



PrEP-ping T cells for HIV Exposure

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Nearly half a century after its emergence as a recognized global health crisis, HIV remains a major challenge. UNAIDS estimates that in 2024, there were 40.8 million people living with HIV worldwide, and over 1 million people newly acquired HIV. Despite major advances in treatment, a protective vaccine and functional cure remain out of reach.

In recent years, the uptake of oral pre-exposure prophylaxis (PrEP) has revolutionized HIV prevention. By taking PrEP, people at greater risk of HIV acquisition can reduce the chances of viral transmission by up to 70%. PrEP consists of the same drugs used for HIV treatment, which work by blocking the spread of the virus between cells. In people living with HIV, this suppresses the virus in the body and reduces virus-related health issues, allowing them to live long and healthy lives. It is presumed that PrEP prevents the establishment of HIV infection by blocking early viral replication in people exposed to the virus. However, there is limited research confirming this or investigating other mechanisms of how PrEP may protect against HIV.

Various factors contribute to the risk of HIV transmission. These include the presence and number of infectious viral particles, as well as the presence and number of susceptible cells at the site of exposure. HIV primarily infects immune cells called CD4+ T cells, and mostly when these cells are in an activated state. The presence and activity of other types of immune cells at the site of exposure also affects the likelihood of transmission. Other immune cells can quash infection before it spreads, or they can unwittingly promote viral spread by recruiting additional activated CD4+ T cells to the site of exposure.

“Oral pre-exposure prophylaxis is a powerful drug for HIV prevention, but little is known about how protective it is in the actual site of HIV exposure,” said graduate student Lakshmi Warriar in the [Lund lab](#) in the Vaccine and Infectious Disease Division. In a recent study published in [the Journal of Infectious Disease](#), Warriar and colleagues investigated whether PrEP affects the immune landscape within the female genital tract, the predominant site of HIV transmission in women.

The study team leveraged a Kenyan cohort of 22 HIV-negative female participants with HIV-positive male partners. They evaluated the immune cells in cervical biopsies from the participants, collected before PrEP initiation and after 6 months of taking daily oral PrEP. While the results showed no change in the frequency of total CD4+ T cells in the cervix, they did reveal important changes in other aspects of the immune environment.

Warrier commented, “We found two major associations with PrEP usage: first, a reduction in activated cervical CD8+ T cells which could limit inflammation and general immune cell recruitment (subsequently limiting HIV target cell recruitment and activation), and second, a reduction in cervical CCR6+CD161+ Th17 cells, a subset that is also targeted by HIV.” These changes may reduce cell susceptibility to HIV at the site of exposure and may work synergistically with the direct antiviral function of PrEP to prevent HIV transmission.

The team hopes to further explore the mechanism driving this observed decrease in T cell activation after PrEP use. These results may have implications beyond HIV prevention. Warrier noted, “it would be interesting to see if the T cells in the tissue after PrEP exposure are still functional/protective, as this could impact the immune response to other sexually transmitted infections.”

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[Warrier L, Saito A, Graham JB, Swarts JL, Vick SC, MacLean F, Potchen NB, Cruz Talavera I, Tasfahun Tsegaye A, Thomas KK, Chohan BH, Ngure K, Mugo N, Lingappa JR, Lund JM. 2026. Initiation of oral pre-exposure prophylaxis associated with changes in genital tract T cell phenotypes in women exposed to HIV. *The Journal of Infectious Diseases*. doi: 10.1093/infdis/jiag204](#)

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