

$\alpha 4\beta 7$ expression on blood T cells is increased during herpes simplex virus 2 infection and correlates with markers of HIV susceptibility in the female genital tract

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HIV and STIs

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CHANGING THE COURSE OF THE
HIV PREVENTION, ENGAGEMENT AND
TREATMENT CASCADE

Herpes Simplex Virus-2 (HSV-2)

- Most cases have no symptoms (80%)
- Prevalence of HSV-2
 - >60% of adults are infected in Africa
 - ~15-20% of adults HSV2+ in North America, but higher in the most HIV-affected communities
 - 40-50% in Toronto MSM and African/Caribbean
 - Within any age stratum – women are at more risk
- HSV-2 is associated with 3 fold increase in HIV acquisition
- May relate to increased HIV target cells in the cervix

Impact of HSV-2 on HIV Target Cells

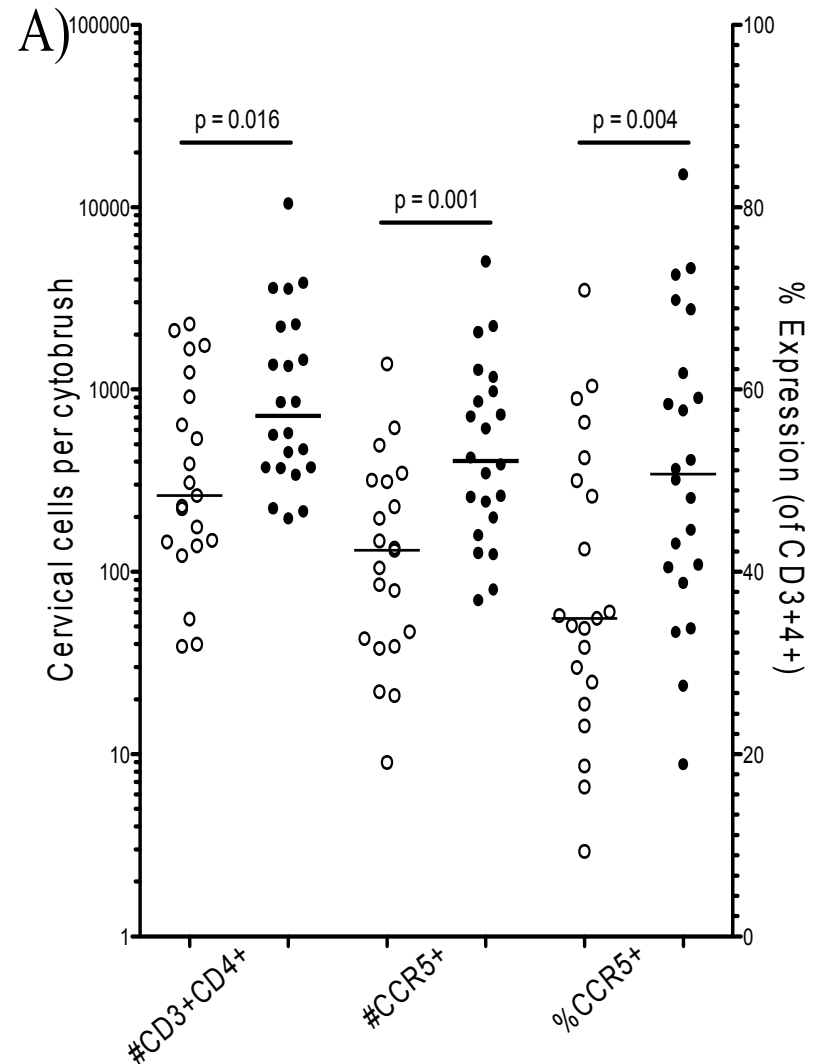
HSV-2 positive women have:

- ↑ number of CD4+ T cells in the cervix
- ↑ number and proportion of genital CD4+ T cells expressing CCR5, CD38/HLA-DR
- Refer to a poster by Shannon et al.

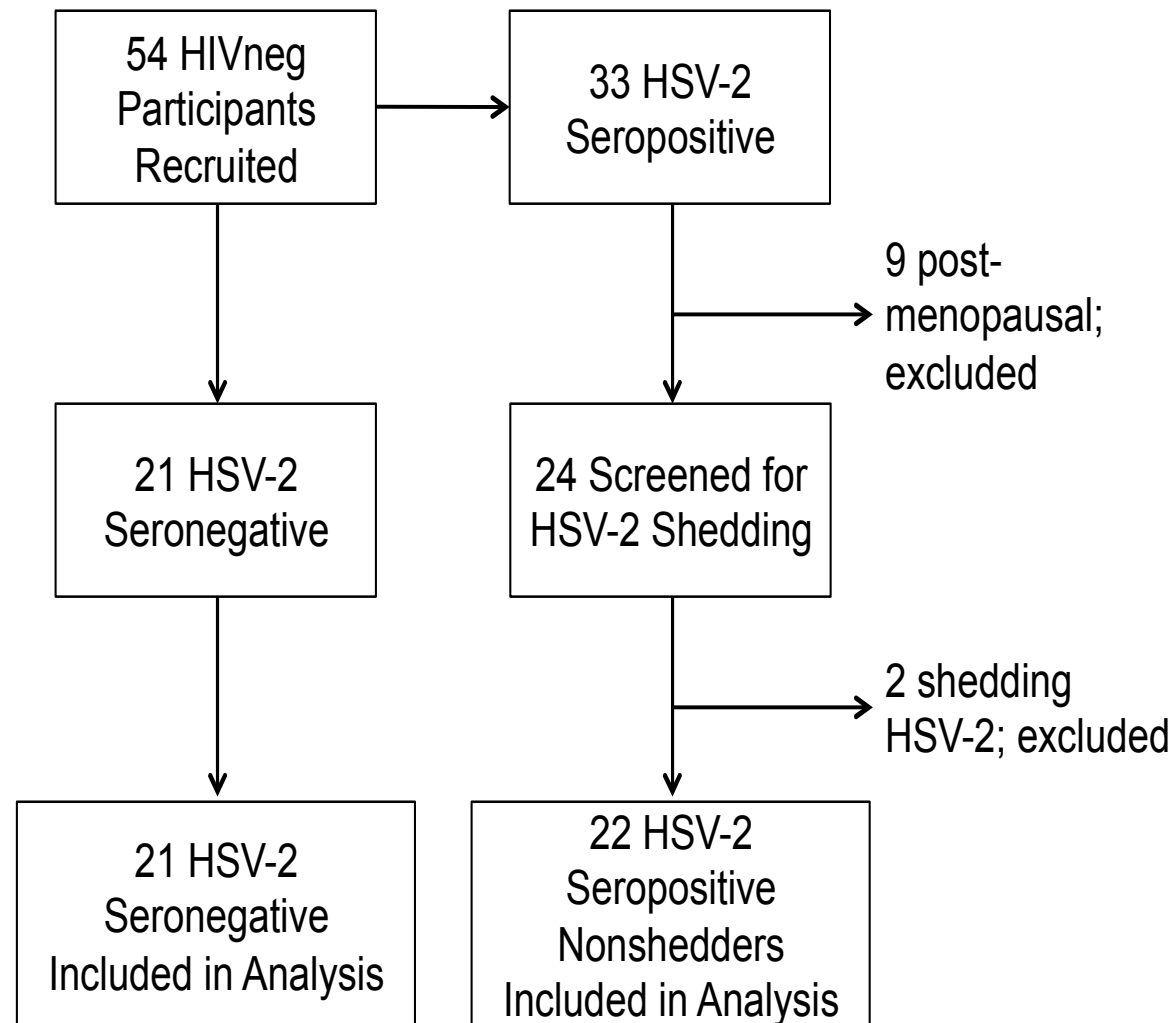
• $\alpha 4\beta 7$ is a mucosal homing integrin that can also bind to HIV gp120

HYPOTHESIS:

- HSV-2 infection is increasing genital “homing” of targets through $\alpha 4\beta 7$ expression in blood



Recruitment / Inclusion



Participant Characteristics

Variable	HSV-2 Negative (N = 21)	HSV-2 Positive (N = 22)
Age (range)	29 (20-38)	38 (24-59)*
Condom Use	33.3% (7/21)	36.4% (8/22)
Hormonal Contraceptives	14.3% (3/21)	13.6% (3/22)
Intravaginal Washing (douching)	9.5% (2/21)	13.6% (3/22)
Bacterial Vaginosis	14.3% (3/21)	18.2% (4/22)
HSV-1	85.7% (18/21)	100% (22/22)

Blood CD4+ T cell Subsets

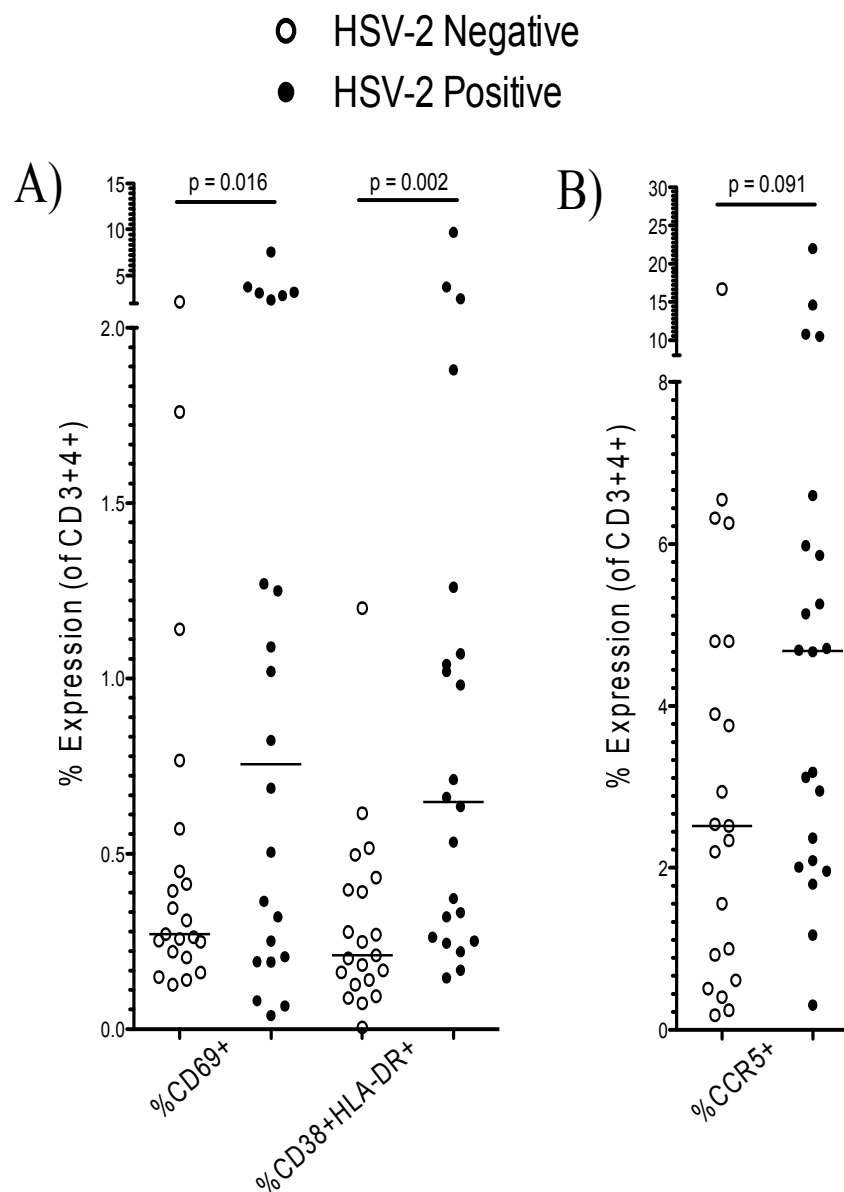
Activation markers:

- CD69
- CD38+HLA-DR+

HIV co-receptor:

- CCR5+

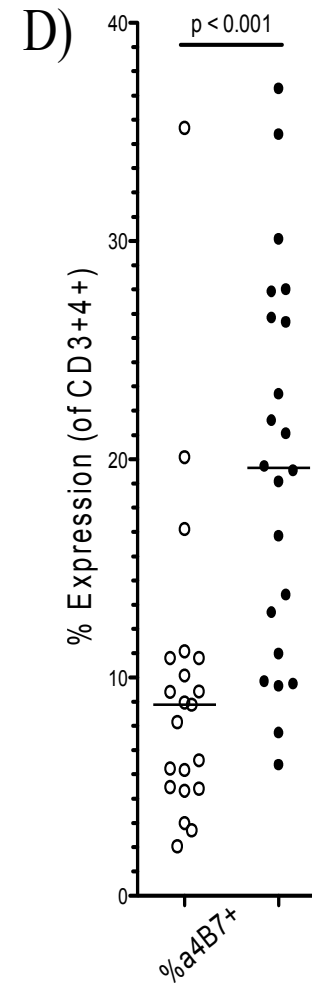
All increased in the blood of HSV2+ women



Blood CD4+ T cell $\alpha 4\beta 7$ Expression

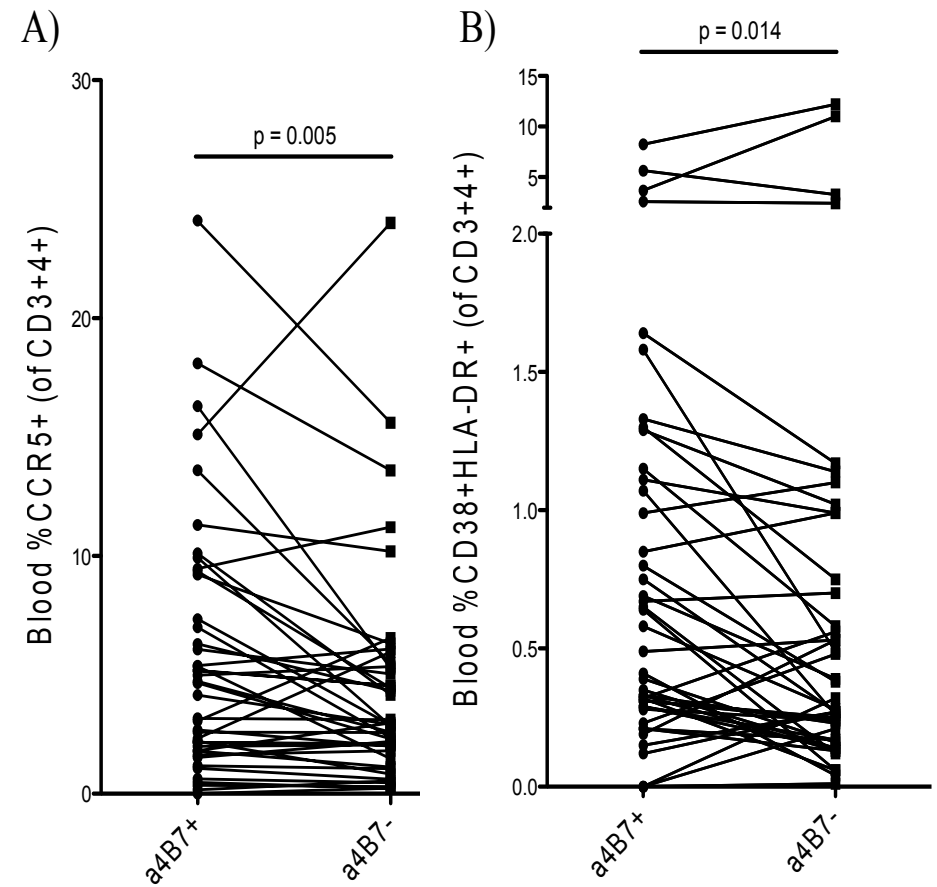
- Increased expression of $\alpha 4\beta 7$ in HSV-2 positive individuals

- HSV-2 Negative
- HSV-2 Positive



Characterization of blood $\alpha 4\beta 7$ T cells

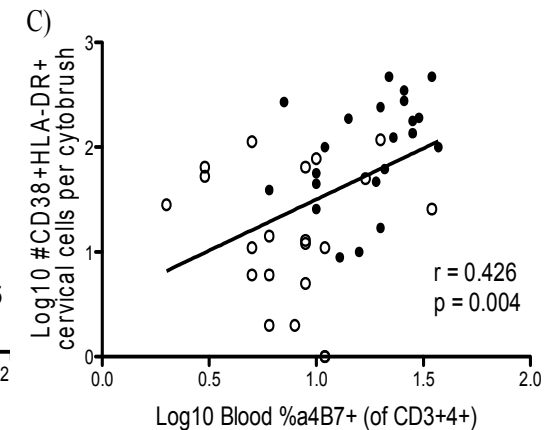
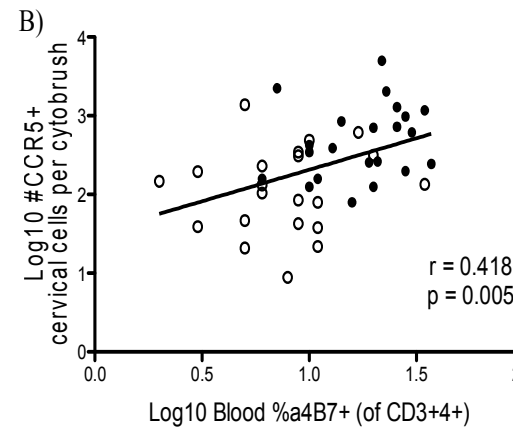
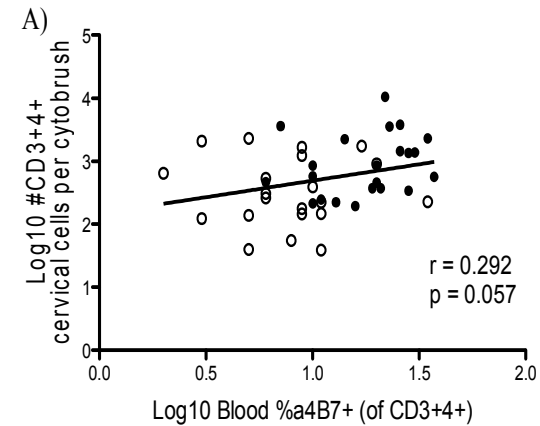
- Blood $\alpha 4\beta 7$ + T cells display increased expression of CCR5 and CD38+HLA-DR+ compared to $\alpha 4\beta 7$ - T cells



Correlation between Blood $\alpha 4\beta 7$ + T cells and Cervical Mononuclear Cells

- Blood $\alpha 4\beta 7$ expression strongly correlated with CCR5+ and CD38+HLA-DR+ CD4+ T cells in the cervix

- HSV-2 Negative
- HSV-2 Positive



Conclusions

- HSV-2 seropositivity was associated with increased activation and expression of $\alpha 4\beta 7$ in the blood CD4+ T cells
- Cells expressing $\alpha 4\beta 7$ in the blood expressed higher levels of CCR5 and CD38/HLA-DR
- $\alpha 4\beta 7$ in the blood correlated with elevated numbers of activated and CCR5+ expressing CD4+ T cells in the cervix

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