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Contact

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Author presents

Tuesday, December 16

3:45 pm

Minisymposium #20

Cellular Response to Infectious

Agents

Room 104, Moscone Center

*Analysis of the Interaction of
HIV with Female Genital Tract
Tissue as a Model to Under-
stand Sexual Transmission*

A. Trull, S. McCoombe,

M. McRaven, T. Hope

Northwestern University

Medical School, Chicago, IL

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Tulane University,

New Orleans, LA

The virus beneath the skin

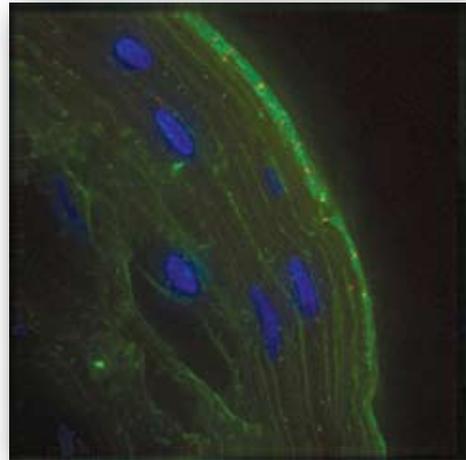
Genital tissue no foolproof barrier to sexual transmission of human immunodeficiency virus

The rise of human immunodeficiency virus (HIV) transmission through heterosexual sex has researchers scrambling for new vaccines and microbicides to block its spread, but findings by researchers at the Northwestern University School of Medicine in Chicago challenge a widely held assumption that the normal mucosal lining of the female genital tract is an effective barrier to viral penetration.

Women and female adolescents now account for 26% of all new HIV cases in the United States, according to the Centers for Disease Control and Prevention (CDC). From its most recent analysis of 2005 data, CDC estimated that there were 56,300 new HIV infections that year and traced 31% of those to high-risk heterosexual contact. Yet the actual mechanism underlying male-to-female sexual transmission of HIV is not well understood.

The Northwestern researchers report that HIV penetrates the genital skin barriers of female humans and macaques, primarily by moving between skin cells to quickly reach depths in the tissue where immune target cells are located. HIV penetration was more common in the outermost superficial squamous epithelial layers where, in the process of normal turnover and shedding, skin cells are no longer tightly bound together and water can normally enter. "This is an unexpected and important result," says Thomas Hope, "because it is generally believed that the squamous epithelium of the female genital tract is an efficient barrier to viral penetration."

By labeling individual HIV virions with photoactivated fluorescent tags,



A cross section of human ectocervical tissue, stained green to show tissue structure. Blue marks cell nuclei. The viral particles of HIV are red.

Hope and colleagues watched the virus penetrate the squamous epithelium, the outermost lining of the female genital tract. The researchers saw virus interacting in both human tissue culture derived from hysterectomies and in nonhuman tissue from rhesus macaque monkeys. In as little as four hours, the labeled virions reached 50 μ m beneath the skin barrier to areas where the immune system cells that HIV typically targets are located. Until now, we have known little about how the virus penetrates epithelial barriers to find its specific immune cell targets: CD4-positive T cells, macrophages, Langerhans cells, and dendritic cells.

Hope says that his studies show that female genital tissue does not offer a foolproof barrier against HIV. New therapeutics or prevention strategies to block the entry of HIV through the superficial layers protecting the female genital tract are urgently needed. 