Glycomic Markers of Biological Aging in Trans Women with HIV Versus Cis Men and Cis Women with HIV

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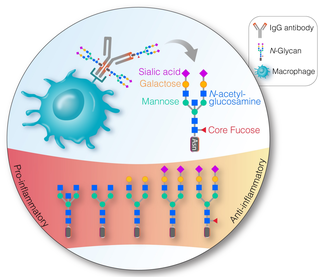
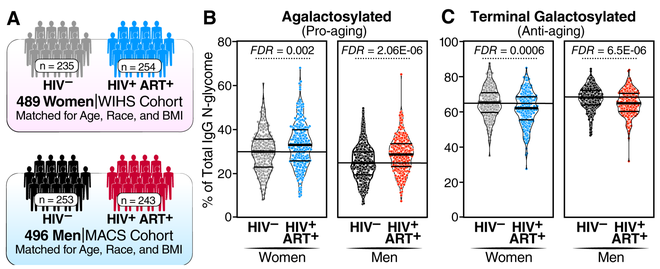
BACKGROUND

- In the general population, host glycomic alterations – including loss of galactose (agalactosylation; measured as high levels of G-terminal ratio and G0 glycan groups) – on circulating IgGs drive inflammation and precede the onset of premature aging-associated diseases.

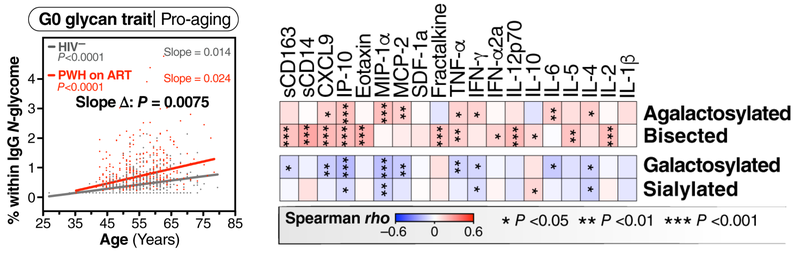


Colomb et al., Current HIV/AIDS Reports, 2019

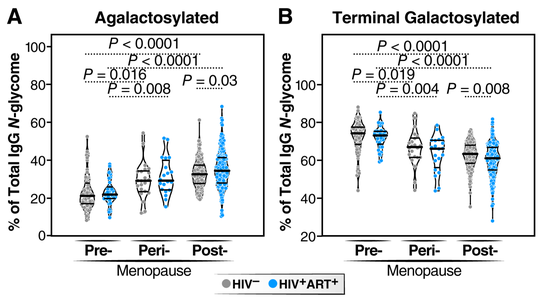
- Living with ART-suppressed HIV is associated with pro-aging and pro-inflammatory IgG glycomic alterations.



- Associations between IgG glycans and age and markers of inflammatory aging..



- Menopause/age induces pro-aging IgG glycomic alterations, specifically agalactosylation.

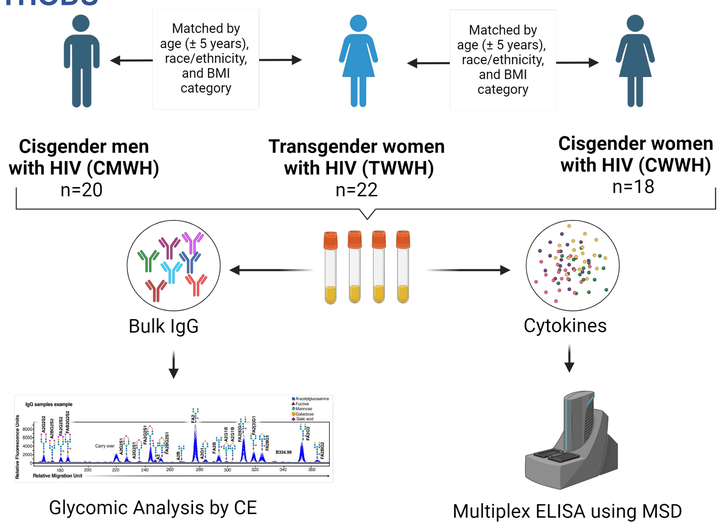


OBJECTIVE

The effects of gender-affirming hormonal therapies (GAHT) on systemic markers of inflammation and aging among transgender women with HIV (TWWH) who are virally suppressed by antiretroviral therapy (ART) are unknown

- **Transgender women with HIV exhibit anti-aging profiles that resemble those of pre-menopausal cisgender women with HIV but differ markedly from matched cis-gender men with HIV.**
- Longitudinal studies are needed to better understand the relationships between gender-affirming hormonal therapies, biological aging, and the risk of developing age-associated diseases. Mechanistic investigation is also warranted to explore the potential impact of sex hormones on aging processes.

METHODS



All TWWH were ART suppressed, were on estrogen, 50% were on spironolactone/antiandrogen, and 32% had testosterone levels <50ng/dL.

RESULTS

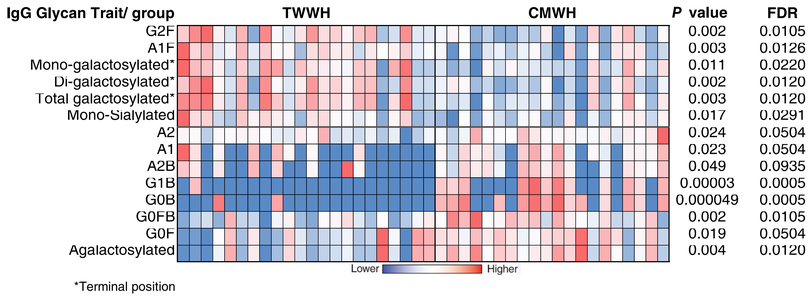


Figure 1. IgG glycan traits are different between TWWH and CMWH. While we observed no differences in levels of inflammation markers between TWWH and CMWH, there were significant differences in levels of several IgG glycomic markers in the two groups.

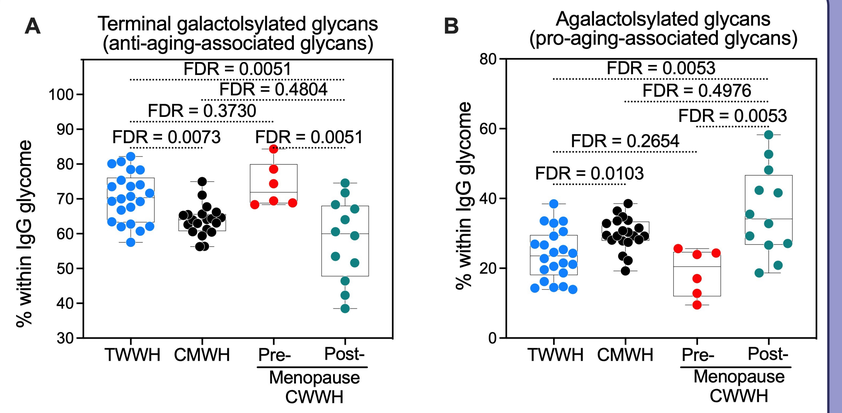


Figure 2. Levels of galactose were higher in TWWH compared to CMWH. (A) Several galactosylated glycans, which are linked to younger chronological and biological age, were higher in TWWH compared to CMWH. Conversely, several agalactosylated glycans, linked to older age, were lower in TWWH compared to CMWH **(B)**. These effects were consistent among TWWH, regardless of whether they had testosterone suppression or not. The anti-aging glycomic profiles of TWWH resembled those of pre-menopausal CWWH, while the pro-aging profiles of CMWH resembled those of post-menopausal CWWH

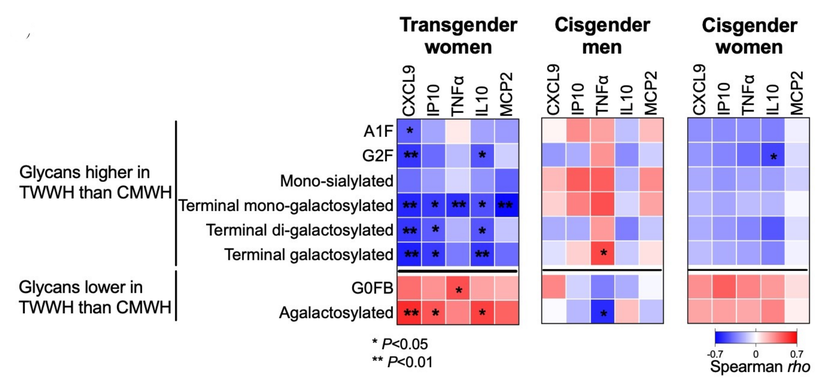


Figure 3. Correlation between IgG glycomic traits and inflammatory markers. The anti-aging profile, enriched in TWWH, was correlated with lower levels of several inflammation markers, including CXCL9, TNFα, and IP10, while the pro-aging profile, lower in TWWH, was associated with higher inflammation, especially in TWWH.

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