Discovery may help prevent HIV 'reservoirs' from forming

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Researchers at Albert Einstein College of Medicine of Yeshiva University have discovered how the protein that blocks HIV-1 from multiplying in white blood cells is regulated. HIV-1 is the virus that causes AIDS, and the discovery could lead to novel approaches for addressing HIV-1 "in hiding" – namely eliminating reservoirs of HIV-1 that persist in patients undergoing antiretroviral therapy. The study was published today in the online edition of the journal *Cell Host & Microbe*.

Antiretroviral therapy can reduce blood levels of HIV-1 until they are undetectable. But despite drug therapy, reservoirs of HIV-1 can persist in several types of white cells, notably macrophages – important immune cells that help clear pathogens and other potentially harmful substances from the body.

"If you stop antiretroviral therapy, the virus emerges from these reservoirs and returns to the general circulation in a matter of days, as if the patient had never been treated," said senior author Felipe Diaz-Griffero, Ph.D., assistant professor of microbiology & immunology at Einstein. "Now we know the protein that we need to control so we can prevent HIV-1 reservoirs from forming or eliminate them entirely."

Scientists have known that a protein called SAMHD1 prevents HIV-1 from replicating in certain immune cells. But until now, it was not understood why SAMHD1 fails to function in immune cells like macrophages that are vulnerable to HIV-1 infection.

Using mass spectrometry, a tool for determining molecular composition, Dr. Diaz-Griffero found that SAMHD1 can exist in two configurations known as phosphorylated and unphosphorylated. (Phosphorylation is an important cellular process in which phosphate groups attach to other molecules, thereby activating various signaling and regulatory mechanisms within the cell.) When SAMHD1 is phosphorylated – the situation in immune cells that divide – the cell is not protected from being infected with HIV-1. When the protein is not phosphorylated – as occurs in the nondividing macrophages – the cell is protected from HIV infection.

"We are currently exploring ways to keep this protein unphosphorylated so that HIV reservoirs will never be formed," said Dr. Diaz-Griffero.

More information: The title of the paper is "The Retroviral Restriction ability of SAMHD1 is Regulated by Phosphorylation."

Provided by Albert Einstein College of Medicine