these cells in the immune response."

Scientists already knew that laboratory cultured cells stopped dividing when large amounts of Vpr were artificially introduced into cells. Greene 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 cells circulating in the blood of HIV-infected patients. The new research shows cell division is stopped in HIV-infected cells taken directly from patient blood samples. The finding helps explain how HIV is able to reproduce so efficiently in the human body and may provide clues to one mechanism contributing to the ultimate HIV-1 induced demise of these CD4 T cells.

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

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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 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.

Greene 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 does within the CD4+ T cell will put us in a stronger position to prevent those events from occurring,” he said.

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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