MedicalXpress

Researchers discover new details about HIV-1 entry and infection

February 15 2007

The primary targets of HIV-1 infection in the human vagina have been definitively identified in a new study published in the February 2007 issue of the journal *Immunity*, published by Cell Press. The findings are likely to guide development of new strategies that will prevent HIV-1 transmission.

"The majority of HIV-1 infected individuals worldwide are women who acquire HIV infection following sexual contact," explain study authors Dr. Florian Hladik and Dr. M. Juliana McElrath from the Fred Hutchinson Cancer Research Center. "Blocking HIV transmission and local spread in the female lower genital tract is key to prevent infection and ultimately to ease the pandemic."

Dr. Florian Hladik and colleagues in the McElrath laboratory developed a unique model system to study the precise mechanisms by which HIV-1 enters the lower reproductive tract of human females. The researchers separated and removed the outer lining of vaginal cells, which serves as the first barrier to the virus. The isolated preparation of intact, viable, vaginal epithelium permitted examination of immune cells that normally migrate out of the vaginal epithelium into deeper tissues shortly after exposure to HIV-1.

The researchers found that HIV-1 simultaneously enters two different types of intraepithelial cells associated with the immune system, Langerhans cells (LC) and CD4+ T cells. However, the path of entry and fate of infection was different for the two cell types. Infection of CD4+

T cells appears to rely at least in part on expression of major HIV-1 coreceptors like CCR5, whereas pathways for infection of vaginal LC appear to be more diverse and complex. In contrast to previous studies, infection of CD4+ T cells does not appear to require passage of the virus from LC.

Both LC and CD4+ T cells can migrate out of the vaginal epithelium. Study findings suggest that CD4+ T cells may be principally responsible for local shedding of the virus in the vagina of women infected with HIV-1 while LC may harbor viable virus for some time before spreading it to other cells.

These results reveal that it is necessary to consider mechanisms of viral entry into both CD4+ T and LC when searching for an effective way to interfere with infection through the vaginal epithelium. "Our findings provide exciting definitive insights into the initial events of HIV-1 infection in the human vagina, which can guide the design of effective strategies to block local transmission and prevent HIV-1 spread," concludes Dr. McElrath.

Source: Cell Press