The mucosal microbiome at sites of HIV acquisition among key populations

Vanessa E Van Doren[1], **Cassie G Ackerley[1,5]**, Robert A Arthur[2], Henry Claussen[2], Suparat Khemnark[3], Phillip M Murray[1], S Abigail Smith[1], Vin Tangpricha[4], Colleen F. Kelley[1,5]
[1]The Hope Clinic of the Emory Vaccine Center, Decatur, GA, USA, [2]Emory Integrated Computational Core, Atlanta, GA, USA, [3]Bamrasnaradura Infectious Diseases Institute, Bangkok, Thailand, [4]Division of Endocrinology, Emory University, Atlanta, GA, USA, [5]Grady Health System, Atlanta, GA, USA

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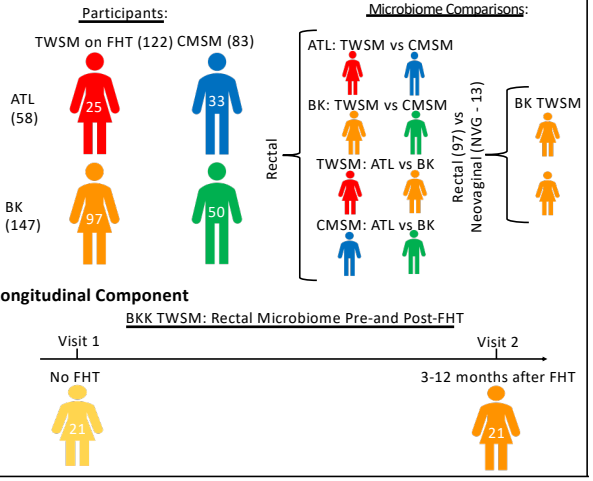
BACKGROUND

- The effects of the microbiome on vulnerability to HIV acquisition at mucosal sites have received significant attention.
- The gut has extensive estrogen receptors, feminizing hormone therapy (FHT) has been shown to influence the gut microbiome in mice, and endogenous estrogen has been shown to affect the gut microbiome in cis women.
- However, little is known about mucosal microbiome variations between key populations, including (1) cisgender men who have sex with men (CMSM) and transgender women who have sex with men (TWSM) using FHT or (2) across geographical locations.

METHODS

Using linear decomposition modeling (LDM), we compared rectal and neovaginal microbiome α diversity and relative abundance (RA) of TWSM and CMSM in Atlanta, Georgia, USA (ATL) and Bangkok, Thailand (BK) via two study designs – cross-sectional and longitudinal – as described below:

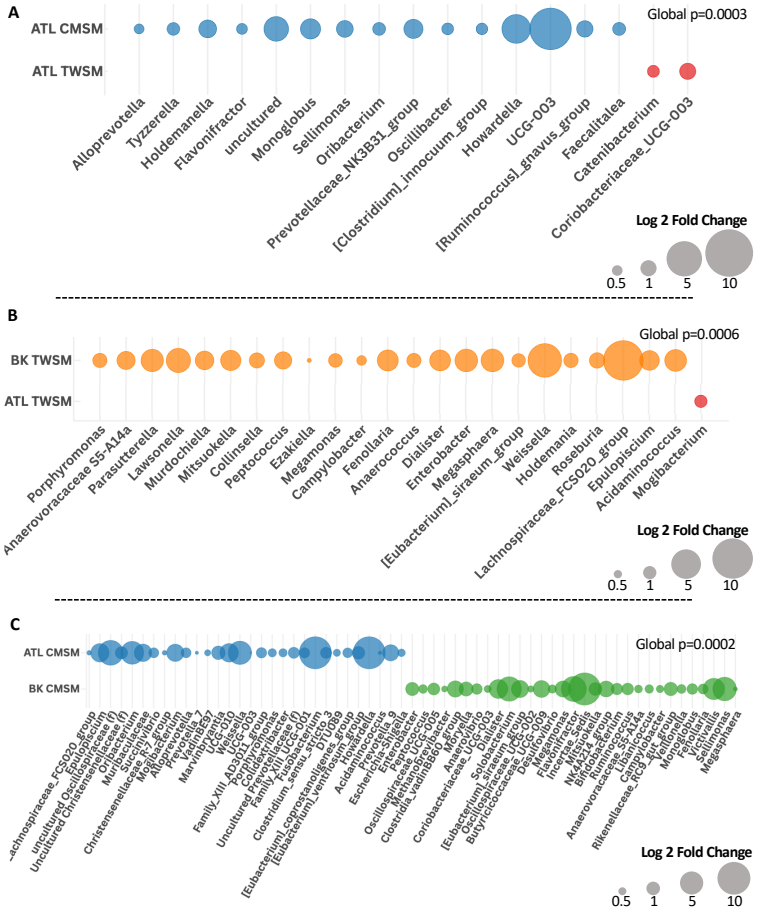
1. Cross-Sectional Component



2. Longitudinal Component

Figure 1: Differences in rectal microbiome composition between key populations. Differences in rectal microbiome relative abundance (RA) were assessed via linear decomposition modeling (LDM). Significant differences in RA were identified between **(A)** CMSM and TWSM in ATL (global p=0.0003), with 17 differentially-abundant taxa (FDR<5%); **(B)** TWSM in BK and ATL (global p=0.0006), with 24 differentially-abundant taxa (FDR<5%); **(C)** CMSM in BK and ATL (global p=0.0002), with 61 differentially-abundant taxa (FDR<5%). The size of the circle indicates the log2 fold change between groups. Significance decreases from left to right across the x-axes of each plot (all FDR<5%). There was no significant difference in RA via LDM between CMSM and TWSM in BK or in TWSM in BK pre- versus post-FHT. α diversity was only significantly different between CMSM in ATL versus BK (p=0.04).

Key populations have distinct microbiomes at sites of HIV acquisition that vary by both geography and gender identity.



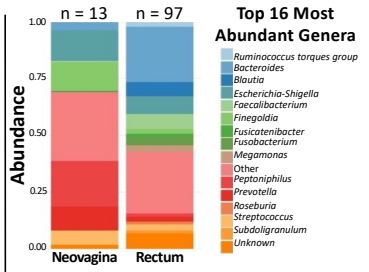


Figure 2: Differences in neovaginal and rectal microbiome relative abundance in TWSM in BK. Differences in neovaginal (NVG) and rectal microbiome relative abundance were assessed via LDM. A significant difference was seen (global p=0.0002), with 125 differentially-abundant taxa (FDR<5%). The most abundant taxa are shown here. There was also a significant difference in α diversity (p=0.005). Of the participants with NVG sampling, 9/13 (69.2%) had penile inversion, 3/13 (23/1%) had sigmoid colon pull-through, and 1/13 (7.7%) did not have a surgical technique reported.

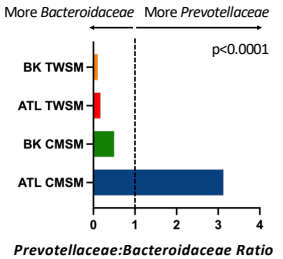


Figure 3: Rectal *Prevotellaceae to Bacteroidaceae* abundance ratios in key populations. Rectal *Prevotellaceae* to *Bacteroidaceae* ratios were >1 for CMSM in ATL but were <1 for CMSM in BK as well as TWSM in both ATL and BK.

RESULTS

- The rectal microbiomes of TWSM & CMSM differed significantly in ATL but not BK.
- The *Prevotellaceae:Bacteroidacaeae* ratio was >1 for ATL CMSM and <1 for BK CMSM & TWSM at both sites.
- The rectal microbiomes of TWSM & CMSM differed significantly between ATL & BK.
- Rectal and neovaginal microbiome compositions differed significantly.
- We detected no difference in the rectal microbiome before & after FHT initiation.

CONCLUSIONS

- Geographic rectal microbiome differences were more notable than those between MSM and TWSM using FHT.
- However, differences in rectal enrichment for *Prevotellaceae* and the distinct neovaginal microbiome underscore the need to distinguish TWSM from MSM in HIV prevention research.
- We found no effect of FHT initiation, which may be due to small sample size.
- We will next assess the influence of systemic estradiol levels on microbiome composition and evaluate for differences in neovaginal microbiome by surgical approach.
- Future studies examining the influence of the microbiome on mucosal HIV acquisition should account for variations in composition among key populations.

ACKNOWLEDGEMENTS

We express our sincerest gratitude to the study participants as well as the Emory Center for AIDS Research and the clinical research and community engagement teams in Atlanta and Bangkok.

This work was funded by 1R01AI128799-01, R38 AI140299, and T32 DK108735.