

Do candidate rectal microbicides also
need to protect the anal canal?

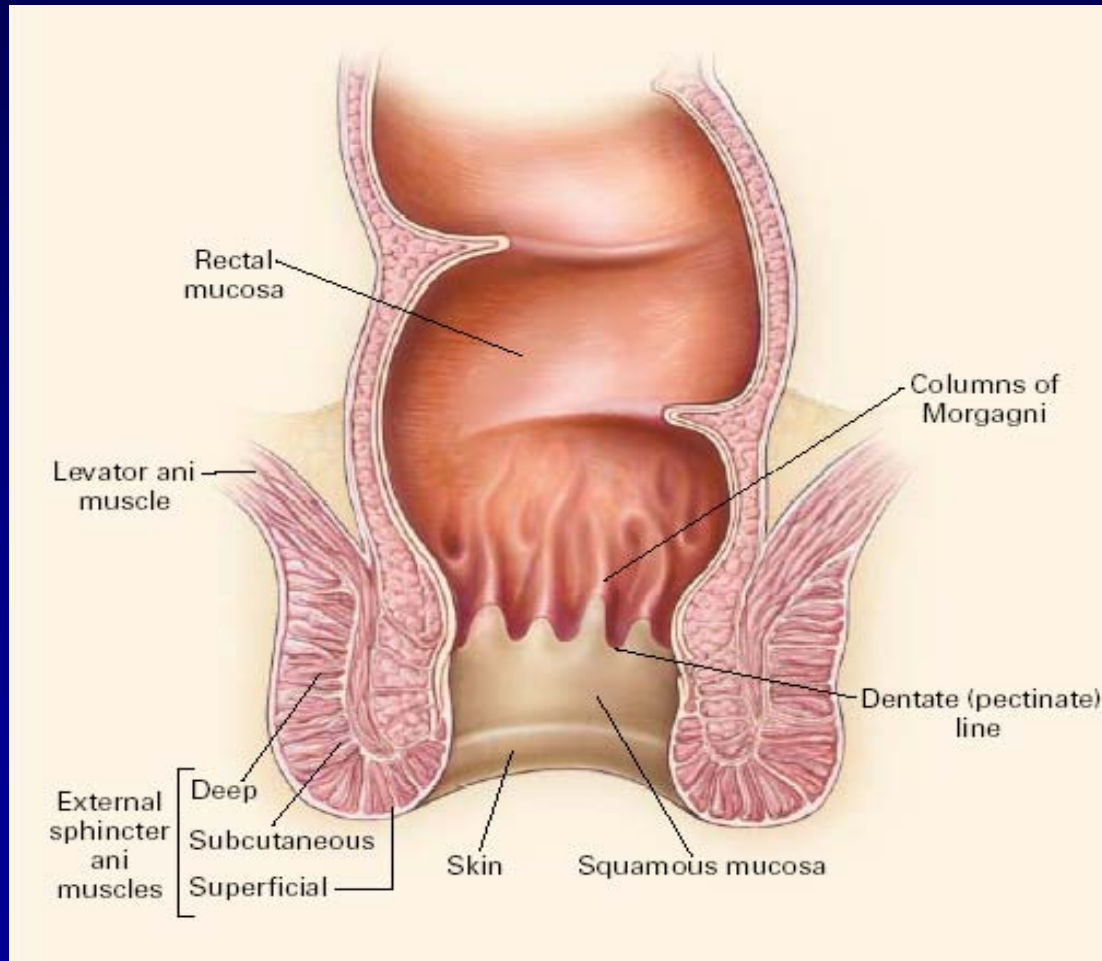
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Background

- Anal intercourse is the highest risk sexual activity for HIV transmission.
- Infection with squamous epitheliotropic sexually transmitted infection (HSV-2 and HPV) increases the risk of HIV-1 infection
- In contrast to the rectal mucosa, the role of the anal canal as a target or vector of HIV-1 infection is unknown

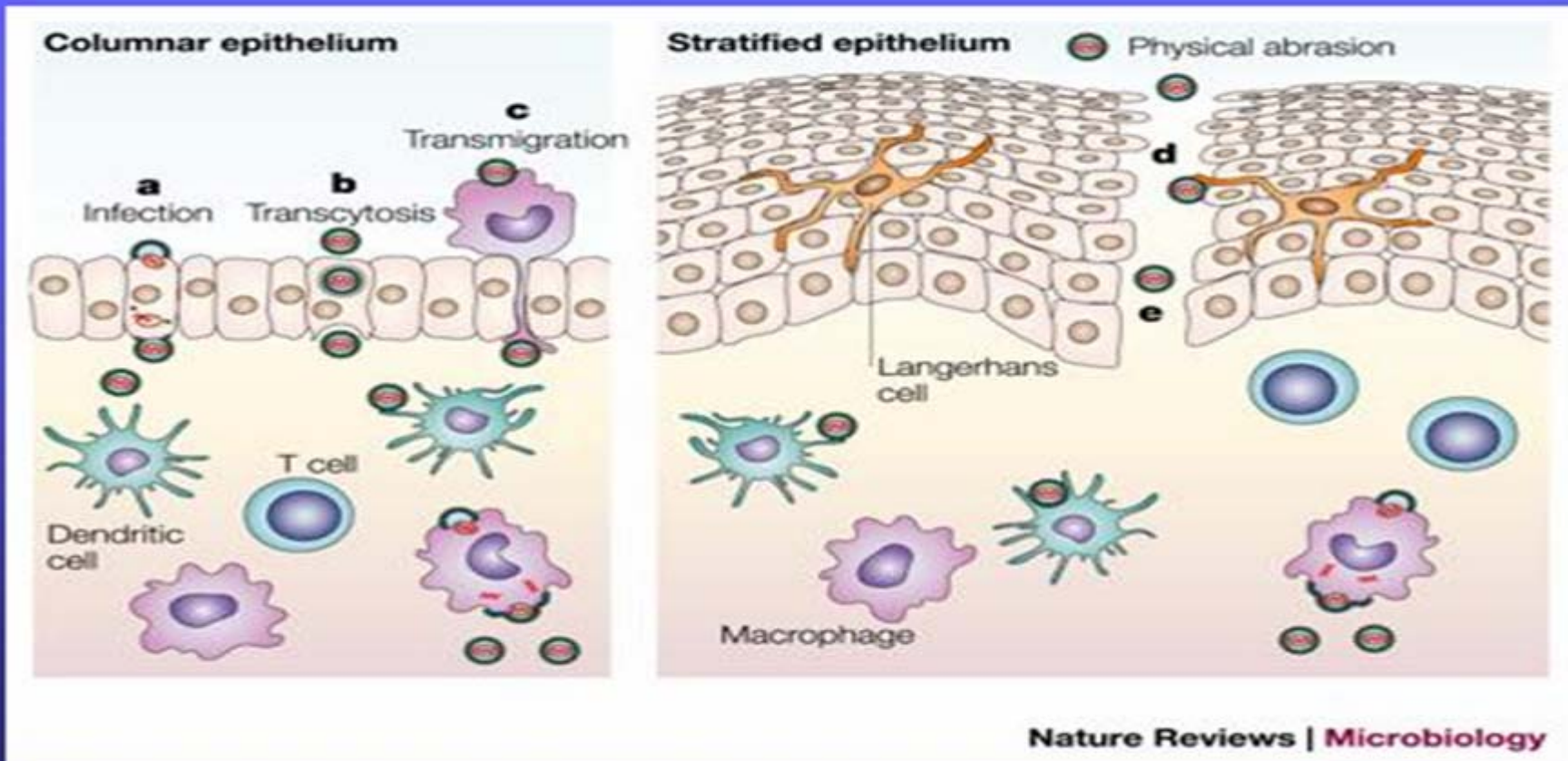
Normal anal canal



Normal anorectal transition zone



Mechanisms of HIV infection



Factors that may increase risk of
incident anal canal HIV infection

1. Epithelial abrasion

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2. STI co-infection

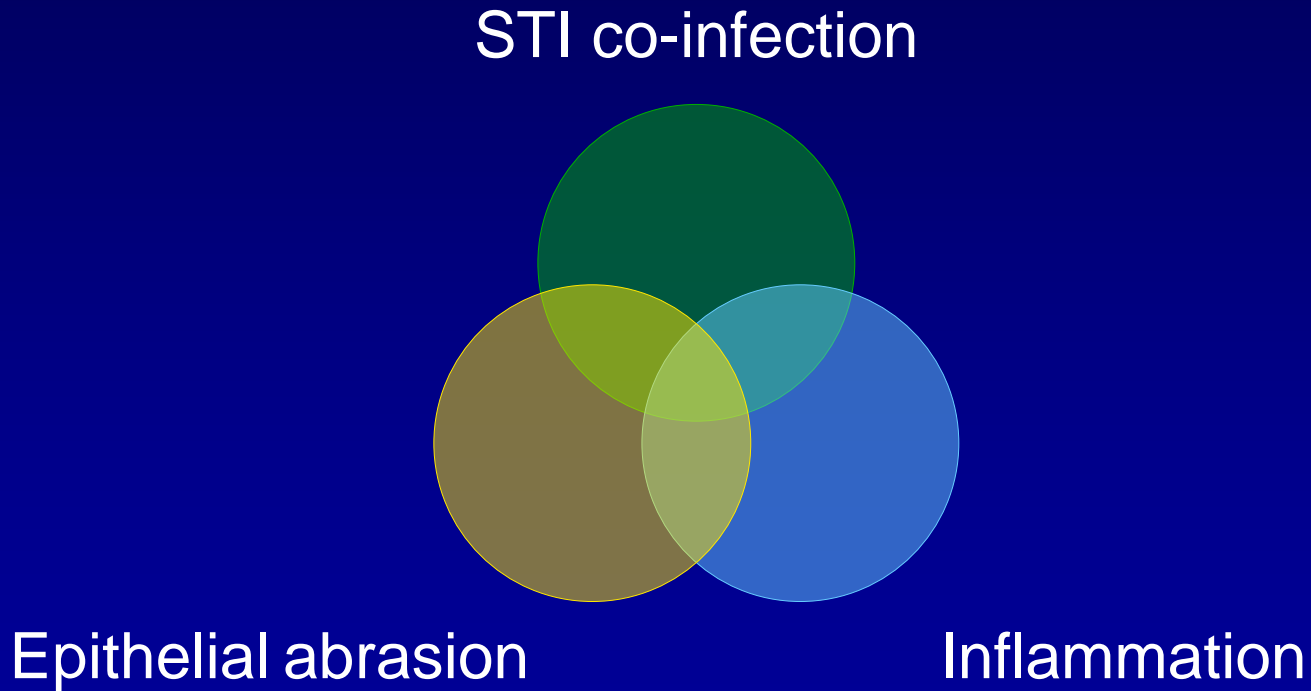
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3. Anal inflammation



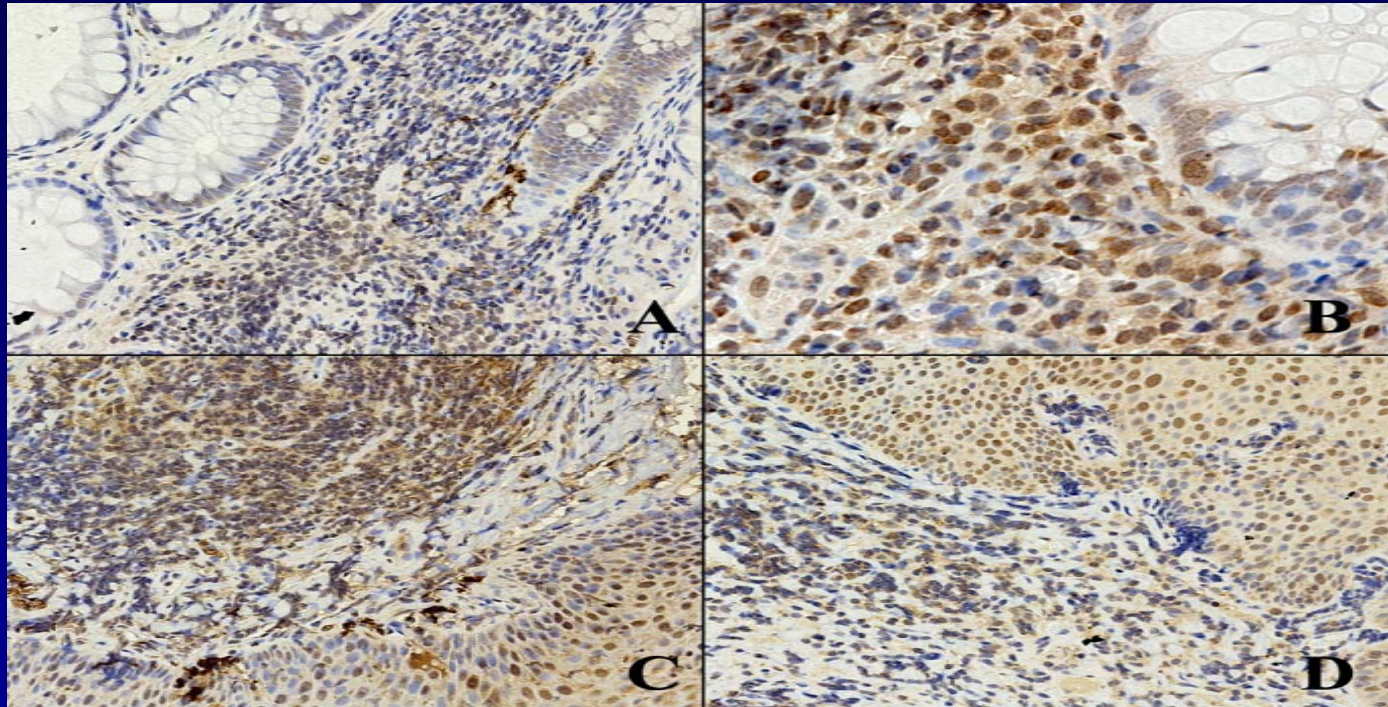
The perfect (anal) storm



Study population

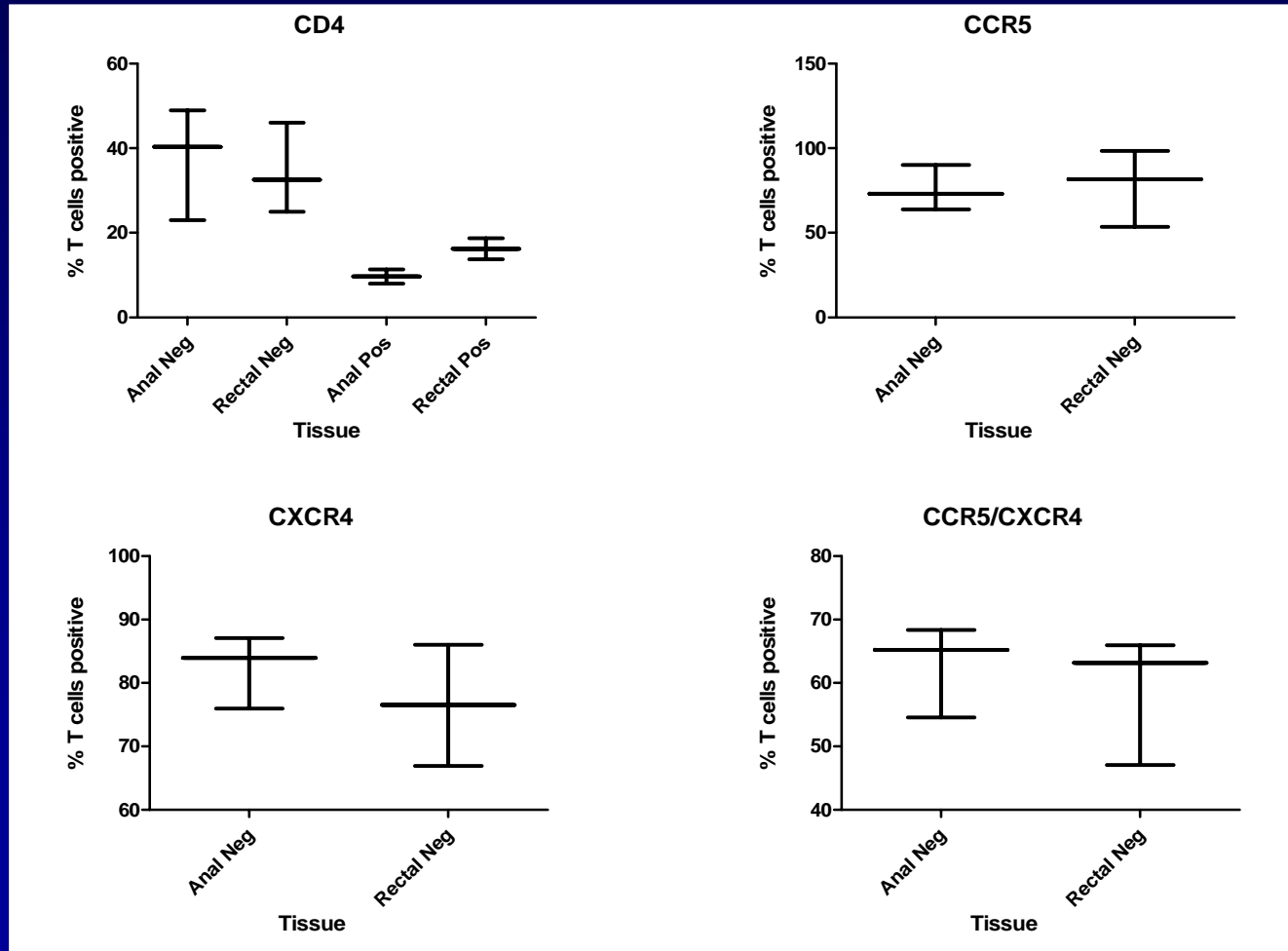
- Population: Chronically infected HIV-positive participants with PVL <50 or >10,000 copies per mL, and HIV-negative participants, over 18 years of age
- Screening: Rectal GC/CT by culture, HSV-2 by culture and Ag detection, HIV-1 PVL
- Biopsies: Paired visually normal anal and rectal tissue biopsies taken with 2.3 mm cup endoscopy forceps under direct vision with high-resolution anoscopy (x16)

Immunostaining

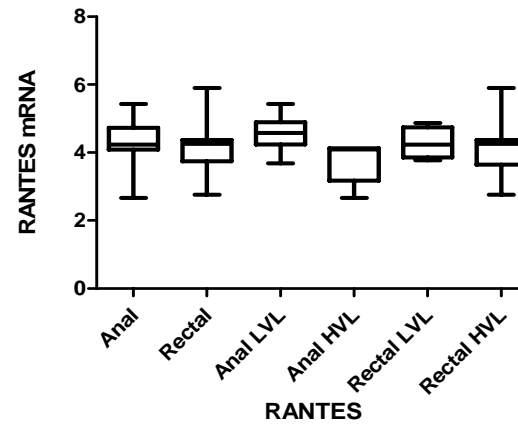
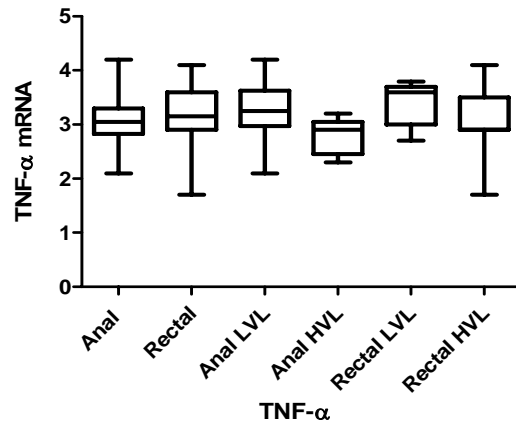
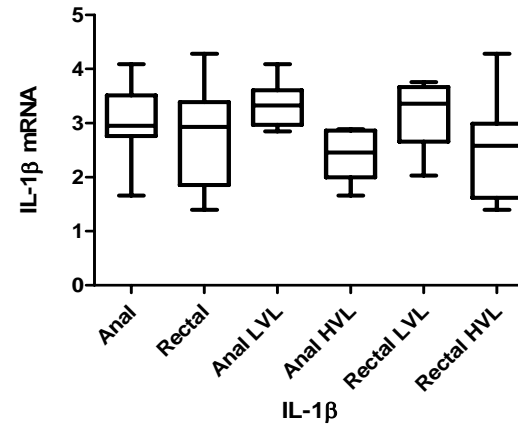
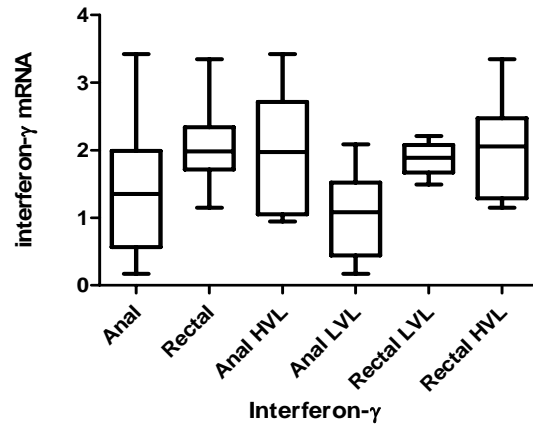


A: Rectal tissue stained for CXCR4 shows positive staining lymphocytes within the lamina propria B: Rectal tissue stained for CCR5 shows positive lymphocytes beneath the rectal epithelium C: Anal tissue stained for CXCR4 reveals positive lymphocytes in the lamina propria D: Anal tissue stained for CCR5 reveals positive lymphocytes beneath the squamous epithelium.

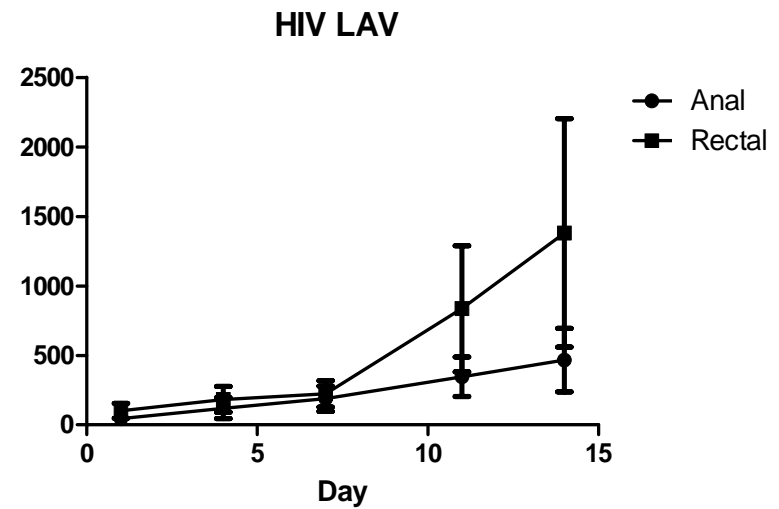
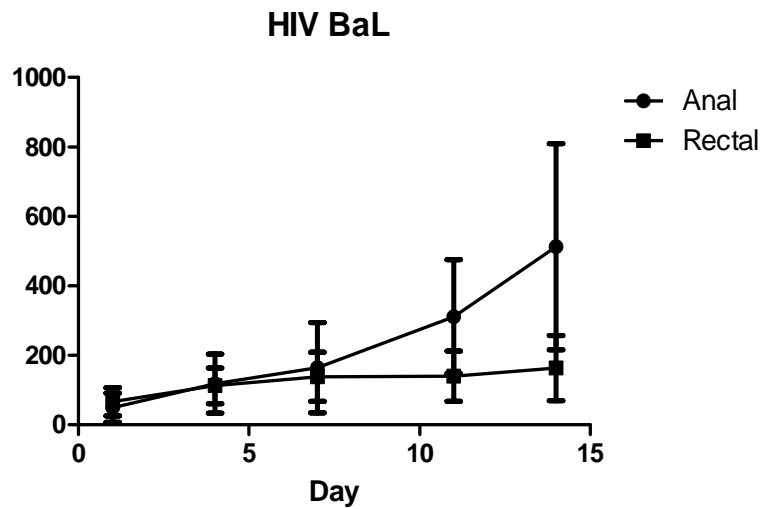
Anal and rectal T cell phenotype



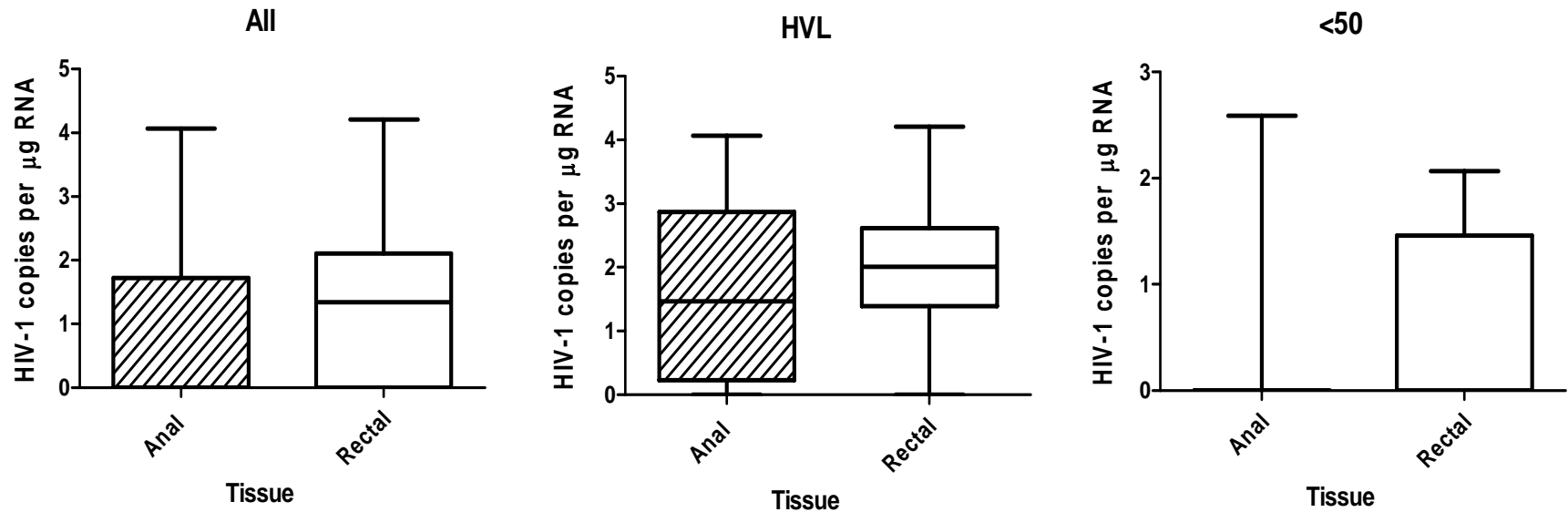
Anal and rectal cytokines



Anal and rectal explant infection



Anal and rectal HIV quantification



Conclusions

- Anal and rectal tissue biopsies contains activated CD4 T cells expressing both R5 and X4 co-receptors and can be infected ex vivo / in vitro with both R5 and X4 tropic HIV-1
- The cytokine environment is similar in both anal and rectal tissue types
- Mucosal HIV-1 infection can be demonstrated in anal and rectal tissue biopsies obtained from participants with chronic HIV-1 infection
- These data suggest that the anal canal is both receptive and permissive for HIV-1 infection and replication
- The anal canal is a potential site of incident HIV infection that should be considered in the development of candidate rectal microbicides

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