Glycomic Biomarkers of Biological Aging Are Altered During Suppressed HIV Infection

260

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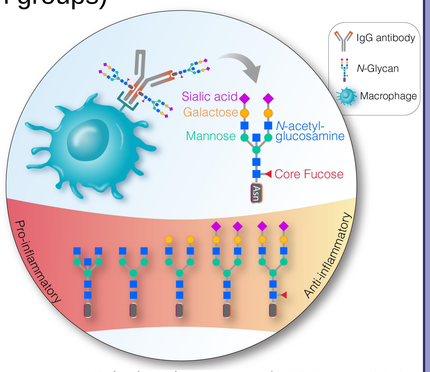
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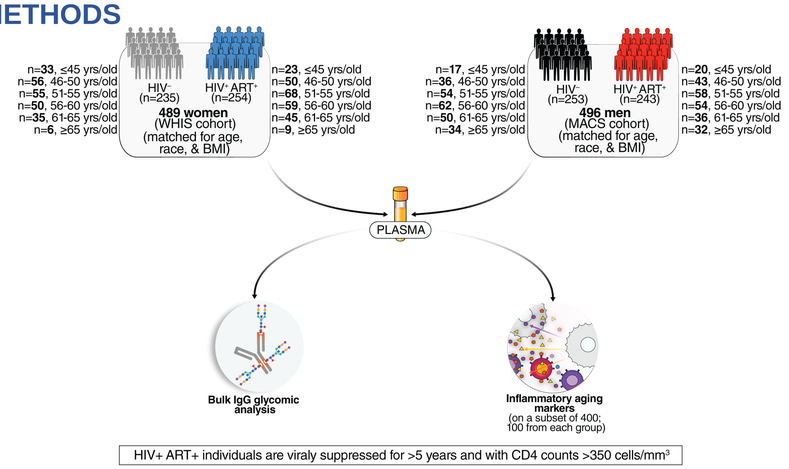
BACKGROUND

- 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.
- However, the impact of antiretroviral therapy (ART)-suppressed HIV infection on these glycomic biomarkers of biological aging is unknown.



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

METHODS



HIV+ ART+ individuals are viraly suppressed for >5 years and with CD4 counts >350 cells/mm^3

RESULTS

Table 1: Demographical characteristics of study participants. Characteristics of the 988 participants from the MACS/WIHS Combined Cohort Study.

		Men				Women			
		HIV Negative		HIV Positive		HIV Negative		HIV Positive	
		n (%)	Median, IQR	n (%)	Median, IQR	n (%)	Median, IQR	n (%)	Median, IQR
N		253	57 (10)	243	56 (11)	235	53 (10)	254	55(9)
Age (years)	≤45	17 (6.7%)	44 (2)	20 (8.2%)	44 (2.5)	33 (14.0%)	43 (5)	23 (9.1%)	44 (4)
	46-50	36 (6.7%)	48 (3)	43 (17.7%)	47 (3)	56 (23.8%)	48 (2)	50 (19.7%)	48 (2)
	51-55	54 (6.7%)	53 (3)	58 (23.9%)	53 (2)	55 (23.4%)	53 (2)	68 (26.8%)	53 (2)
	56-60	63 (6.7%)	58 (3)	54 (22.2%)	58 (2)	50 (21.3%)	58 (3)	59 (23.2%)	58 (3)
	61-65	49 (6.7%)	62 (3)	36 (14.8%)	63 (2)	35 (14.9%)	63 (3)	45 (17.7%)	62 (3)
	>66	34 (6.7%)	69 (4.5)	32 (13.2%)	68.5 (4)	6 (2.6%)	69 (6)	9 (3.5%)	71 (6)
Race	White, non-Hispanic	166 (65.6%)	-	128 (53%)	-	22 (9.4%)	-	30 (11.8%)	-
	White, Hispanic	11 (4.3%)	-	14 (6%)	-	12 (5.1%)	-	19 (7.5%)	-
	Black, non-Hispanic	68 (26.9%)	-	78 (32%)	-	175 (74.5%)	-	169 (66.5%)	-
	Black, Hispanic	2 (0.8%)	-	4 (2%)	-	4 (1.7%)	-	5 (2%)	-
	American Indian or Alaskan Native	1 (0.4%)	-	1 (0%)	-	1 (0.4%)	-	1 (0.4%)	-
	Asian or Pacific Islander	1 (0.4%)	-	1 (0%)	-	0 (0%)	-	0 (0%)	-
	Other	3 (1.2%)	-	2 (1%)	-	1 (0.4%)	-	1 (0.4%)	-
	Other Hispanic	1 (0.4%)	-	15 (6%)	-	20 (8.5%)	-	29 (11.4%)	-
BMI			26.2 (5.25)		25.5 (5.85)		30.5 (9.7)		30.3 (9.5)
Diabetes	No	196 (77.5%)	-	191 (79%)	-	162 (69.9%)	-	181 (71.3%)	-
	Yes	30 (11.9%)	-	34 (14%)	-	73 (31.1%)	-	73 (28.7%)	-
	Insufficient data	27 (10.7%)	-	18 (7%)	-	0 (0%)	-	0 (0%)	-
CD4 Count (cells/mm3)		-	-		698 (364)	-	-	-	725.5 (381.75)
Viral Load (HIV copies/ml)		-	-	-	<50	-	-	-	<50
Nadir CD4 (cells/mm^3)		-	-	-	306.5 (234)	-	-	-	216 (213.75)

Sex-dependent premature-aging-associated glycomic dysregulation is accelerated during ART+ HIV infection and is associated with inflammatory aging (**inflammaging**) and subclinical atherosclerosis.

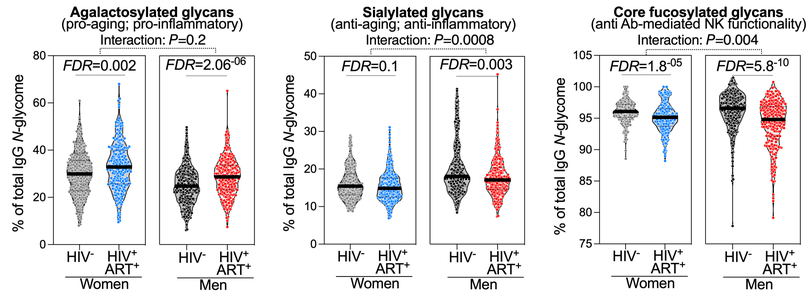


Figure 1. ART-treated HIV infection is associated with sex-dependent glycomic alterations. Induction of the pro-inflammatory agalactosylated glycans in both women and men, a reduction of the anti-inflammatory sialylated glycans in men, and a reduction of the fucosylated glycans in both women and men but more reduction in men than women.

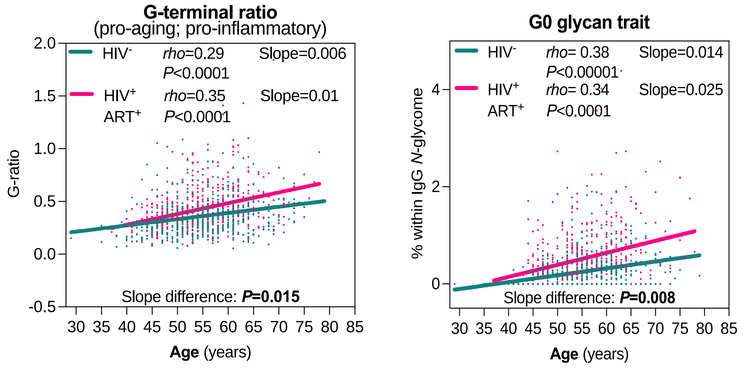


Figure 2: ART-suppressed HIV infection accelerated the pace of age-associated agalactosylation. Spearman correlations showing a difference in the slopes over time in the accumulation of the pro-inflammatory agalactosylated glycans in HIV- and HIV+ART+ individuals.

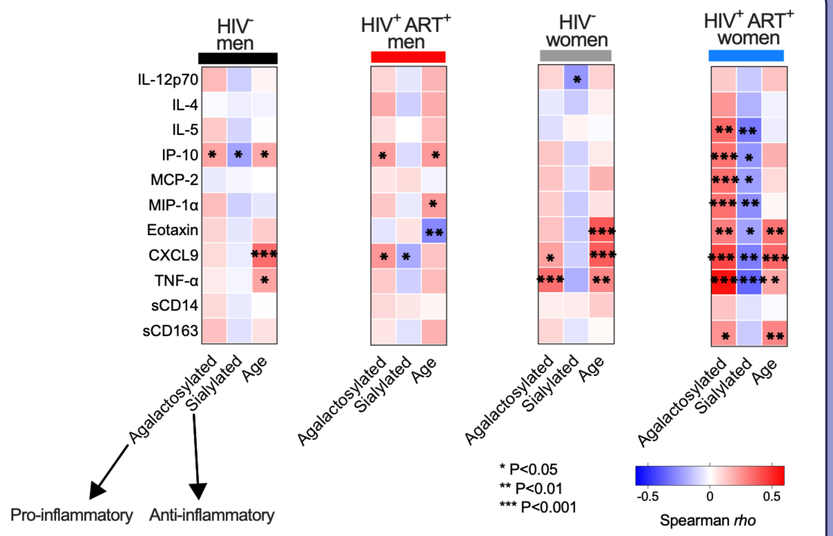


Figure 3. Aglycosylated glycans correlate with inflammatory markers of biological aging. HIV-associated IgG agalactosylation correlated with higher inflammatory markers of aging, such as CXCL9 and IP-10, especially in HIV+ ART+ women.

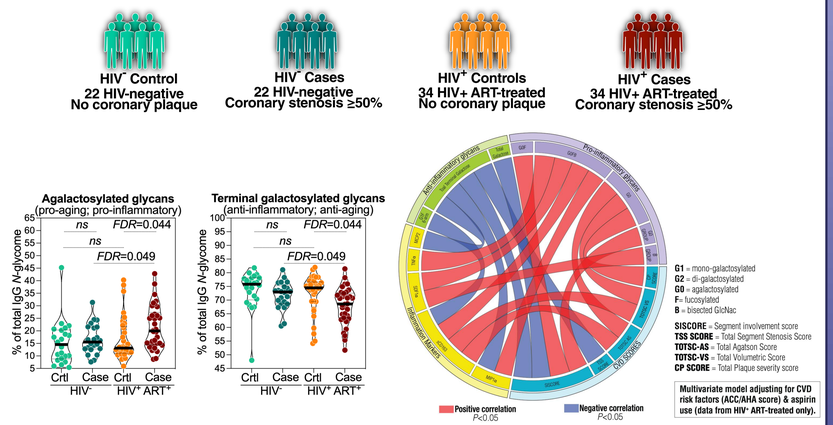


Figure 4. Agalactosylated glycans were higher in HIV+ men with coronary stenosis compared to controls. In a subset of the MACS cohort, we analyzed the IgG glycomes of 112 samples from HIV- and HIV+ ART+ male cases and controls; cases had coronary stenosis ≥50% in ≥1 coronary segments, and controls had no coronary plaque (by CT angiography). Pro-inflammatory agalactosylated glycans correlate with subclinical atherosclerosis during ART-suppressed HIV infection in men.

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