

## ABSTRACT

HIV-infected (HIV+) men are more susceptible to sexually transmitted infections (STIs), and may also become superinfected by HIV. We hypothesized that HIV induces immune alterations in the foreskin that may impact the subsequent acquisition/clearance of genital co-infections. Methods. Tissue and blood were obtained from 70 HIV-uninfected and 20 HIV+ men undergoing elective circumcision. Tissue and blood T cells were characterized by flow cytometry, immunohistochemistry, and PCR. Results. There was substantial influx of CD8 T cells into the foreskins of HIV+ men (108.8 vs. 23.1 cells/mm<sup>2</sup>, p<0.001); but foreskin CD4 T cell density was unchanged (43.0 vs. 33.7/mm<sup>2</sup>, p=0.67), despite substantial blood depletion (409.0 vs. 877.8 cells/mm<sup>3</sup>, p<0.001). While frequencies of foreskin CCR5+ T cells, Tregs and Th17 cells were unaltered in HIV+ men; CD8 T cell production of TNF $\alpha$  was decreased. HIV-specific CD8 T cells were present in the foreskins of HIV+ men, although their frequency and function was reduced compared to Foreskin CD4 T cell density and CCR5 expression in the blood. Conclusions. CD8 T cell density was not reduced during HIV infection, perhaps explaining susceptibility to HIV superinfection. Foreskin CD8 T cell density was increased, but decreased production of TNF $\alpha$  may enhance susceptibility to foreskin-acquired genital co-infections in HIV+ men.