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Poster Session C

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Sperm May Act as a Vector for HIV Transmission to the Genital Epithelium

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ABSTRACT

HIV infection in women occurs primarily through vaginal intercourse. The exact mechanisms of viral transmission from semen through the vaginal mucosa are poorly understood. HIV primarily targets CD4+ immune cells via the interaction between viral gp120 and CD4. Vaginal/cervical (V/C) epithelial cells do not possess CD4, although other surface molecules may act as HIV receptors. Several lines of research studies indicate that gp120 can bind sulfoglycolipids, sulfogalactosylceramide (SGC) and sulfogalactosylglycerolipid (SGG), results implicating their roles as HIV receptors. In semen, HIV can be in the form of free virions and/or cell associated. Since SGG is abundantly present on the sperm surface, we hypothesize that HIV binds to sperm via interaction between gp120 and SGG and sperm can act as vectors transferring the captured HIV to genital epithelial cells. The objective of our study is to determine whether 1. HIV can bind to sperm in vitro. 2. HIV bound to sperm is still infectious and 3. Sperm can act as a vector transmitting HIV to V/C cells. To demonstrate HIV binding to sperm, live motile Percoll gradient pelleted sperm from fertile donors were incubated with dual tropic HIVcs204 (0-10 ng of p24). Sperm were then washed with fresh medium and treated with 0.5% Triton X-100 to extract the plasma membrane. HIV p24 present in the plasma membrane extract was then determined by ELISA. Our results indicated the presence of p24 in the sperm plasma membrane with its level increasing correspondingly to the amount of incubated HIV. The sperm bound HIV was still infectious, as shown by its ability to infect peripheral blood mononuclear cells (PBMCs), following the incubation of HIV-sperm complexes. This was determined by measuring p24 in the co-culture medium; the results indicated increasing amounts of p24 corresponding to the initial viral inputs used for sperm pre-incubation. As sperm were able to bind to vaginal, ectocervical and endocervical epithelial cell lines (Vk2/E6E7, Ect1/E6E7 and End1/E6E7 cells, respectively), as shown microscopically, we also asked whether HIV bound to the sperm surface could be transported into these cells. Following co-incubation with HIV bound sperm; DNA was isolated from these 3 cell lines and subjected to PCR for HIV Gag sequence. The Gag PCR product was detected in the 3 cell lines, indicating that HIV from the sperm surface had the ability to enter the cells. Of note is the presence of SGC on the surface of the V/C cell lines as shown by immunofluorescence and further confirmed by electrospray ionization mass spectrometry. It is possible that V/C cell surface SGC may act as a receptor for the viral entry. In summary, we have shown that sperm can capture and transmit HIV to cells of the vaginal mucosa. This research could lead to new approaches for microbicide development by including compounds that can target both cell free and sperm associated HIV. This research was supported by a grant from the Canadian Institute of Health research (CIHR).