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Rectal Tissue HIV RNA is Associated with Systemic Inflammation in Persons with HIV

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BACKGROUND

- Despite antiretroviral therapy (ART), non-AIDS comorbidities account for significant morbidity and mortality in persons with HIV (PWH)
- Chronic inflammation plays a large role in the increased risk of non-AIDS comorbidities
- Gut mucosa, including the rectum, is a key reservoir and site of ongoing immune dysregulation
- We assessed associations between rectal tissue HIV RNA and 1) systemic inflammatory and hypercoagulation biomarkers and 2) replication-competent virus

METHODS

- Treatment-naïve PWH initiating ART had paired blood and rectal tissue (RT) sampling, **Fig 1.**

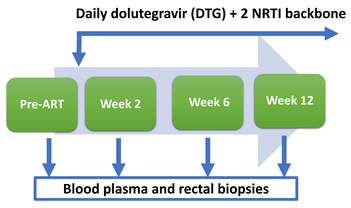


Figure 1. Study Schema

- Plasma and RT HIV RNA was quantitated with Abbott Real-Time HIV RNA assay (limit of detection <40 c/mL or c/gram)
- Modified quantitative viral outgrowth assays (QVOA) were performed on a subset of rectal samples, **Fig 2**.

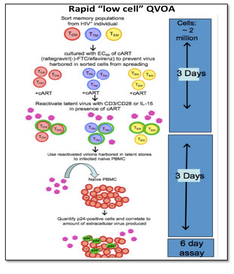


Figure 2. Rapid low cell QVOA

- Plasma biomarkers (CRP, sCD163, IL-6, D-Dimer, TNF-α) were measured by ELISA
- Linear regression models included each biomarker as the dependent variable and RT suppression status, biopsy week, and RT suppression status* week as independent variables.
- Models included random intercepts for the participant with a variance components covariance structure

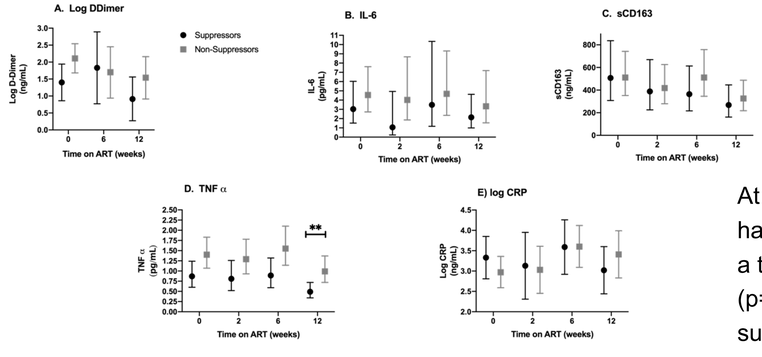
Persistent detectable **rectal tissue HIV RNA** during early ART is **replication-competent** and is associated with increased ***systemic inflammation*** and ***hypercoagulation*.**

RESULTS

- Fourteen (14) participants contributed 37 paired plasma and RT samples
- RT suppressors (n=5) had lower plasma HIV RNA at baseline but similar time to virologic suppression compared to RT non-suppressors (n-9), **Table 1**
- QVOA was performed in 11 rectal tissue samples with detectable HIV RNA and 100% had replication-competent virus

Variable n(%) or median (Q1, Q3)	Overall n=14	Rectal tissue suppressor, n=5	Rectal tissue non-suppressors, n=9	P-value
Age, years	37 (29, 47)	45 (34, 51)	30 (26, 44)	0.23
Cis-gender male	10 (71)	3 (60)	7 (78)	0.48
Black, Non-Hispanic	12 (86)	4 (80)	8 (89)	0.65
CD4, cells/mm^3	211 (67, 372)	357 (130, 389)	210 (43, 368)	0.52
Log plasma HIV RNA, copies/mL	4.6 (4.4, 4.7)	4.4 (3.7, 4.4)	4.7 (4.5, 4.9)	**0.02**
Time to virologic suppression, weeks	6 (2, 6)	6 (6, 6)	6 (2, 6)	0.87
Log rectal tissue HIV RNA, copies/gram	6.4 (5.4, 7.2)	5.5 (4.4, 6.1)	6.4 (5.4, 7.3)	0.15

Figure 3. Model-based estimates of biomarkers by rectal tissue suppression status over time.



At week 12, RT suppressors had lower TNF-α (p=0.008) and a trend toward lower D-Dimer (p=0.16) than RT non-suppressors, **Fig 3**.

CONCLUSIONS

- Persistent detectable rectal tissue HIV RNA reflects replication-competent virus in the first 12 weeks following ART initiation and is associated with increased systemic inflammation and hypercoagulation
- Early tissue HIV RNA viral dynamics may predict patterns of systemic inflammation and hypercoagulation even during rapid plasma virologic suppression
- Larger studies of virally-suppressed individuals on long-term ART are needed to confirm findings and assess additional endpoints of subclinical and clinical end-organ disease

ADDITIONAL KEY INFORMATION

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NIH National Institute of Allergy and Infectious Diseases

Grady

CFAR Emory Center for AIDS Research