

Bacteriome Composition in Acute/Early PWH: Insights from PIRC Rectal Swabs

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Background: HIV-associated mucosal damage alters the gut microbiome. Knowledge of gut microbiome composition differences between acute and early HIV stages is limited. Yet, mucosal damage, decrease in CD4⁺ T cells, and perturbations in the gut immune system occur with different kinetics after acquiring HIV. We investigated the implications of acute (group 1 (G1)) and early (group 2 (G2)) HIV acquisition on the rectal bacteriome.

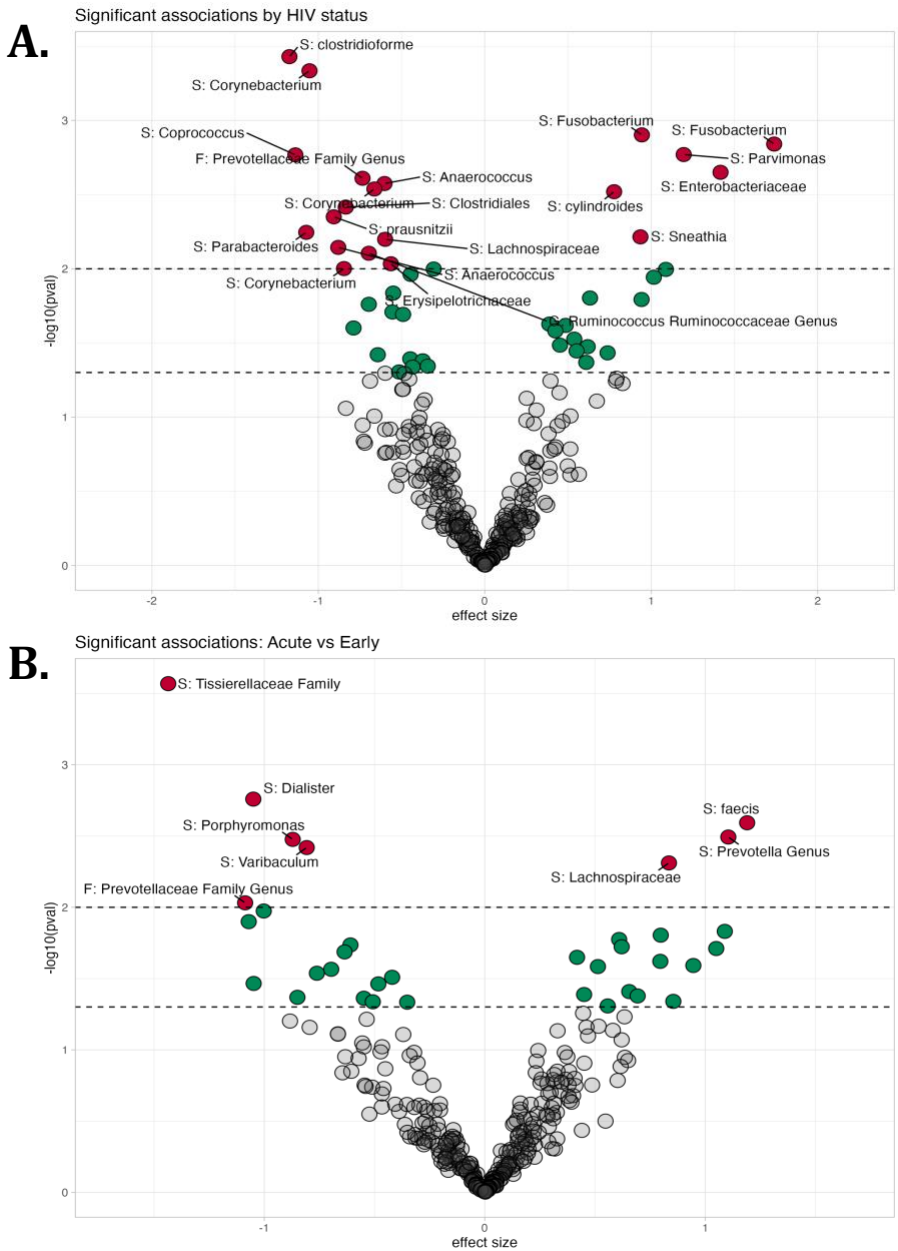
Methods: Rectal swabs were collected from persons with HIV (PWH) identified with acute and early HIV before starting antiretroviral therapy and enrolled in the San Diego Primary Infection Resource Consortium (PIRC) and from people without HIV (PWoH) who screened negative between 1996 and 2022. For each swab, bacteriome composition was analyzed by 16SrRNA sequencing to compare positive or negative HIV status. Among PWH, we compared individuals identified <90 days after HIV acquisition (G1) versus acquisition >90 but up to one year (G2). Dimension reduction of taxa was performed by filtering by thresholds of relative abundance (RA), prevalence, and number of reads. Multivariable associations between the RA of taxa and factors including age, sex, HIV status, and recency of HIV acquisition were performed using MaAsLin2 R package.

Results: 414 participants were included (97.5% male, 65.7% White, average 34±11 years, 79.2% PWH, of which 32% G1 and 68% G2). We observed differences between PWH and PWoH in the bacteriome composition; 6 and 11 taxa were significantly more and less common in PWH ($p < 0.01$). Notably, *Fusobacteria*, which has been associated with poorer CD4 T-cell recovery following antiretrovirals, was more abundant in PWH (**Figure 1A**). Additionally, 3 and 4 taxa were significantly more and less common in G2 compared to G1 ($p < 0.01$, **Figure 1B**). Differences were seen at the family level; among them, RA of *Lachnospiraceae*, associated with anti-inflammatory properties and maintaining gut homeostasis, was significantly lower in G1 compared to G2.

Conclusions: Our study demonstrates (1) significant differences in the bacteriome associated with HIV status and (2) the impact of acute and early HIV acquisition on rectal bacteriome composition. These findings suggest an early but distinct effect of HIV on the gut microbiome

during initial stages of acquisition. Longitudinal studies are needed to validate our results through within-individual analyses, to better understand the interaction between HIV and the gut microbiome over time.

Figure 1: Significant Associations of Bacterial Taxa with HIV Status and Recency of Acquisition



Significant (p -value < 0.01 , red data points) associations between relative abundance and HIV status (Top Figure) and recency of HIV acquisition (Bottom Figure) are shown. The x-axis indicates association between negative effect sizes (Acute infection or Negative HIV status) and positive effect sizes (Early

*infection or positive HIV status). The y-axis indicates p-value on a -log₁₀ scale with the top and bottom horizontal dash lines representing $p < 0.01$ and $p < 0.05$ thresholds respectively. Significant taxa with $p < 0.05$ threshold is colored green while taxa with $p < 0.01$ are colored red. **A.** The relative abundance (RA) of 11 and 6 taxa were significantly higher in PWoH (top left, in red) and PWH (top right, in red) respectively (p value < 0.01). **B.** Similarly, RA of 3 and 4 taxa were significantly higher in early (top right, in red) and acute infection (top left, in red) respectively.*