Rectal Microbiome Alterations Associated with TDF/FTC for Pre-Exposure Prophylaxis

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Background

- Oral daily tenofovir (TFV) disoproxil fumarate/emtricitabine (TDF/FTC) for HIV pre-exposure prophylaxis (PrEP) is a highly effective HIV prevention strategy; however, long-term adverse effects are not fully defined.
- The rectal microbiome helps maintain gut immune homeostasis, and perturbations may influence HIV susceptibility.
- Numerous factors influence microbiome composition including behavioral factors, which are important considerations in study design and analysis.
- This study sought to examine the effects of oral TDF/FTC for PrEP on the rectal microbiome using a well-characterized cohort of men who have sex with men (MSM).

Methods

- Participants: HIV-negative participants currently on PrEP (n=37) were selected from an ongoing cohort (The mSTUDY). Control participants (n=37) not on PrEP were selected using 1:1 matching on a propensity score which included:
  - Age
  - Race/ethnicity
  - Recent receptive anal intercourse (RAI)
  - Frequency of RAI
  - Drug use
- Specimens: Rectal swabs and hair samples used in this study were collected August 2014 – July 2017.
- Microbiome: Microbiome profiling was performed using 16S RNA gene sequencing and data processed using DADA2.
- Associations between PrEP use and bacterial abundance were examined using zero-inflated negative binomial regression (ZINB) and binomial least absolute shrinkage and selection operator (LASSO) regression.

Results

- Oral TDF/FTC for PrEP is associated with changes in the rectal microbiome compared to well-matched controls.
- Streptococcus abundance was increased in PrEP use (adjusted p=0.015).
- Other important alterations include increased Mitsuokella and Fusobacterium, as well as decreased Escherichia/Shigella.
- Increased Fusobacterium was similarly associated with TFV levels by hair analysis in a small subset (n=15) of PrEP users.
- This study highlights the need for investigation of the role of microbiome changes in HIV susceptibility and effectiveness of PrEP.

Table 1. Study participant demographics and characteristics

| Characteristic | Control (n=37) | PrEP (n=37) | p-value
<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>Age (mean, range)</td>
<td>28.8 (20-54)</td>
<td>28.8 (20-54)</td>
<td>0.91</td>
</tr>
<tr>
<td>Race/Ethnicity (%)</td>
<td>16 (43.2)</td>
<td>14 (37.8)</td>
<td>0.86</td>
</tr>
<tr>
<td>Black/Non-Hispanic</td>
<td>17</td>
<td>19</td>
<td>0.05</td>
</tr>
<tr>
<td>Hispanic</td>
<td>12 (32.4)</td>
<td>12 (32.4)</td>
<td>1.00</td>
</tr>
<tr>
<td>Other/Multiracial</td>
<td>7 (18.9)</td>
<td>4 (10.8)</td>
<td>0.52</td>
</tr>
<tr>
<td>Gender (M/F) (%)</td>
<td>26 (70.3)</td>
<td>24 (65.0)</td>
<td>0.51</td>
</tr>
<tr>
<td>Male</td>
<td>35</td>
<td>35</td>
<td>1.00</td>
</tr>
<tr>
<td>Female</td>
<td>2</td>
<td>2</td>
<td>1.00</td>
</tr>
</tbody>
</table>

Table 2. TFV and FTC concentrations in hair samples

<table>
<thead>
<tr>
<th>Sample Type</th>
<th>PrEP (ng/mg hair)</th>
<th>Control (ng/mg hair)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-PrEP</td>
<td>0.031</td>
<td>0.016</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Post-PrEP</td>
<td>0.020</td>
<td>0.009</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Conclusions

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Acknowledgments

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