GENITAL SECRETIONS FROM WOMEN WITH BACTERIAL VAGINOSIS ENHANCE HIV INFECTION EX VIVO

P-T04

Marla J. Keller[1,2], Richard Hunte[1], Rebecca Barnett[1], Joyce Serebrenik[1], Jessica McWalters[2], April Dobkin[1], Jessica Goymer[1], Laurie L. Ray[1], Lilia Espinoza[1], Jessica M. Atrio[2], Kerry Murphy[1,2], Betsy C. Herold[1,2]

[1]Albert Einstein College of Medicine, Bronx, NY, USA, [2]Montefiore Medical Center, Bronx, NY, USA

BACKGROUND

- Women with bacterial vaginosis (BV) are more susceptible to HIV infection.
- We hypothesize that increased HIV susceptibility is mediated by direct or indirect effects of bacteria on mucosal immunity and the epithelial barrier.
- The aim of this study was to assess differences in mucosal immunity and vaginal microbiota in US women at the time of symptomatic BV and after treatment.

METHODS

- Twenty HIV- women with BV diagnosed by Amsel criteria were evaluated before, 1 week, and 4 weeks after completion of treatment with oral metronidazole.
- Cervicovaginal fluid (CVF) cytokines and chemokines by Luminex, CVF inhibitory or enhancing activity against HIV infection using an ex vivo assay, and select vaginal microbiota were measured by quantitative PCR (qPCR).
- Results were compared between visits by Friedman's ANOVA test. Spearman correlation coefficients were calculated to assess associations between CVF HIV activity and the microbiome and other measures.

RESULTS

Table 1. Demographics and Other Characteristics

	n=20
Age (median, IQR)	39 (30, 43)
Race	5 White, 13 Black, 2 mixed
Ethnicity	8 Hispanic, 12 Non-Hispanic
History of smoking	8 (40%)
Prior bacterial vaginosis	12 (60%)
Ever had anal sex	7 (35%)
Douching month prior to visit 1	4 (20%)
Current hormonal contraception	4 (20%)
Vaginal pH at visit 1	5.5 (4.9, 6)
Nugent score at visit 1	8 (8, 10)

Figure 1. Mucosal immune mediator levels at time of BV diagnosis, 1 week, and 4 weeks after treatment. Each circle represents an individual participant. The lines indicate the median with interquartile range. The asterisks indicate p<0.05, Friedman's ANOVA test.

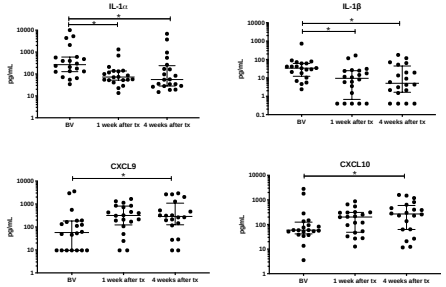


Figure 2. Vaginal swab eluants from women with BV enhance HIV infection. Vaginal eluants or control fluid were incubated with TZMbl cells prior to inoculating with HIV_{BaL}. Viral infection was quantified by measuring relative light units (RLU) as percentage of RLU in control fluid. Results from each participant (mean of triplicate wells) is shown at each time point. The lines indicate the median with interquartile range. The asterisk indicates p<0.05, Friedman's ANOVA test.

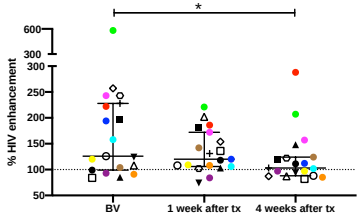


Figure 3. Microbiome shifts from diverse anaerobes to Lactobacillus-dominant following metronidazole treatment. Relative proportion of select species were determined by qPCR; each column represents an individual participant.

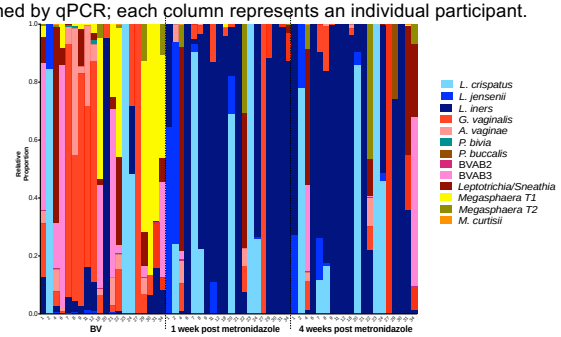
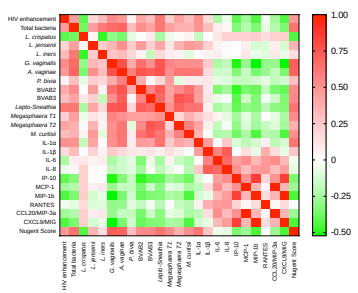


Figure 4. HIV enhancement correlates with diverse anaerobes. Color-coded heat map of Spearman correlation coefficients between HIV enhancing activity and total or specific bacteria quantified by PCR and other measurements.



HIV enhancement correlated positively with:
total bacteria (r = 0.46)
G. vaginalis (r = 0.55)
A. vaginae (r = 0.48)
Sneathia (r = 0.62)
BVAB2 (r = 0.4)
Nugent score (r = 0.48)
IL-1α (r = 0.5)
and correlated negatively with: *L. crispatus* (r = -0.4)
IP-10 (r = -0.397)
CXCL9 (r = -0.43)
CXCL10 (r=-0.4)
All p-values ≤ 0.002

CONCLUSIONS

- Inflammatory cytokines were higher and chemokines were lower in women with BV which significantly changed after treatment with oral metronidazole.
- Genital secretions from women with BV enhanced HIV infection ex vivo and the enhancement was associated with increased concentrations of select anaerobes.
- Treatment with oral metronidazole led to a reduction in the HIV enhancing activity and correlated with a shift to *Lactobacillus*-dominant microbiome.
- These findings have implications for adolescents and women of color who have higher rates of non-*Lactobacillus*-dominant microbiome.
- Mechanistic studies are in progress to better understand links between HIV enhancing activity and the vaginal microbiome.

ACKNOWLEDGEMENTS

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