

# HSV-2-driven changes in $\alpha_4\beta_7$ expression correlate with increased susceptibility to SHIV

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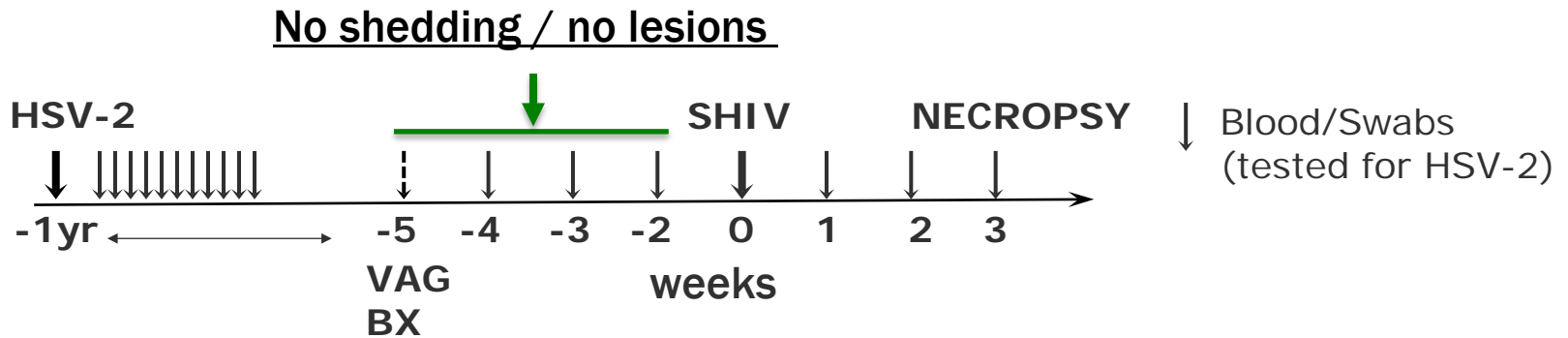
# HSV-2 Increases Risk of HIV-1 Acquisition

Even in absence of detectable HSV-2 replication, inflammation and lesions.

- HSV-2 as *tool* to investigate changes that correlate with susceptibility to HIV infection
- HSV-2 rectal infection increases the % of  $\alpha_4\beta_7^{\text{high}}$  CD4<sup>+</sup> T cells in the rectal tissue (Martinelli et al. Plos Path 2011)
- SIV acquisition correlates with the % of  $\alpha_4\beta_7^{\text{high}}$  CD4<sup>+</sup> T cells before challenge (Martinelli et al. J AIDS 2013)

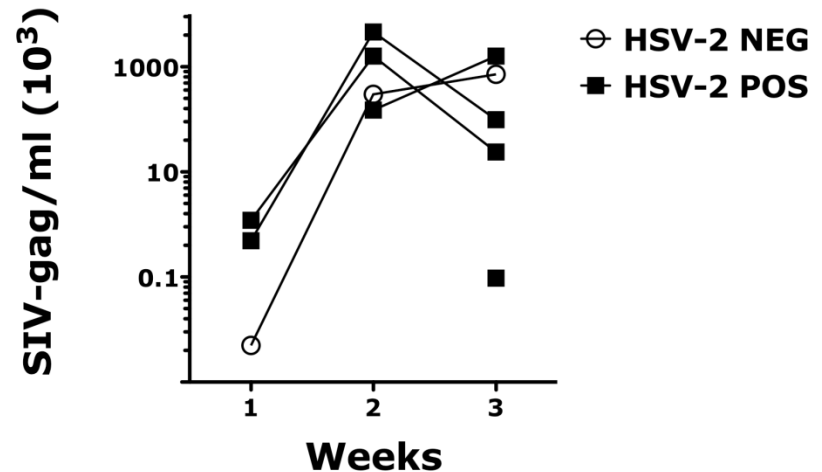
# What About Vaginal Infection?

# HSV-2 Infected Macaques are More Susceptible to Vaginal SHIV Infection



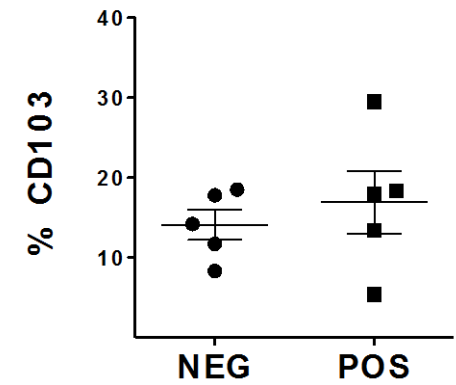
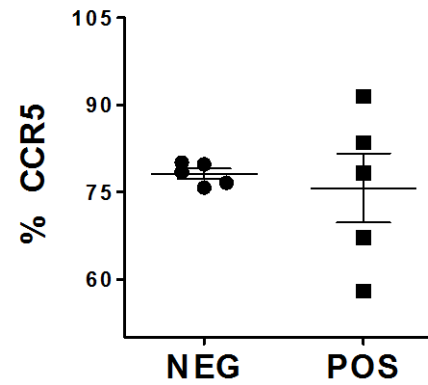
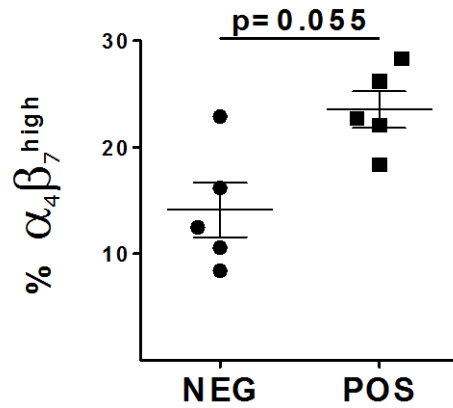
1 vaginal challenge: 250 TCID<sub>50</sub> of SHIV<sub>SF162P3</sub>

HSV-2	SHIV+
POS	4/5
NEG	1/5

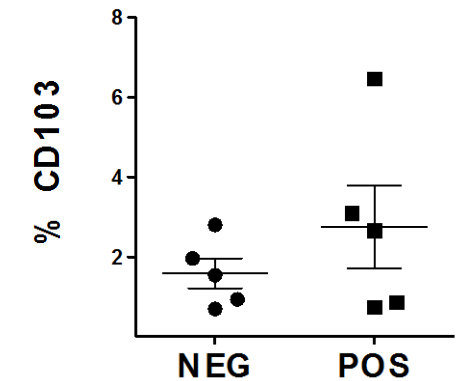
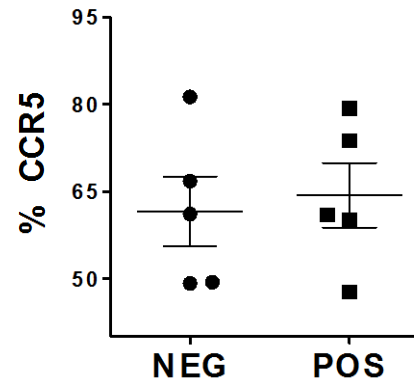
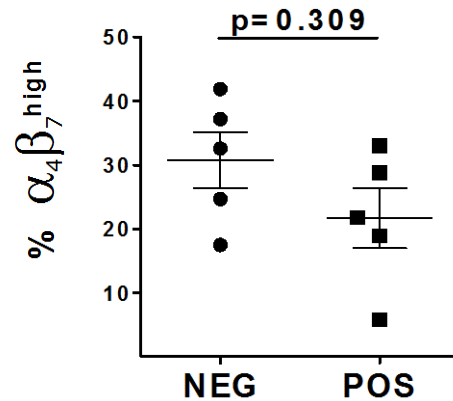


# HSV-2 Increases the % of $\alpha_4\beta_7^{\text{high}}$ $\text{CD4}^+$ T cells in Vaginal Tissue

VAG

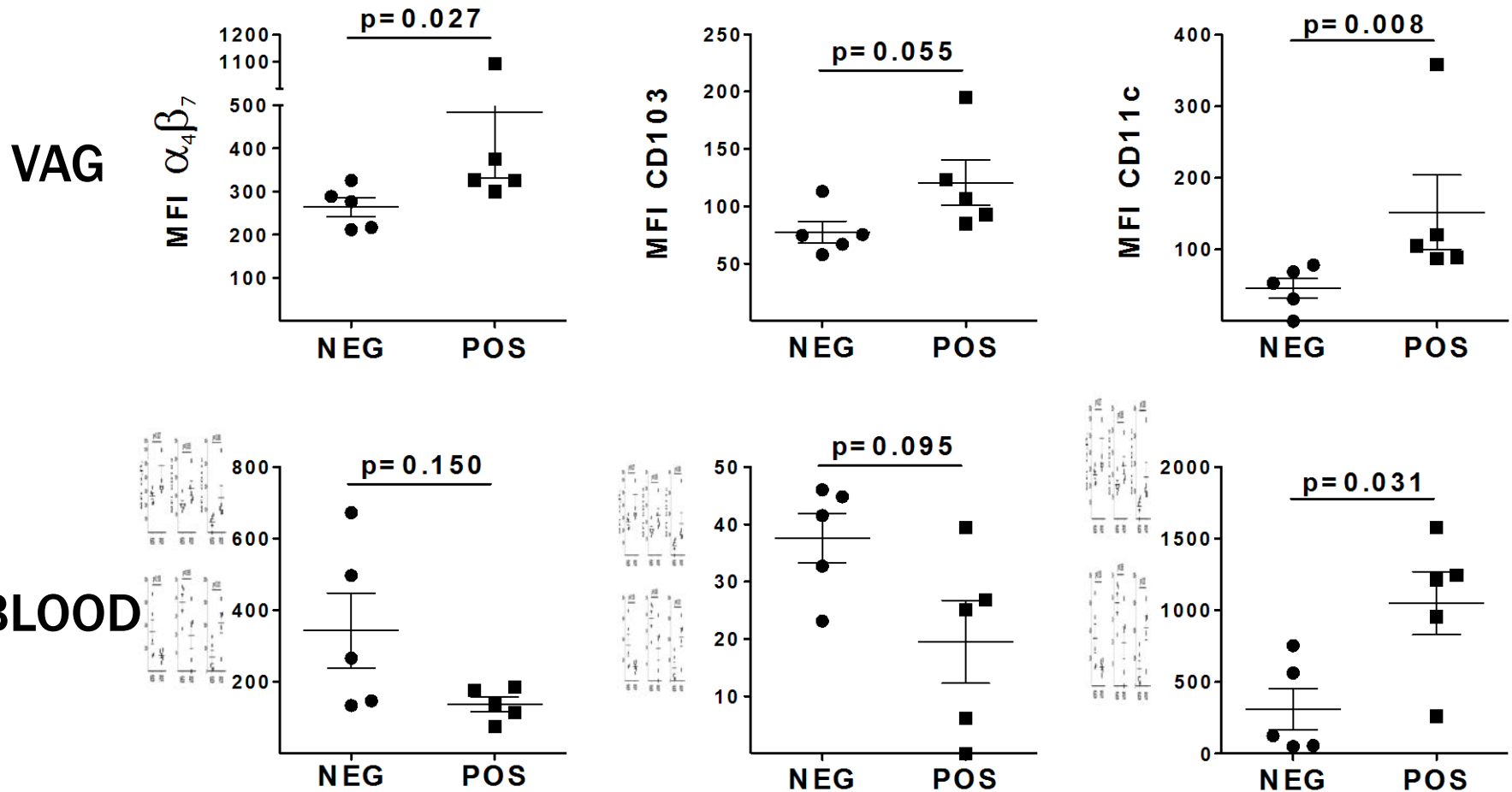


BLOOD



**The % of  $\alpha_4\beta_7^{\text{high}}$  CD4<sup>+</sup> T Cells in  
Blood and Vaginal Tissue do not  
Correlate**

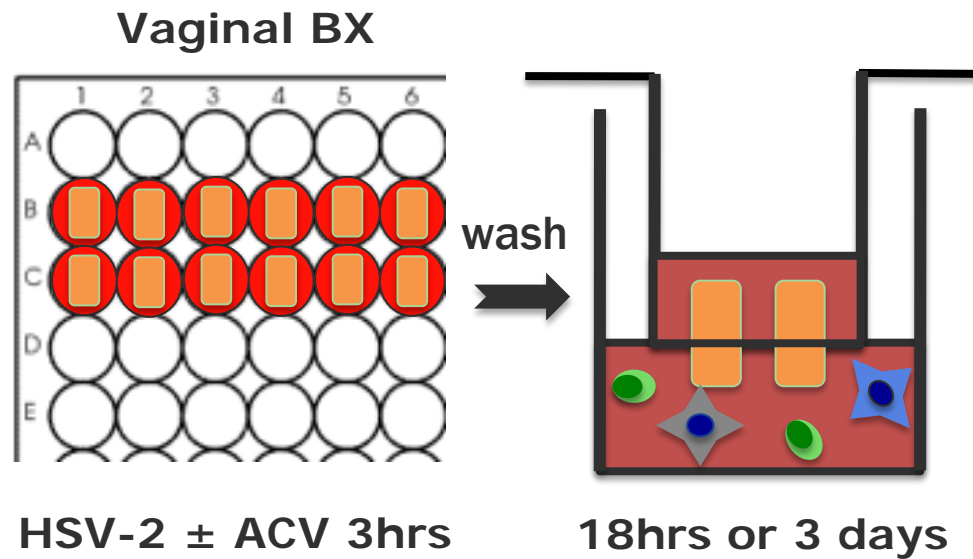
# HSV-2 Infection Increases Expression of $\alpha_4\beta_7$ and CD11c on Vaginal DCs



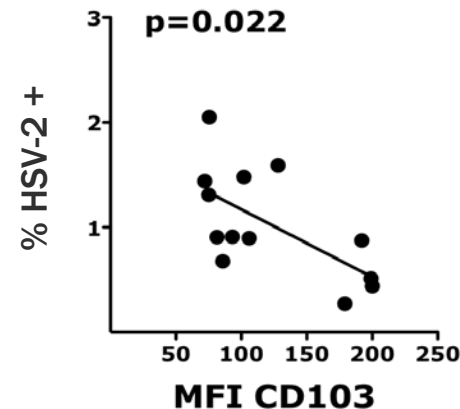
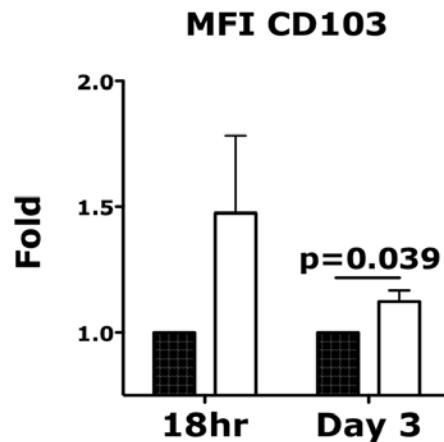
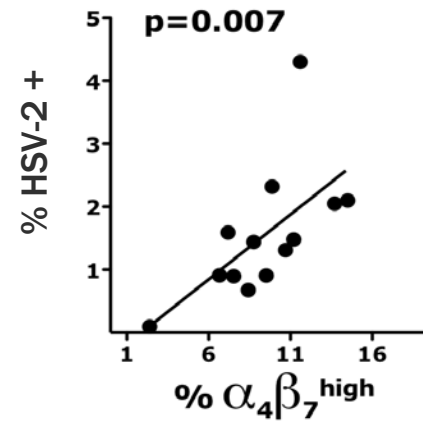
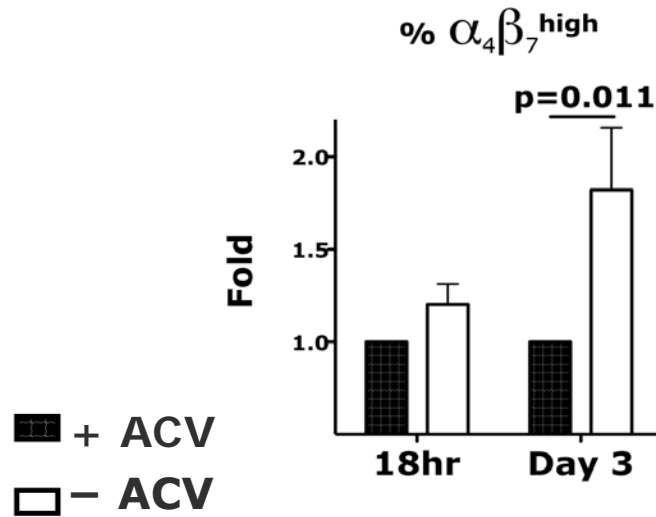
**HSV-2-driven changes in  
vaginal mucosa correlate  
with susceptibility to  
SHIV?**



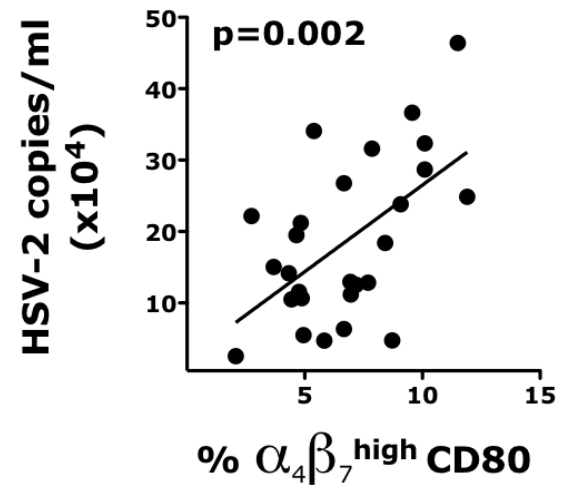
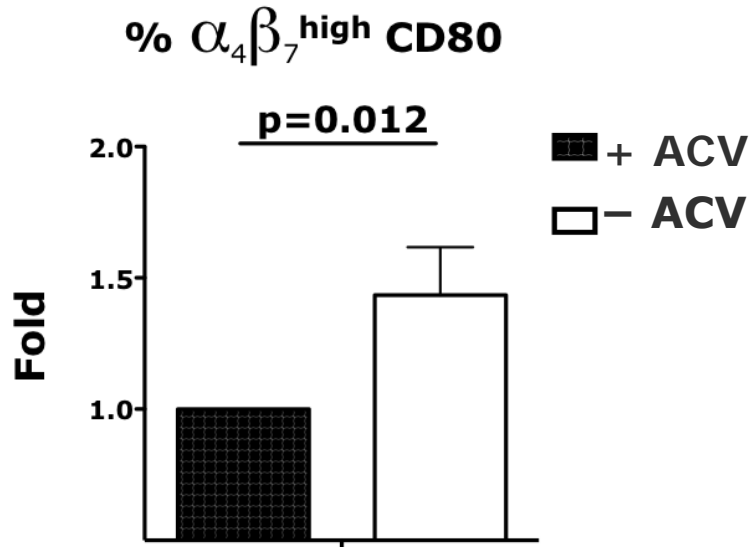
# Ex Vivo HSV-2 Infection of Macaque Vaginal Tissue



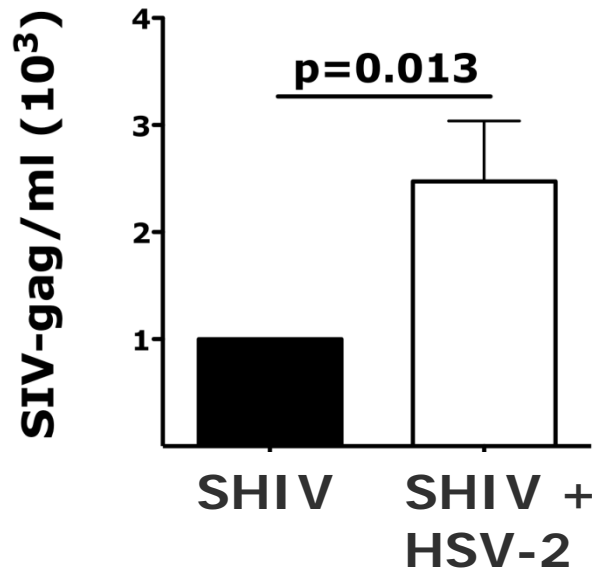
# Ex Vivo HSV-2 Increases the % of $\alpha_4\beta_7^{\text{high}}$ and CD103<sup>+</sup> CD4<sup>+</sup> T cells in Vaginal Mucosa



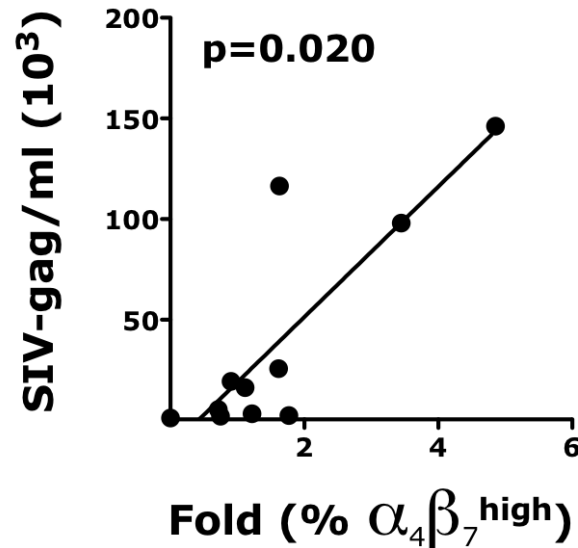
# Ex Vivo HSV-2 Increases the % of $\alpha_4\beta_7^{\text{high}}$ CD80<sup>+</sup> CD3<sup>-</sup> HLA-DR<sup>+</sup> in the Vaginal Mucosa



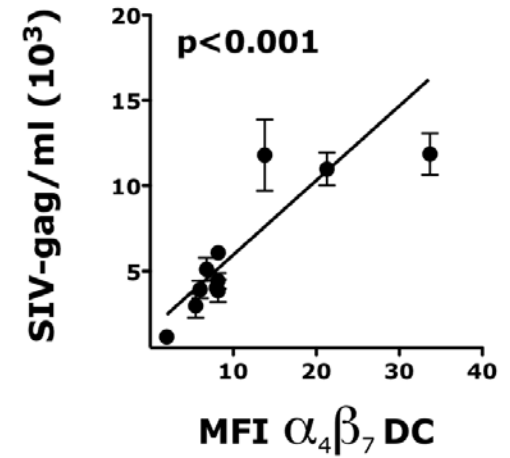
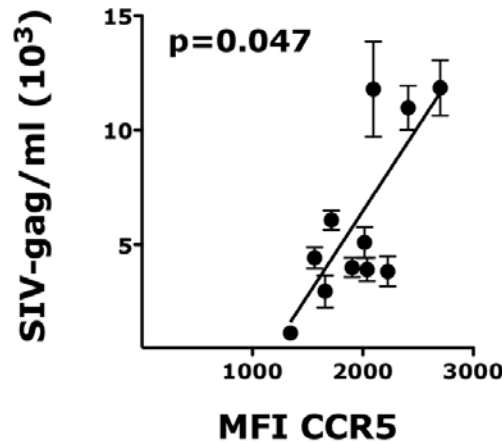
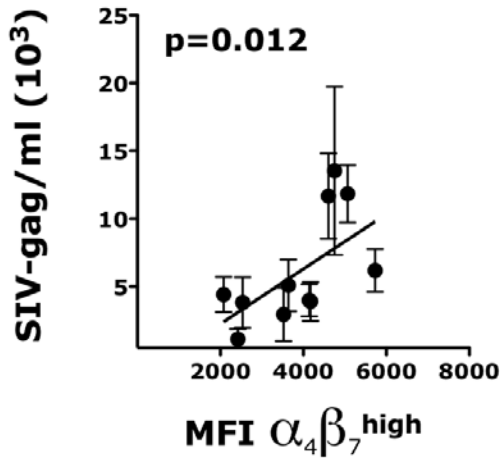
# Ex Vivo HSV-2 Infection Increases the Susceptibility of the Vaginal Mucosa to SHIV



# SHIV Infection Correlates with the HSV-2-Driven Increase in % of $\alpha_4\beta_7^{\text{high}}$ CD4<sup>+</sup> T cells



# Base Line $\alpha_4\beta_7$ expression Correlates with SHIV infection Ex Vivo



Independent of HSV-2 infection

# Summary:

- HSV-2 chronically infected macaques:
  - More susceptible to SHIV infection.
  - Higher % of  $\alpha_4\beta_7^{\text{high}}$  CD4<sup>+</sup> T cells in vaginal tissue
  - Higher  $\alpha_4\beta_7$  expression on vaginal DCs
  - More inflammatory factors in vaginal fluids
- HSV-2 infection of vaginal tissue ex vivo:
  - Increases SHIV replication
  - Increases the % of  $\alpha_4\beta_7^{\text{high}}$  CD4<sup>+</sup> T cells and  $\alpha_4\beta_7^{\text{high}}$  CD80<sup>+</sup> APCs
  - Increased  $\alpha_4\beta_7^{\text{high}}$  CD4<sup>+</sup> T correlate with SHIV replication in HSV-2/SHIV infected tissues.

# Summary:

- Ex vivo SIV replication correlates with:
  - BL expression of  $\alpha_4\beta_7$  on  $\alpha_4\beta_7^{\text{high}}$  CD4 T cells
  - Frequency of  $\alpha_4\beta_7^+$  CD4 T cells.

*Availability of  $\alpha_4\beta_7^+$  cells facilitates HIV infection?*



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