Stability of Penile Bacteria Associated with HIV Seroconversion, Inflammation, and Cells (BASICs)

Sydney G Nelson[1], Ronald M Galiwango[2], Daniel E Park[1], Sanja Huibner[3], Maliha Aziz[1], Edward Sung[1], Juan E Salazar[1], Aggrey Anok[2], James Nnamutete[2], John Bosco Wasswa[2], Godfrey Kigozi[2], Aaron A R Tobian[4], Jessica L Prodger[5], Rupert Kaul[3], Cindy M Liu[1]

[1]George Washington University, Washington, DC, USA, [2]Rakai Health Sciences Program, Kalisizo, Uganda, [3]University of Toronto, Toronto, Canada, [4]The Johns Hopkins University School of Medicine, Baltimore, MD, USA, [5]Western University, London, Canada

1174

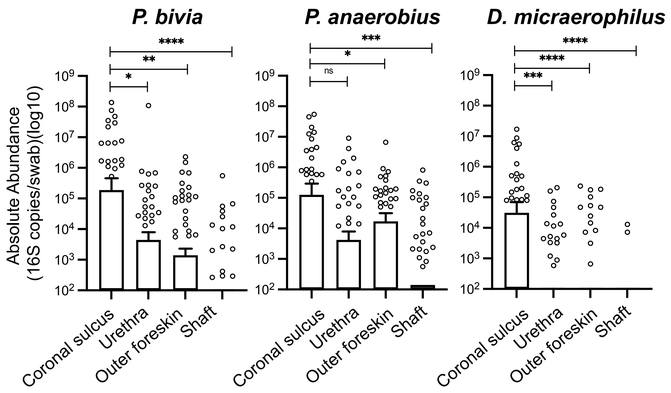
BACKGROUND

- **B**acteria **A**ssociated with HIV **S**eroconversion, **I**nflammation, and immune **C**ells (BASICs) are penile bacteria associated with increased HIV risk in men.
- Little is known regarding the colonization dynamics of BASICs, or if they colonize other male genital tract sites outside of the coronal sulcus.

METHODS

- Swabs from 97 uncircumcised men were collected cross-sectionally at the coronal sulcus, outer foreskin, shaft, and distal urethra in Rakai, Uganda; 47 were then sampled longitudinally over 8 weeks.
- We characterized the penile microbiome and determined prevalence, proportional and absolute abundance of BASICs using 16S rRNA qPCR and V3V4 amplicon sequencing.
- Residence time, defined as time between emergence and disappearance of a taxon, was used to compare stability of BASICs in the coronal sulcus to commensal penile bacteria.
- Abundance thresholds associated with HIV seroconversion risk for three key BASICs, called the BASIC triad, were imputed using published data (Prodger et al., 2021) to characterize BASIC dynamics.

Figure 1: Absolute abundance of BASIC triad across the penis



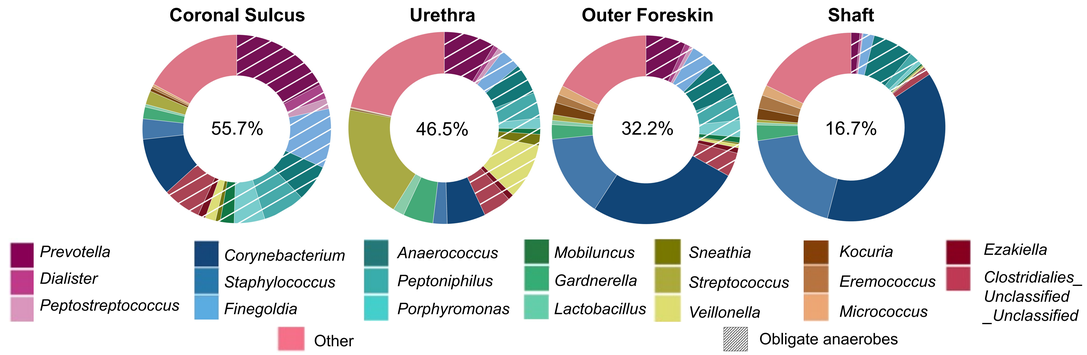
Mann-Whitney Test: n.s. = p>0.05; * = p≤0.05; ** = p≤0.01; *** = p≤0.001; **** = p≤0.0001

Bacteria **A**ssociated with HIV **S**eroconversion, **I**nflammation, and immune **C**ells (**BASICs**) were most prevalent and abundant in the **coronal sulcus** compared to other penile sites.

Colonization by BASICs in the coronal sulcus is **dynamic**.

Fluctuation of BASIC triad abundance respective to high-risk HIV seroconversion thresholds suggests there is a **window of time a participant spends at higher risk of HIV**.

Figure 2: Proportional abundance of the 20 most abundant penile bacterial genera across sites.



RESULTS

- Across penile sites, the coronal sulcus had the highest bacterial load ($1.72x10^8$ 16S rRNA copies/uL), including BASIC triad species *P. bivia*, *P. anaerobius*, and *D. micraerophilus*, and obligate anaerobes.
- *P. bivia*, *P. anaerobius*, and *D. micraerophilus* were detected at least once in 62%, 70%, and 64% of participants over the 8-week study period, but only 17%, 17%, and 9% were colonized at all visits.
- 43% of participants had at least one visit with a BASIC above the high-risk abundance threshold.
- BASICs had a shorter residence in the coronal sulcus than *Corynebacterium*, a ubiquitous skin microbe.

Figure 3: Percent of visits above the high-risk HIV-seroconversion abundance threshold for triad species

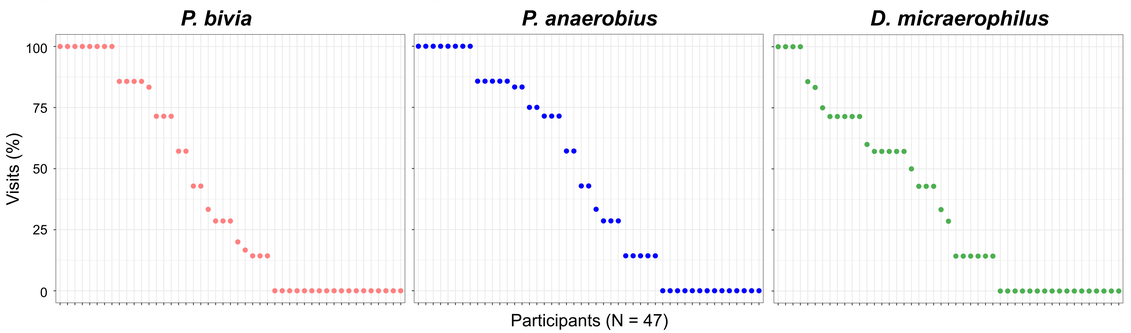
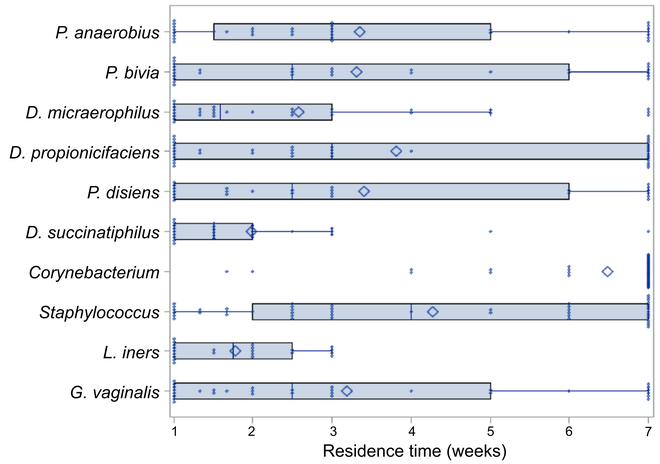


Figure 4: Residence time of BASICs and comparator taxa.



CONCLUSIONS

- The coronal sulcus microbiome is distinct compared to other penile sites.
- High abundances of BASIC triad are uncommon outside of the coronal sulcus; removing the sub-preputial space by medical male circumcision eliminates the primary habitat for BASICs.
- High abundance colonization by BASICs is transient and uncommon in the coronal sulcus.
- Targeted interventions reducing BASIC abundance in the coronal sulcus may be an effective approach to decrease HIV risk.

ADDITIONAL KEY INFORMATION

We thank the staff of the Rakai Health Science Program in Uganda and all study participants. This work was supported by the National Institutes of Health (R01A123002 and R01DK131936 to CML; 1R01AI128779 to AART), the Canadian Institutes for Health Research (PJT-180629 to RK) and Fogarty HIV Research Training Program of the National Institutes of Health (4D43TW009578-04 to RMG). JLP is supported, in part, by the Canada Research Chairs Program (CRC-2020-00175). The funders had no role in the study design, data collection, or analysis.