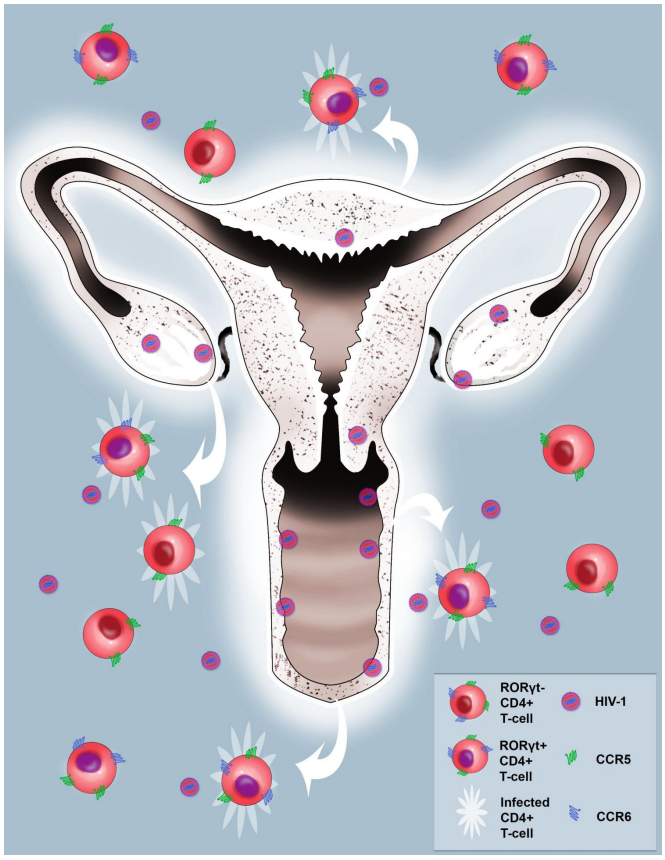
Fireflies light the way to female HIV transmission

27 April 2016



The illustration shows that infection of target cells can take place throughout the female reproductive tract. And at all sites the primary target of early infection is Th17 cells. The Th17 cells are identified by the markers of CCR5 and CCR6. The infected cells are illustrated by the white burst. Credit: Tom Hope, Northwestern University

Finding the vulnerable points where HIV enters the female reproductive tract is like searching for needles in a haystack. But Northwestern Medicine scientists have solved that challenge by creating a glowing map of the very first cells to be infected with a HIV-like virus.

Through an animal model, the scientists showed for the first time that HIV enters cells throughout the entire female reproductive tract from the labia to the ovary, not just the cervix, as previously thought.

"It's a technical achievement that provides immediate insights into the earliest transmission events," said lead investigator Thomas Hope, professor of cell and molecular biology at Northwestern University Feinberg School of Medicine. "Now we know which areas are vulnerable to HIV and can investigate why does the virus get in here and not everywhere else?"

The HIV transmission study was recently published in *Cell Host & Microbe*.

"If we are going to stop women from getting infected, we have to stop the very first cells from getting infected," Hope said. "A week after the initial infection, there are hundreds of thousands of infected cells, and it's very difficult to stop. If you can stop it earlier, then you have a chance."

Any strategies to efficiently prevent HIV acquisition in women likely needs to protect the entire female reproductive tract, Hope said.

Hope and colleagues removed the guts from the virus and inserted a gene from lightning bugs and another gene from a fluorescent protein to generate a reporter virus. Then they mixed the reporter virus with the real HIV-like virus. The glowing cells infected by the reporter revealed the site of infection with the real virus. The result: after being transmitted to the host, the real virus appeared in clusters of about 20 to 30 infected cells within 48 hours.

Without the new technology, "scientists would have to take a million little sections to see if they found evidence of the virus," Hope said.

In the research, scientists used rhesus macaques and a simian immunodeficiency virus (SIV) that is

generally analogous to HIV.

The discovery will help scientists design a more effective vaccine to protect women from HIV.

"For a vaccine to be effective, you don't just need your arsenal of weapons but they need to be in the right place at the right time," Hope said. "If you show up a day late or don't bring enough weapons, it's too late. Now we can see the chink in the armor of the virus. If you can attack it early instead of late, you can stop it."

Northwestern scientists discovered the primary target of transmission is the Th17 cell, a minority but important population of T cells in the first line of immune defense. It was previously known that they are depleted early in HIV and SIV infections.

Within 48 hours of infection, scientists can see evidence of the battle between the virus and the Th17 cell.

"We can see infected dead cells, infected cells being eaten by other cells to control them, and cells that kill themselves (apoptosis)," Hope said. "The virus is causing all those things, and it shows the battle between the virus and infected host begins immediately upon infection."

More information: "Th17 Cells Are Preferentially Infected Very Early after Vaginal Transmission of SIV in Macaques," *Cell Host & Microbe*, 2016.

Provided by Northwestern University