

HIV transmission through vaginal/cervical epithelial cells

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Abstract

The lower female genital tract is a site of HIV-1 transmission. The tract consists of the vaginal, ectocervical and endocervical mucosa. To date, it is not known whether HIV-1 directly infects the vaginal/cervical epithelial cells or the virus transcytoses through the epithelia to infect underlying CD4⁺ cells. We begin by showing that HIV-1 does not replicate in these cells. In our study the epithelial cells were co-incubated with HIV-1 isolates for a 24 hour time period and subsequently washed free of the virus. On days 4, 7 and 10 the spent culture media was collected and the cells were given fresh medium. Aliquots taken from the spent media were assayed for viral replication using p24 ELISA. p24 is an HIV-1 antigen frequently used as an indicator of HIV-1 multiplication. p24 from the input viruses was detected after HIV-1 incubation. However, after washing free viruses, p24 titers were undetectable in the spent media collected on days 4, 7, and 10. Thus, no new viral proteins were released into the supernatant. These results indicate that HIV-1 does not replicate in vaginal/cervical epithelial cells. However, upon analyzing the morphology of these epithelial cells we found that they tended to round up and slough off after approximately 4 days of HIV-1 infection even though we did not detect any viral replication at that time. Furthermore, we also show that HIV-1 DNA (reverse transcribed from viral RNA) is incorporated into the vaginal/cervical epithelial cell genomes (using *Alu*-LTR nested PCR technique).

HIV-1 appears to enter vaginal/cervical epithelial cells but these cells do not express the known HIV-1 receptor (CD4). Our previous results indicate that galactosylceramide (GC), sulfogalactosylceramide (SGC), and sulfogalactosylglycerolipid (SGG) may be potential HIV-1 receptors since they can bind to gp120 (the surface glycoprotein of HIV-1). Our objective is to demonstrate that these glycolipids (GC, SGC, and SGG) are expressed on the vaginal/cervical epithelial cells and that they are receptors for HIV-1. Lipid extracts and HPTLC results revealed the presence of GC, SGC, and SGG on these epithelial cells. Furthermore, indirect immunofluorescence indicated that these glycolipids are localized on the surface of vaginal/cervical epithelial cells. In view of our recent findings, our next objective is to use a transwell system to determine if HIV-1 uses GC, SGC, and SGG as binding molecules to transcytose through the vaginal/cervical epithelial cells and infect CD4⁺ T cells in the compartment below the epithelium.