

Poster presentation

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P07-08. Spermatozoa capture HIV-1 through heparan sulfate and efficiently transmit the virus to dendritic cells

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Background

Semen is the main vector for HIV-1 dissemination worldwide. It contains three major sources of infectious virus: free virions, infected leukocytes, and spermatozoa-associated virions. In this study we focused on the interaction of HIV-1 with human spermatozoa and the ability of spermatozoa to transmit the virus to dendritic cells (DCs).

Methods

Spermatozoa purified from healthy subjects were incubated with HIV-1 BaL, IIIB or different strains from primary isolates, then washed to remove free virus, and the amount of HIV associated to spermatozoa as well as the ability of spermatozoa to transmit the virus to monocyte-derived DCs was analyzed by measuring p24 antigen by ELISA.

Results

Flow cytometry showed that heparan sulfate is expressed in spermatozoa. Heparan sulfate plays an important role in the capture of HIV-1, as demonstrated by the inhibitory effect induced by heparine (50 U/ml) (>70% capture inhibition, n = 15) and heparinase II pre-treatment of the spermatozoa (>50% capture inhibition, n = 6). By contrast, treatment with the inhibitor of mannose receptor mannan (5 mg/ml) slightly inhibited virus attachment (>20% capture inhibition, n = 10). Spermatozoa-attached

viruses were efficiently transmitted to DCs through a cell-to-cell contact-dependent mechanism. Fluorescence, confocal and electronic microscopy showed that this process was associated to the internalization of a fraction of the spermatozoa. This interaction also resulted in the phenotypic maturation of DCs (up-regulation of CD80, CD86, CD40, CD83 and CCR7), and the production of IL-10 but not IL-12p70. Finally, we found that acidic extracellular pH levels, similar to those found in the vaginal mucosa after sexual intercourse, increased more than four times (n = 12) the binding of HIV-1 to the spermatozoa and the subsequent transmission of HIV-1 to DCs.

Conclusion

Our observations support the notion that far from being a passive carrier, spermatozoa acting in concert with DCs might affect the early course of sexual transmission of HIV-1 infection.