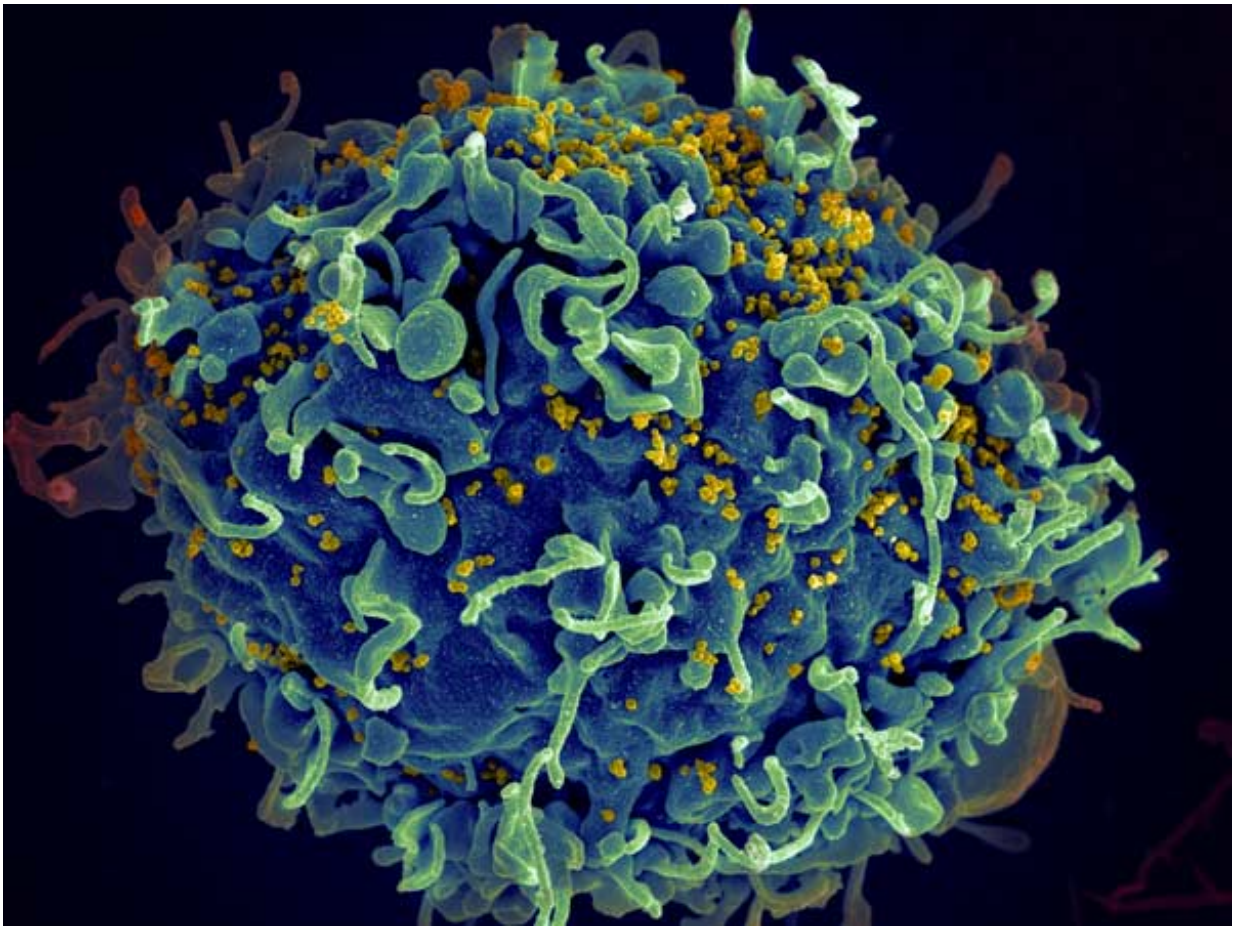
Researchers track HIV in real time as it infects and spreads in living tissue

June 9 2016



HIV infecting a human cell. Credit: NIH

By watching brightly glowing HIV-infected immune cells move within

mice, researchers at the Icahn School of Medicine at Mount Sinai have shown how infected immune cells latch onto an uninfected sister cell to directly transmit newly minted viral particles. These interactions allow HIV to spread efficiently between these immune cells, known as CD4+ helper T cells. The research, published online today in *Cell Reports*, challenges the long-held perception that the primary route of HIV infection of immune cells is from free-floating viral particles that move within tissue and blood fluids.

While HIV cell-to-cell transmission has been observed in test tube experiments, this is the first study to capture these interactions in a living animal. Although cell-to-cell infection does result in release of abundant solo viral particles, direct transmission from HIV-infected immune cells to other cells—which can then replicate in clusters of these cells—is a much more efficient route to quickly spread the virus, researchers say. It may be particularly important in allowing the virus to spread in the body even before it is detectable in the blood.

Previous studies in cell culture have indicated that cell-to-cell infection may help HIV to resist antibodies and potent therapies. This study provides direct evidence that these interactions do occur in infected immune tissues, and highlight the importance of considering cell-to-cell transmission in developing new treatments.

"All HIV treatment to date has been based on the free-floating virion model," says Benjamin K. Chen, MD, PhD, an Associate Professor of Infectious Diseases, Microbiology, and Immunology at the Icahn School of Medicine at Mount Sinai. "We believe that the sensitivity to antibodies used as potential HIV treatment and to certain antiretroviral drugs can be decreased by cell-to-cell transmission. Agents that efficiently block cell-to-cell transmission may help reduce the HIV viral reservoir, and vaccines that can neutralize this transmission may also help prevent or control HIV."

HIV, or human immunodeficiency virus, is a virus that attacks the body's immune system. If left untreated, HIV can progress and develop into AIDS (acquired immunodeficiency syndrome). More than 1.2 million people in the United States are living with HIV infection. Globally, more than 39 million people have been infected.

Glowing proteins track HIV movement

Lead author Kenneth M. Law, a graduate fellow in Dr. Chen's laboratory, attached green fluorescent molecules derived from jellyfish and red glowing proteins from coral onto variants of HIV. The researchers then introduced the two strains into mice transplanted with a human immune system and watched in real time as HIV spread from one CD4+ helper T cell to another.

"We could visualize hot spots of infection within lymphoid tissue, which has millions of cells moving dynamically within the tissue," says Mr. Law. "By focusing just on the green and red glowing cells, we could monitor how an infected cell influences uninfected cells."

Using an advanced imaging technique called intravital microscopy, the researchers followed the movement and interaction of HIV-infected cells in the spleen of mice. They watched as infected cells induced contact with uninfected cells, and the uninfected cell would then pause for a time on the infected cell—building a physical connection between them.

Scientists describe these infectious connections as virological "synapses" because they resemble the way that cells of the nervous system or the immune system communicate through intimate cell-to-cell connections.

A mutation factory

The investigators believe the proteins that make up the HIV virion are being assembled at the site of the bridge and then directly moved to the cell being infected. Cell-to-cell infection allows several viruses to simultaneously pass between the connected cells. The researchers found that multiple viruses could infect a single cell through virological synapses.

This pathway allows multiple copies of HIV to transmit together from cell to cell, a genetic property that can help mutant viruses to accumulate. This may help explain the high mutation rate that allows the virus to escape from immune responses, says Mr. Law. "The genetic mixing that happens when a cell is infected with multiple HIV virions can lead to novel genetic recombination that then gets passed into the next immune cell that is infected."

Provided by The Mount Sinai Hospital

Citation: Researchers track HIV in real time as it infects and spreads in living tissue (2016, June 9) retrieved 23 April 2024 from https://medicalxpress.com/news/2016-06-track-hiv-real-infects-tissue.html