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Sex and the Penile Microbiome: Potential Sharing of HIV Risk–Associated Anaerobes

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Background

- Are the anaerobic bacteria associated with HIV risk shared between sexual partners?

Anaerobes in the genital microbiome have been associated with HIV acquisition in both men and women.[1-5] *Prevotella bivia* and *Dialister micraerophilus* are associated with HIV risk and genital inflammation in both men and women despite major differences in vaginal and penile microbiome composition. Little is known regarding the potential transmission of HIV-associated anaerobes, particularly the directionality of transmission.

Methods

- We characterized sub-preputial microbiota in uncircumcised HIV negative males, including 95 non-sexually active adolescents and 47 non-sexually active and sexually active adult men in Rakai, Uganda.
- Sub-preputial swabs were collected into 1% BSA in PBS with protease inhibitor.
- Total bacterial density was measured by qPCR. Proportional and absolute abundance of penile bacteria was characterized by sequencing the 16S rRNA V3V6 region.
- Overall penile microbiome composition was compared by PerMANOVA. Prevalence and abundance of penile bacteria were compared by the Chi-square test and Wilcoxon rank-sum test, respectively.

Results

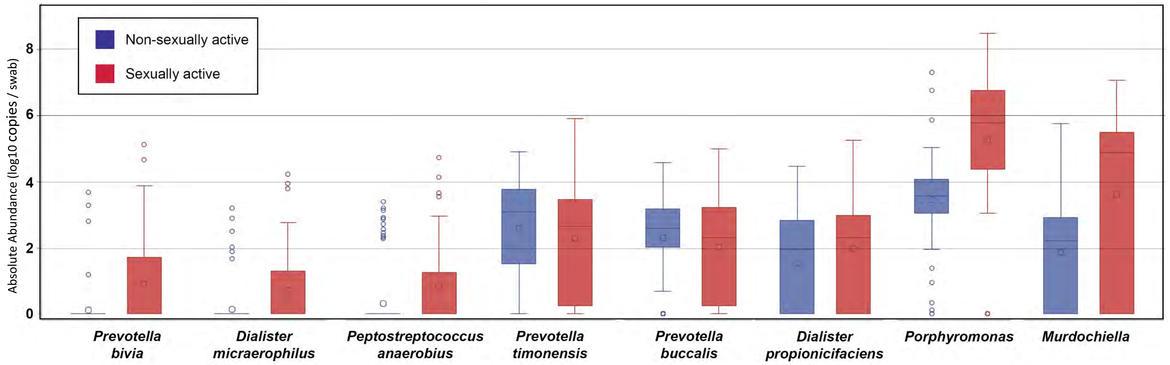
Overall Composition

- Penile microbiome composition differed significantly between sexually active and non-sexually active uncircumcised males in both proportion and absolute abundances (PerMANOVA p<0.001 in both).
- However, total bacterial density was similar across groups.

HIV seroconversion-associated anaerobes may originate in the vaginal microbiome.

Once transmitted to the penile microbiome, the anaerobes could colonize the penis and spur foreskin inflammation.

Figure 1. Absolute abundance of anaerobes by sexual activity status



HIV seroconversion-associated anaerobes

- Non-sexually active adolescents had high abundance of anaerobic penile bacteria, including many *Prevotella* and *Dialister* species.
- However, two species associated with HIV risk and genital inflammation—*P. bivia* and *D. micraerophilus*—were significantly less prevalent and abundant in non-sexually active adolescents.
- *Peptostreptococcus anaerobius*, associated with HIV risk in men, was also less prevalent and abundant in non-sexually active adolescents.

Table 1. Study population characteristics

	Non-sexually active N=100	Sexually active N=42
Age in years, median (SD)	16 (1.22)	20 (5.23)
Retract foreskin when washing*	74 (74.0%)	41 (97.6%)
Antibiotics in the last 3 months	4 (4.0%)	2 (4.8%)

*p<0.001

Table 2. Prevalence of anaerobes

Prevalence	Non-sexually active N=100	Sexually active N=42	P-value
Prevotella bivia	4 (4.0%)	14 (33.3%)	<0.001
Dialister micraerophilus	6 (6.0%)	14 (33.3%)	<0.001
Peptostreptococcus anaerobius	11 (11.0%)	15 (35.7%)	<0.001
Prevotella timonensis	81 (81.0%)	32 (76.2%)	0.516
Prevotella buccalis	83 (83.0%)	33 (78.6%)	0.533
Dialister propionicifaciens	55 (55.0%)	29 (69.1%)	0.120
Porphyromonas	98 (98.0%)	37 (88.1%)	0.013
Murdochiella	71 (71.0%)	30 (71.4%)	0.959

Summary & Conclusions

Prior to initiation of sexual activity, the uncircumcised penile microbiome is dominated by anaerobic bacteria, but the specific species associated with HIV risk and genital inflammation are conspicuously rare.

These data suggest that the seroconversion-associated anaerobes may originate in vaginal microbiome, which once when transmitted to the penile microbiome could colonize the penis and spur foreskin inflammation.

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