HIV Rebound in Controllers Is Associated With Specific Fecal Microbiome Profile

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Disclosure: Employee of Gilead Sciences, Inc.
Study Design for Oral VES in HIV Controllers on ART

Viral and immunologic outcomes
♦ A modest increase in time to viral rebound, as well as a decrease in viral set point and intact proviral DNA\(^1\)
♦ Induction of dose-dependent interferon response and increased immune-cell activation\(^2\)

Aim of study
♦ To characterize the fecal microbiome in HIV VCs on ART and following VES treatment
♦ To investigate if there is any association between fecal microbiome and VES treatment outcomes

ART, antiretroviral therapy; ATI, analytic treatment interruption; c, copies; VES, vesatolimod; VCs, virologic controllers; VL, viral load.
VES Restored Abundance of Some Microbiome Species to Level Close to HVs

**Placebo**
- Baseline, n=2
- Pre-ATI, n=6

**VES 4–10 mg**
- Baseline, n=4
- Pre-ATI, n=7

**HV, Healthy Volunteers**
- n=14

### Species
- Catenibacterium mitsuokai
- Phascolarctobacterium succinatutens
- Parabacteroides distasonis
- Bacteroides eggerthii
- Parabacteroides merdae
- Bacteroides caccae
- Alistipes putredinis
- Bacteroides stercoreus
- Eubacterium siraeum
- Bacteroides ovatus
- Faecalibacterium prausnitzii
- Bacteroides vulgatus
- Eubacterium rectale
- Bacteroides uniformis
- Subdoligranulum unclassified
- Prevotella copri

**Notes**
- HVs, healthy volunteers.
Proteobacteria Abundance Tended to Be Positively Correlated With ISG Expression Level and CD4 T-Cell Activation

*Statistically significant (p ≤0.05). Data were obtained from male participants in the HIV VC study, including both treatment arms and both time points (n=19); only confidence intervals (CIs) ≥0.2 are color coded. ISG, interferon-stimulated gene.
Fecal *Ruminococcus gnavus* Abundance at Pre-ATI Was Negatively Associated With Time to Viral Rebound in HIV VCs

- Higher abundance of *R. gnavus* at pre-ATI was associated with shorter time to rebound
- Low and high abundance for given taxa was determined by medium abundance

FDR, false discovery rate.
Conclusions

- VES restored the abundance of some microbiome species, such as *Prevotella copri*, to a level that was close to that of HVs
- Fecal proteobacteria abundance potentially reflects systemic immune activation and increased antiviral responses in VES-treated HIV VCs
- Enrichment of *R. gnavus* at pre-ATI was negatively associated with time to HIV rebound, suggesting a negative association between *R. gnavus* and HIV reservoir and viral persistence (*R. gnavus* probably led to increased oxidative stress and inflammation)
- Future studies are needed to understand the possible mechanisms driving gut dysbiosis, and investigate the abundance of some microbiome species in predicting antiviral responses and viral reservoir in HIV cure studies, as well as expanding the study to women living with HIV

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