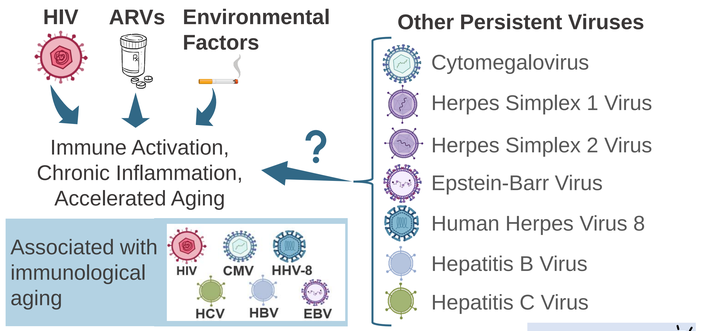
Non-HIV Chronic/Latent Viruses and Immune Aging: Sex Effects Comparable to Those of HIV and CMV

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Introduction



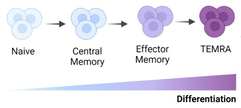
CD4⁺ T-cell **CD8⁺ T-cell** **CD4:CD8 ratio (usually ~1-3)**

- ↓ ratio associated with poorer health outcomes

"proliferative" CD8⁺CD28⁺ "senescent" CD8⁺CD28⁻

CD8⁺CD28⁺:CD28⁻ ratio

- ↓ ratio indicates perturbed function
- "proliferative:senescent" ratio



Naïve:Non-Naïve CD8 T-cell ratio

- ↓ ratio indicates "aged" phenotype

People living with HIV (PLWH) experience accelerated aging

Women living with HIV have shorter life expectancy than men living with HIV and HIV-negative women

Aim

To determine associations between sex, HIV status, number of chronic/latent viral infections, and markers of immune aging in people living with HIV and HIV-negative controls enrolled in the CARMA cohort.

Methods



Thaw live frozen peripheral blood mononuclear cells

Stain for immune markers of interest

Flow Cytometry (BD Cytoflex)

Results

Table 1: Demographic characteristics of study participants in the CARMA cohort

*NHV: Non-HIV Viruses *ACB: African, Carribean, Black	Female			Male			M vs. F
	HIV+ (n=103)	**HIV-** (n=103)	p-value	**HIV+** (n=70)	**HIV-** (n=74)	p-value	p-value
Age (years), median (range)	38 (2-72)	37 (2-76)	0.98	31 (3-70)	31 (1-74)	0.97	0.09
Tobacco Smoking (n) current / past / never	29/16 /58	19/15/69	0.22	22/11/37	25/10/39	0.9	0.15
Ethnicity (n) White / ACB* / Indigenous /	42/36/19/6	53/20/19/11	0.16	25/20/12/13	33/18/10 /13	0.57	0.06
Number of NHV*, median [IQR]	3 [2-4]	2 [1-3]	<0.0001	3 [2-4]	2 [1-2]	<0.0001	<0.0001
Aging Markers, median [IQR]							
CD4:CD8 Ratio	1.1 [0.7-1.5]	2.3 [1.7-3.5]	<0.0001	0.9 [0.5-1.4]	1.7 [1.4-2.4]	<0.0001	<0.0001
CD8, CD28+/- Ratio	1.4 [0.8-3.0]	2.9 [1.4-5.5]	<0.0001	1.3 [0.7-3.1]	2.7 [1.4-6.0]	<0.0001	0.56
CD4 Naïve:Effector Ratio	0.4 [0.2-1.0]	0.6 [0.2-0.9]	0.95	0.4 [0.2-0.9]	0.5 [0.2-1.5]	0.15	0.18
CD8 Naïve:Effector Ratio	0.8 [0.5-1.5]	0.8 [0.4-1.3]	0.92	0.9 [0.4-1.4]	0.6 [0.2-1.3]	0.14	0.19

Female sex is associated with more favorable immune cell ratios, with effect sizes comparable to those of HIV and CMV, despite a higher burden of non-HIV viruses compared to males

Results

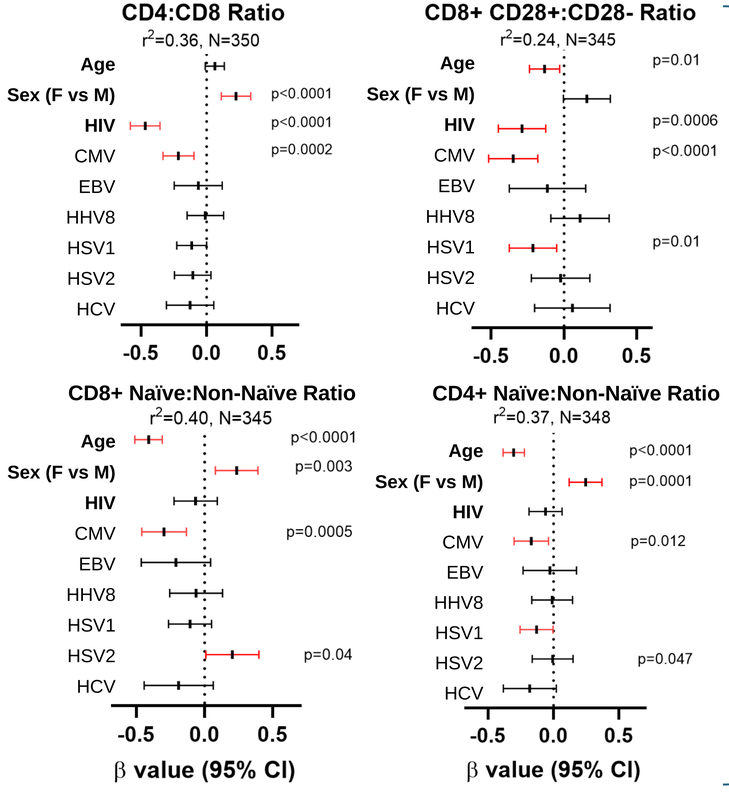


Figure 1: Multivariable linear regression models of markers of immune aging. Models adjust for ethnicity and tobacco smoking status. β:Effect size, CI: Confidence Interval

Male sex, HIV and CMV are independently associated with a lower CD4:CD8 ratio

↑ age, HIV, CMV and HSV1 are independently associated with a lower CD8, CD28+/- ratio

↑ age, CMV are associated with a decreased CD8 Naïve: Effector ratio, while being female and having HSV2 are associated with an increase

↑ age, male sex, CMV and HSV1 are associated with a decreased CD4 Naïve: Effector ratio

Results

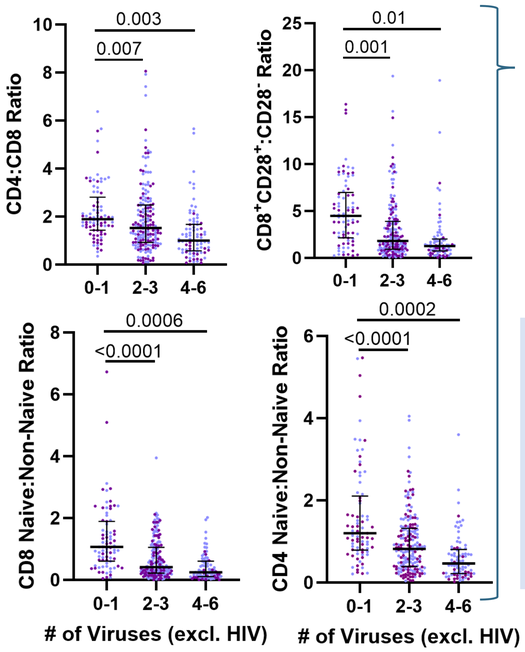


Figure 2: Associations between number non-HIV viruses and markers of immune aging. Lighter and dark purple dots represent females and males, respectively. p-values adjusted for age, sex, HIV, smoking status and ethnicity

An increasing number of non-HIV viruses are independently associated with a decrease in all markers of immune aging measured

Significance

- Viruses that are typically asymptomatic, such as CMV, HSV1 and HSV2 likely to contribute to immune aging
- Although female participants have more non-HIV viruses, they showed healthier immune cell profiles for the markers studied
- We found sex-based differences in immune cell ratios that are similar in effect size to those of HIV and CMV
- We will investigate specific the associations between specific virus combinations and immune aging (CMV + HSV1/2, CMV + HIV)

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