

Understanding HIV Infection in the Female Genital Tract

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Women worldwide represent half of the people living with HIV, with a disproportionate number of infections in endemic areas. Women acquire HIV mainly through sexual contact. However, the critical events that allow or prevent HIV infection in the female genital tract remain largely unknown.

Using endometrial, endocervical and ectocervical tissues obtained from women undergoing hysterectomies we have investigated key aspects of HIV pathogenesis in the female genital tract, including HIV-target cell characterization, mechanisms for viral uptake and innate immune mechanisms that naturally protect against infection.

We have demonstrated that the distribution of HIV-target cells and immune functions differ between anatomical compartments in the female genital tract, and between pre and postmenopausal women. Th17 cells have been identified as the most susceptible target cells that sustain HIV replication in the genital mucosa. Genital dendritic cells expressing CD14 rapidly capture HIV and respond to this viral challenge with the secretion of innate molecules with anti-HIV activity, while other dendritic cell subsets lack HIV-capture potential. Finally, we recently demonstrated that genital neutrophils release Neutrophil Extracellular Traps (NETs) after contact with HIV, and that NETs immobilize and inactivate the virus to prevent infection of susceptible cells, representing a previously unrecognized form of mucosal protection against HIV.

Understanding how HIV infection is established in the female genital tract is key to develop HIV prevention strategies for women. Study of this mucosal surface is complex as the immune system is compartmentalized and regulated by multiple factors, including hormonal regulation and changes after menopause.