The Effect of Condomless Receptive Anal Intercourse on the Rectal Mucosa in MSM
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BACKGROUND:
- The risk of HIV transmission per exposure event for receptive anal intercourse is 1.38%, more than 12-fold higher than other routes of HIV transmission. Nearly 70% of HIV transmissions among MSM are attributed to rectal exposure.
- The vast majority of mucosal HIV transmission research has been conducted in the female genital tract or in non-human primates and extrapolated to rectal transmission among MSM.
- Sexual intercourse with semen exposure is known to cause an inflammatory reaction with influx of HIV target cells in the female genital tract.
- Therefore, we conducted a study to examine the rectal mucosal effects of condomless receptive anal intercourse (CRAI) in MSM.

METHODS:
- We enrolled 41 HIV negative MSM who were engaging in CRAI with an HIV negative partner and 21 men who had never engaged in anal intercourse (controls) into this study.
- Peripheral blood and rectal biopsy samples were collected from 2 time points separated by a median of 9 weeks. MSM abstained from CRAI for ≥72 hours prior to visit 1. MSM engaged in CRAI ≥72 hours prior to visit 2.
- PBMCs were isolated by Ficoll density and rectal MBCs by collagenase digestion. Cells were stained with surface antibodies for CD4+ and CD8+ cell phenotyping and stimulated with PMA/Ionomycin (Figure 1) to evaluate cytokine expression and analyzed with Flowjo software. Linear mixed effects models were used to examine differences in CD4+ and CD8+ cellular phenotype and cytokine expression between MSM engaging in CRAI and controls.
- From a subset of subjects (18 MSM and 10 controls), RNA was extracted from one rectal pinch biopsy and sequenced with Illumina HiSeq. Data were analyzed with DESeq to examine differential mRNA gene expression and Gene Set Enrichment Analysis with MSigDB database.

RESULTS:

- Table 1. Description of the study population. MSM engaging in CRAI were slightly older than MSM who did not engage in CRAI. All MSM engaged in CRAI reported use of lubricants for sex and a history reported anus sex.

- Table 2. Results of rectal MBC phenotyping for MSM engaging in CRAI and men who never engaged in anal intercourse (controls). Cells from MSM engaging in CRAI and higher HIV expression on CD4+ T cells. Upon HIV stimulation, rectal CD8+ T cells from MSM engaging in CRAI overall had higher HIV expression than controls. However, due to the exception of a decline in CD8+ expression in CD4+ T cells, there was no significant differences with timing of CRAI among MSM.

- Table 3. Overall model-averaged mean and standard deviation of the mean (SDM) for Ki67 expression on CD8+ T cells. Upon mitogen stimulation, rectal CD8+ T cells from MSM engaging in CRAI showed a higher Ki67 expression.

- Table 4. percentages of Ki67+CD8+ cells with and without mitogen stimulation. Upon mitogen stimulation, rectal CD8+ T cells from MSM engaging in CRAI showed a higher Ki67 expression.

CONCLUSIONS:
- The rectal mucosa of HIV negative MSM engaging in CRAI showed a distinct mRNA gene expression and CD8+ T lymphocyte profile as compared to men who have never engaged in anal intercourse.
- Our data show evidence of an acute inflammatory response to CRAI, possibly driven by neutrophils and monocytes, that may be the result of microtrauma/mucosal injury during intercourse with exposure to pro-inflammatory semen and the gut microbiota.
- With chronic exposure to CRAI, the frequency of IFNγ producing CD8+ T cells increased, suggesting a pro-inflammatory microenvironment.
- Th17 cells, critical for mucosal defense and inflammation, also likely play an important role in the acute and chronic response.
- Further research will be needed to determine how these factors may impact HIV susceptibility or mucosal vaccine response in the rectal mucosa of HIV negative MSM and how the gut microbiota may contribute.