Distinct Intestinal Microbial Signatures Linked to Accelerated Biological Aging in People with HIV

#336

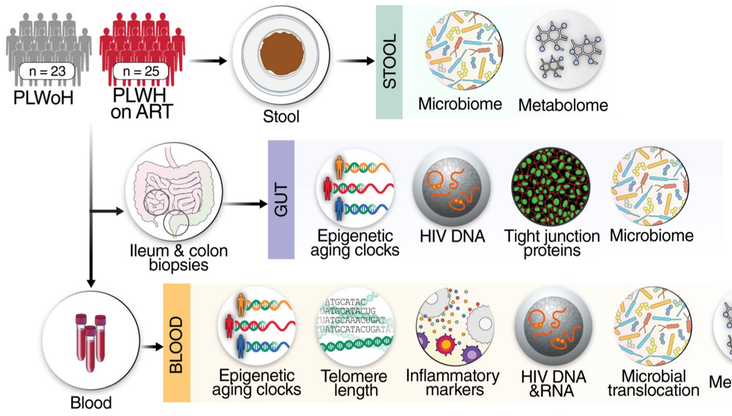
Shalini Singh[1], Leila B. Giron[1], Maliha W Shaikh[2], Shivanjali Shankaran[2,3], Phillip A. Engen[2], Zlata R. Bogin[2], Simona A. Bambi[2], Aaron Goldman[1], Toshitha Kannan[1], Ceylan E. Tanes[4], Kyle Bittinger[4], Alan Landay[2,3], Michael Corley[5], Ali Keshavarzian[2,3], Mohamed Abdel-Mohsen[1]

[1]The Wistar Institute, Philadelphia, PA, USA; [2]Rush Center for Integrated Microbiome and Chronobiology Research, Rush University, Chicago, IL, USA; [3]Department of Medicine, Rush University, Chicago, IL, USA; [4]Children's Hospital of Philadelphia, Philadelphia, PA, USA; [5]Weill Cornell Medicine, New York, NY, USA.

BACKGROUND

- HIV infection disrupts the intestinal barrier, resulting in persistent inflammation, even with antiretroviral therapy (ART). This inflammation contributes to aging-related comorbidities in people with HIV (PWH).
- However, it remains unclear whether ART-suppressed HIV affects intestinal biological aging and whether microbial dysbiosis and translocation contribute to aging in PWH on ART.

METHODS



RESULTS

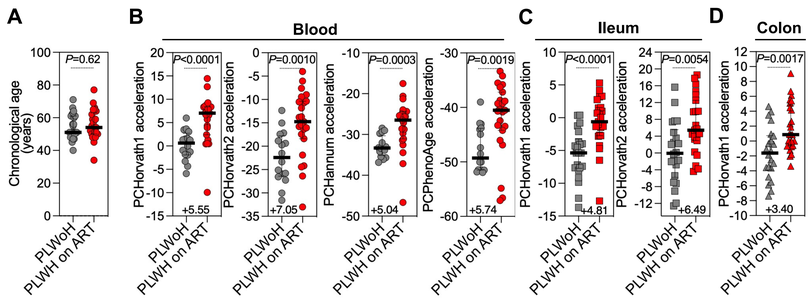


Figure 1: Accelerated intestinal and blood biological aging in PLWH on ART. (A) Chronological age comparison between PLWoH and PLWH on ART. **(B-D)** Dot-plots illustrating the significant acceleration in biological age for blood (B), ileum (C), and colon (D) based on multiple epigenetic clocks

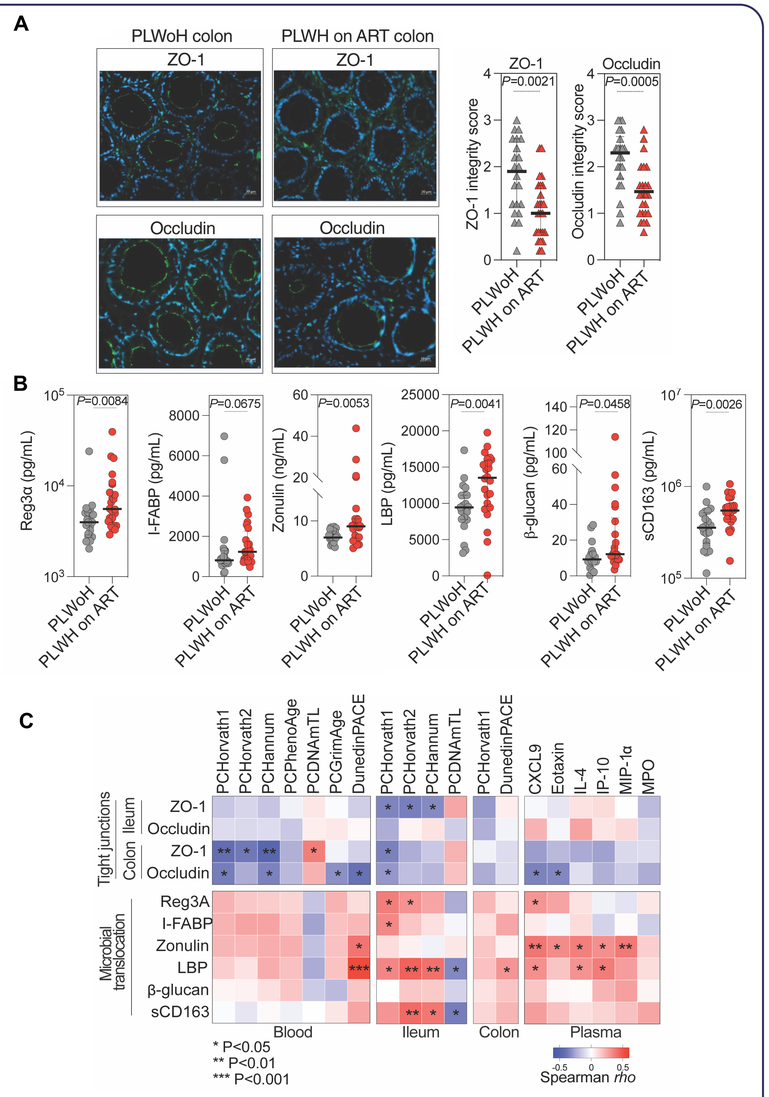


Figure 2. Intestinal permeability and microbial translocation are associated with increased rates of accelerated biological aging. (A) Confocal microscopy of colon biopsies from PLWoH and PLWH on ART depict ZO-1 or occludin expression (green). Nuclei were stained with DAPI (blue). **(B)** Elevated microbial translocation in PLWH on ART plasma compared to PLWoH. **(C)** Spearman's rank correlations heatmap between tight junction integrity and microbial translocation (bottom rows) with accelerated biological aging and inflammation.

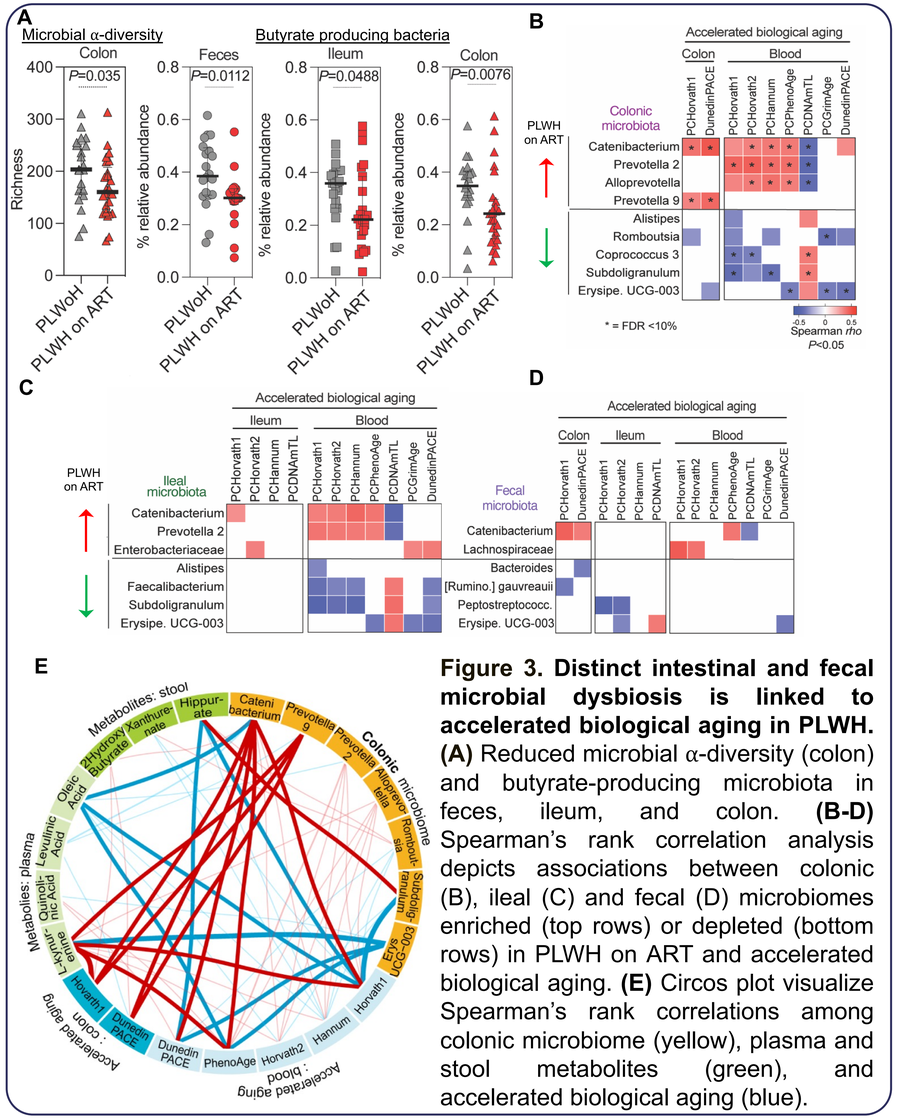


Figure 3. Distinct intestinal and fecal microbial dysbiosis is linked to accelerated biological aging in PLWH. (A) Reduced microbial α-diversity (colon) and butyrate-producing microbiota in feces, ileum, and colon. **(B-D)** Spearman's rank correlation analysis depicts associations between colonic (B), ileal (C) and fecal (D) microbiomes enriched (top rows) or depleted (bottom rows) in PLWH on ART and accelerated biological aging. **(E)** Circos plot visualize Spearman's rank correlations among colonic microbiome (yellow), plasma and stool metabolites (green), and accelerated biological aging (blue).

- PLWH on ART undergo accelerated systemic and intestinal biological aging.
- Disrupted intestinal integrity and microbial translocation associate positively with accelerated biological aging.
- Distinct microbial profiles and gut related metabolites are linked to intestinal and systemic biological aging in PLWH on ART.

Ref: *Singh, S., Giron, L.B., Shaikh, M.W. et al. Distinct intestinal microbial signatures linked to accelerated systemic and intestinal biological aging. Microbiome 12, 31 (2024).*
Author Contact: ssingh@wistar.org, mmohsen@wistar.org