

CD4 T cell counts are inversely correlated with anti-cluster A antibodies in antiretroviral therapy-treated PLWH

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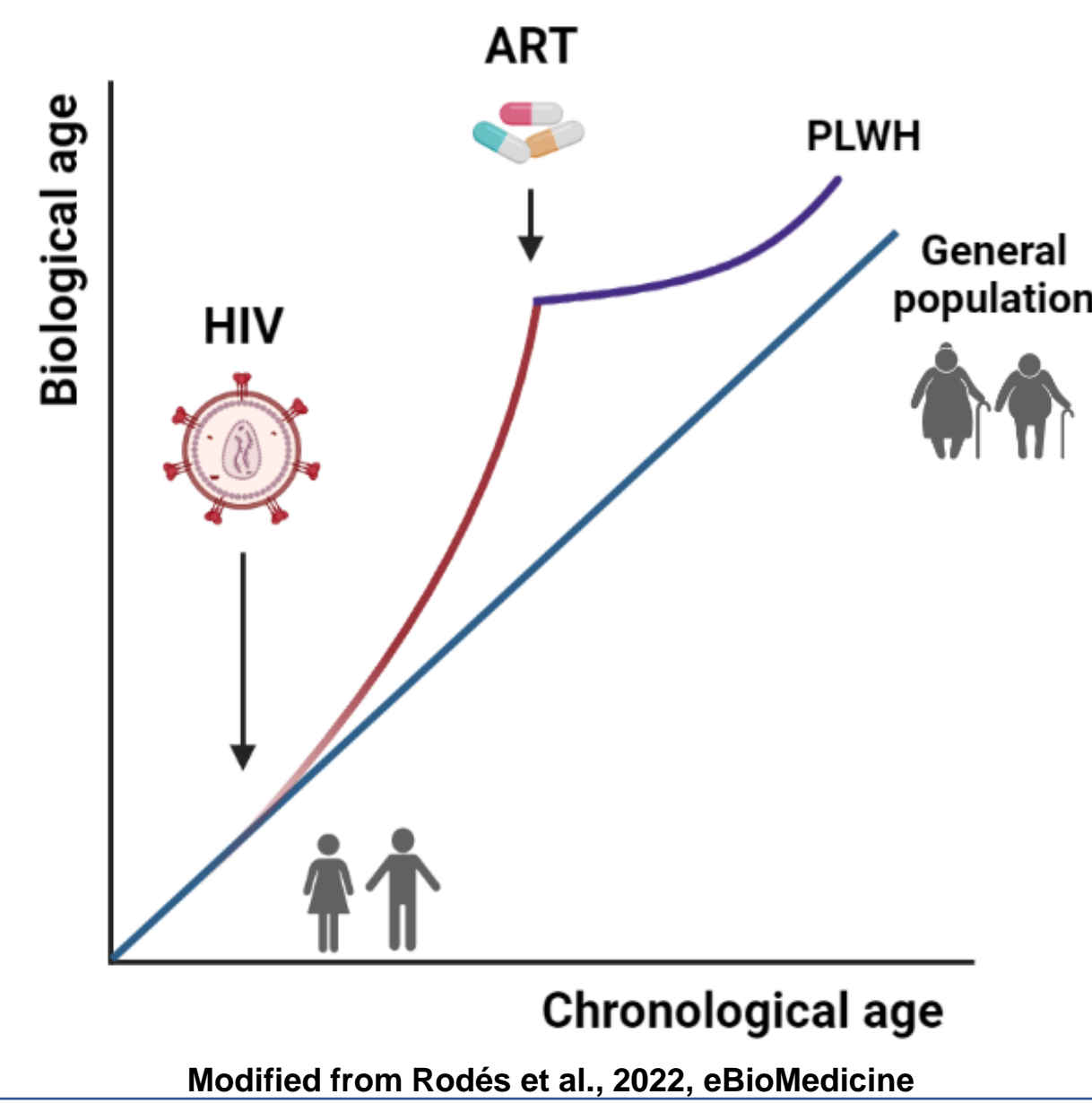
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BACKGROUND

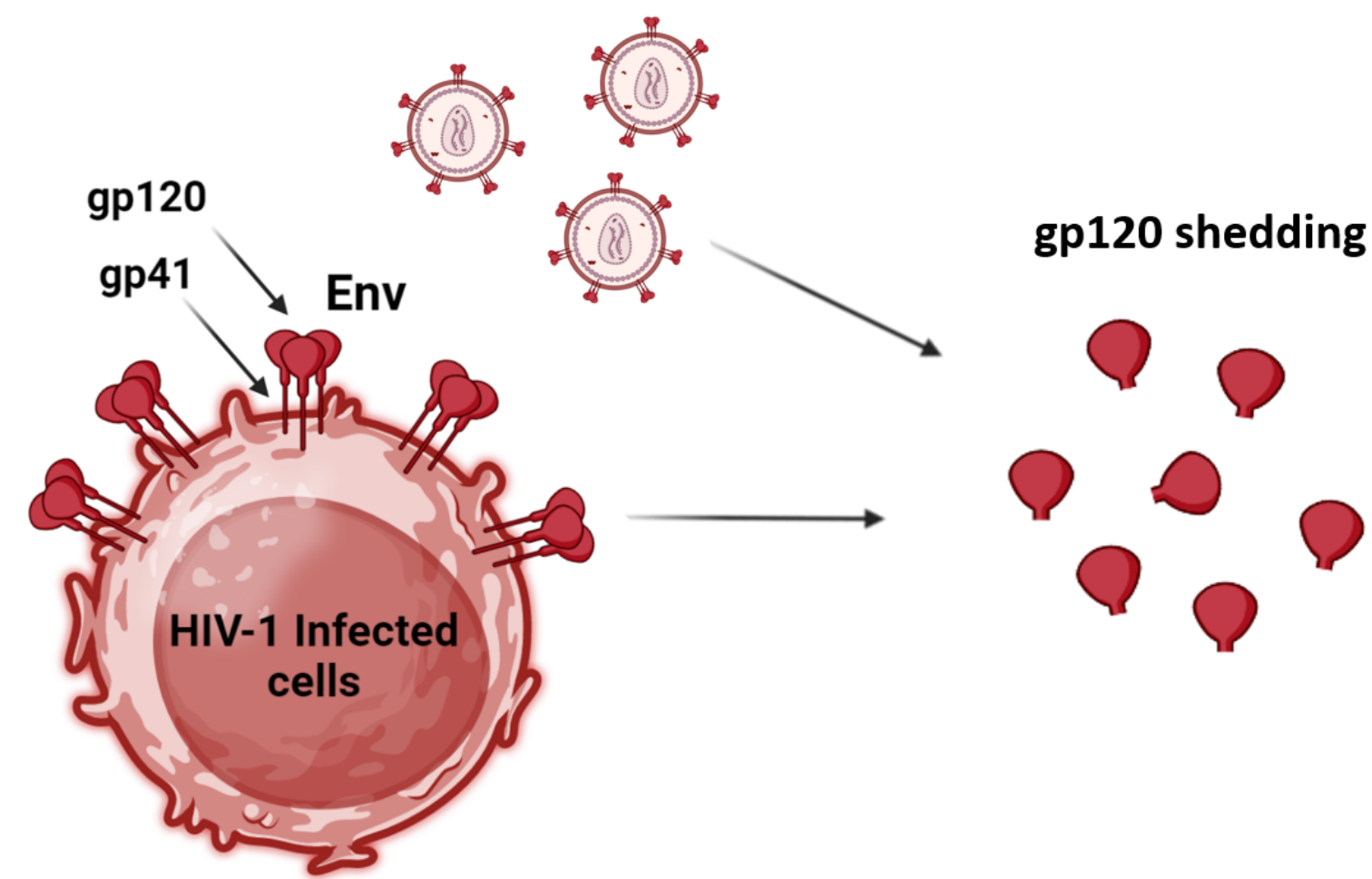
Despite antiretroviral therapy (ART), people living with HIV (PLWH) show signs of chronic immune activation and dysfunction.

PLWH have higher incidence of :

- Cardiovascular events
- Kidney impairments
- Cognitive disorders
- Cancer
- Persistent chronic inflammation

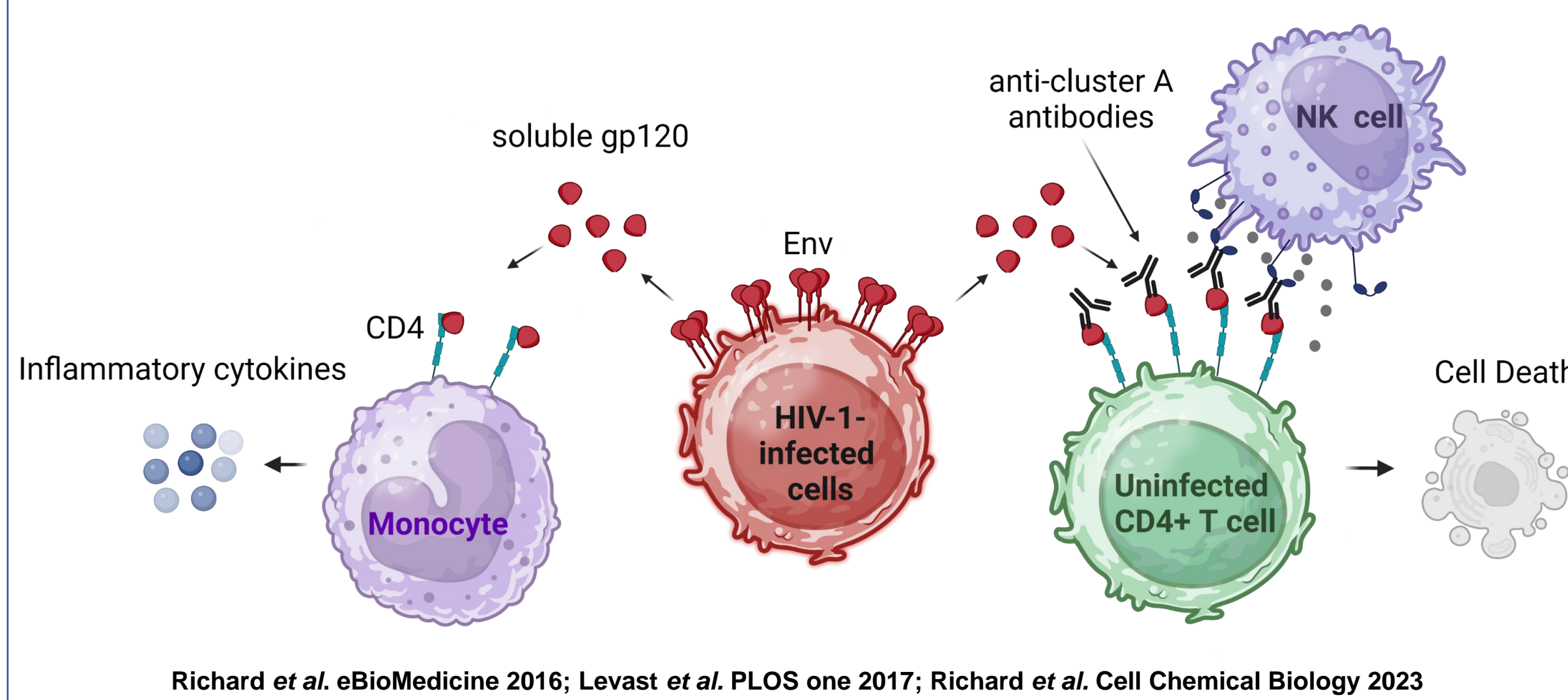


gp120 sheds from infected cells and viral particles

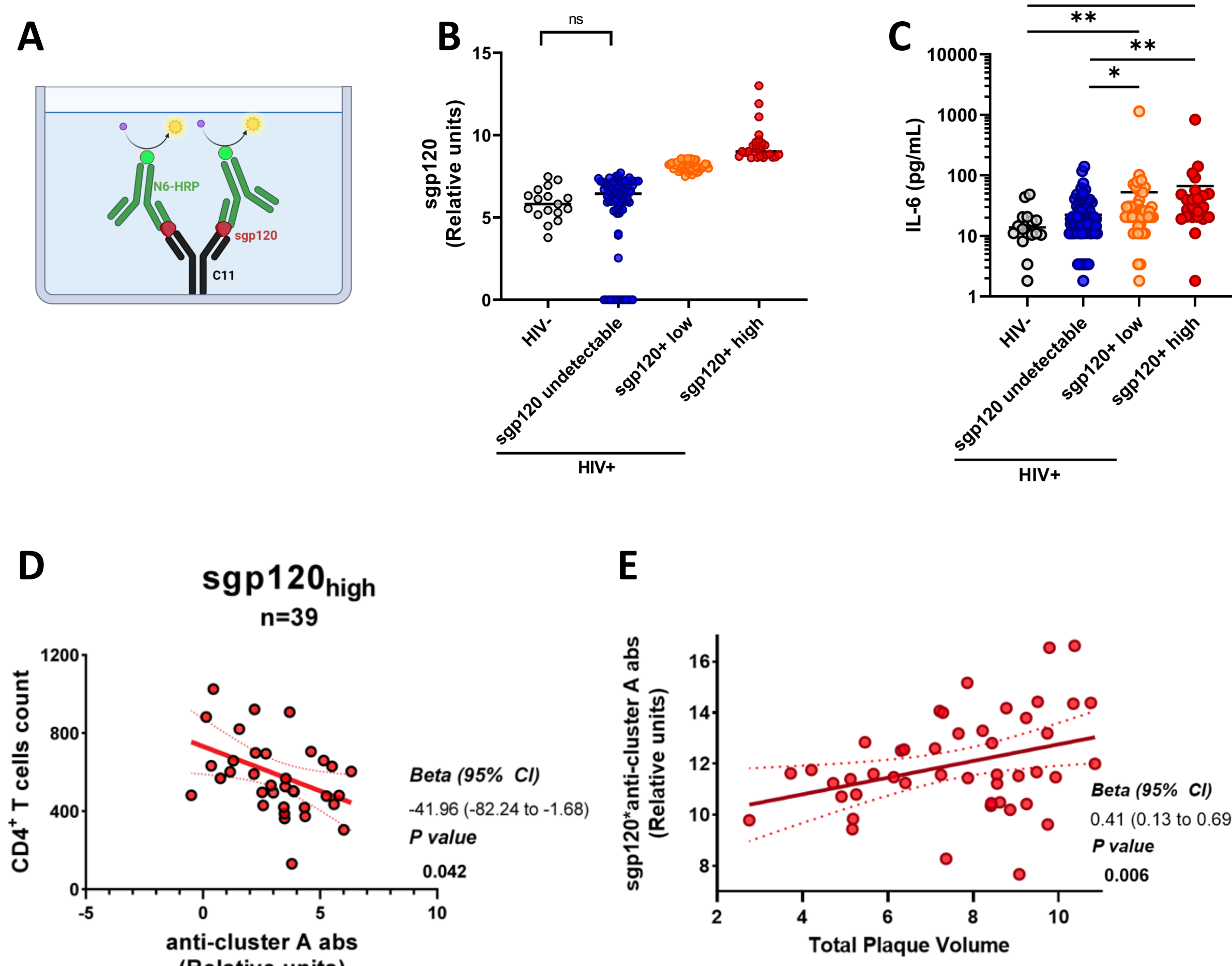


Soluble gp120 has immunomodulatory properties *in vitro*

1. Induces the release of proinflammatory cytokines
2. Sensitizes uninfected bystander cells to ADCC



Soluble gp120 is immunomodulatory in PLWH with undetectable viral load



Benlarbi et al. The Journal of Infectious Diseases 2024

RESULTS

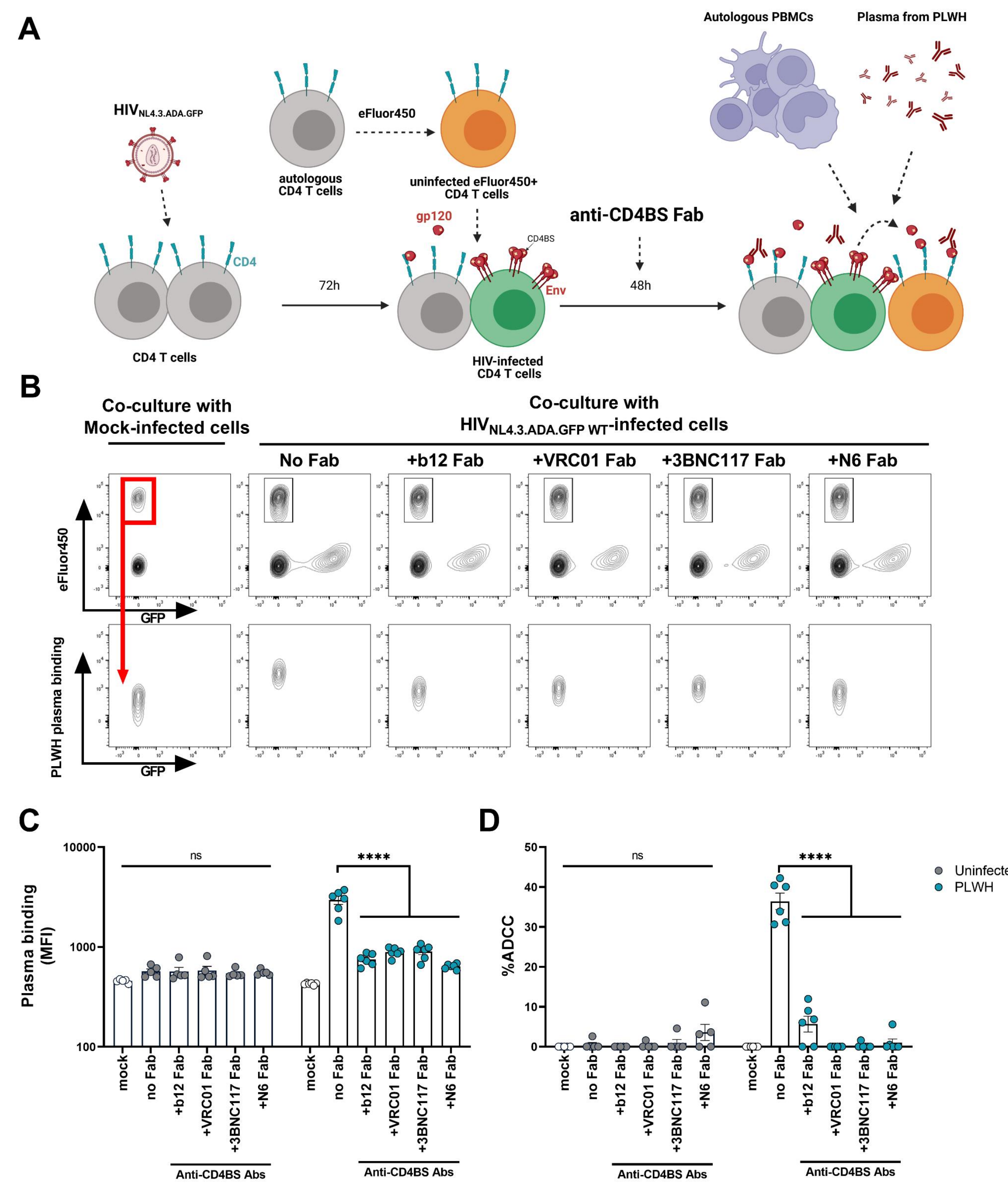


Figure 1. Uninfected bystander CD4⁺ T cells are eliminated by ADCC responses mediated by plasma from PLWH.

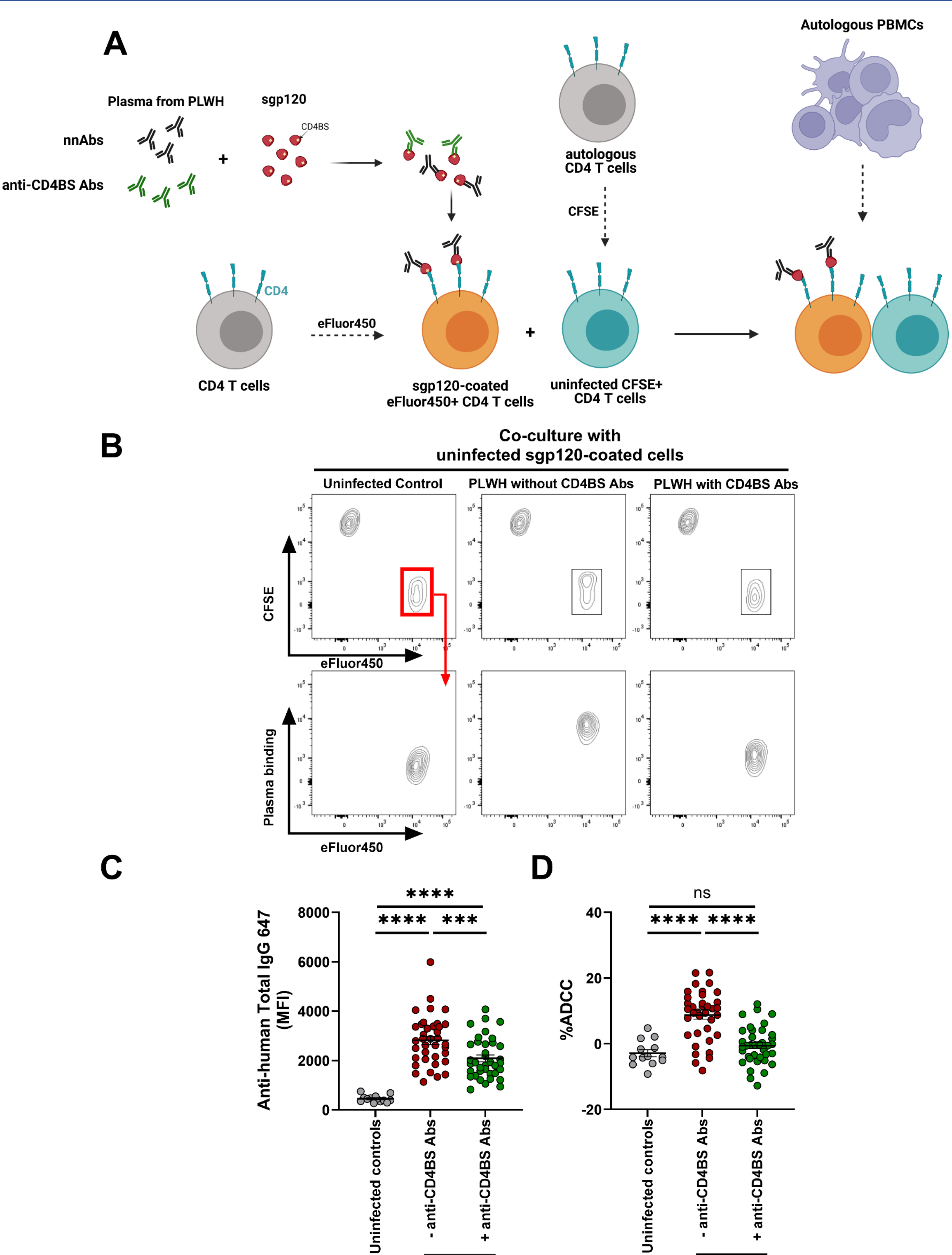


Figure 2. Plasma from PLWH with anti-CD4BS Abs protect uninfected bystander CD4⁺ T cells from ADCC responses.

	CHACS cohort	PRESTIGIO Cohort	NIH cohort
Number of participants	386	80	66
Age (mean, SD) (min-max)	55.8 (7.7) 30-79	56.7 (9.6) 23-77	57.4 (11.1) 21-79
Male sex (n, %)	347 (89.9)	58 (72.5)	57 (86.4)
Ethnicity (n, %)			
Caucasian	317 (82.3)	77 (91.3)	45 (68.2)
Black	32 (8.3)	2 (2.5)	16 (24.2)
Hispanic	16 (4.1)	1 (1.2)	0 (0)
Other	18 (4.6)	0 (0)	2 (4.6)
Undisclosed	3 (0.7)	0 (0)	3 (3)
CD4 count (mean, SD) Min-max	615.4 (251) 29-1459	594 (376) 5-1942	592.4 (270) 81-1515
CD4:CD8 ratio (mean, SD)	0.96 (0.53)	0.68 (0.51)	1.04 (0.56)
Nadir CD4 (mean, SD) Min-max	237 (168) 4-880	118 (125) 1-878	230 (181) 1-878
HIV duration (mean, SD)	18 (8)	30 (6)	N/A
ARV duration (mean, SD)	14 (7)	26 (5)	20 (7)
Viral load below clinical limit of detection (n, %)	386 (100)	60 (75)	60 (91)

Table 1. Characteristics of three cohorts of PLWH.

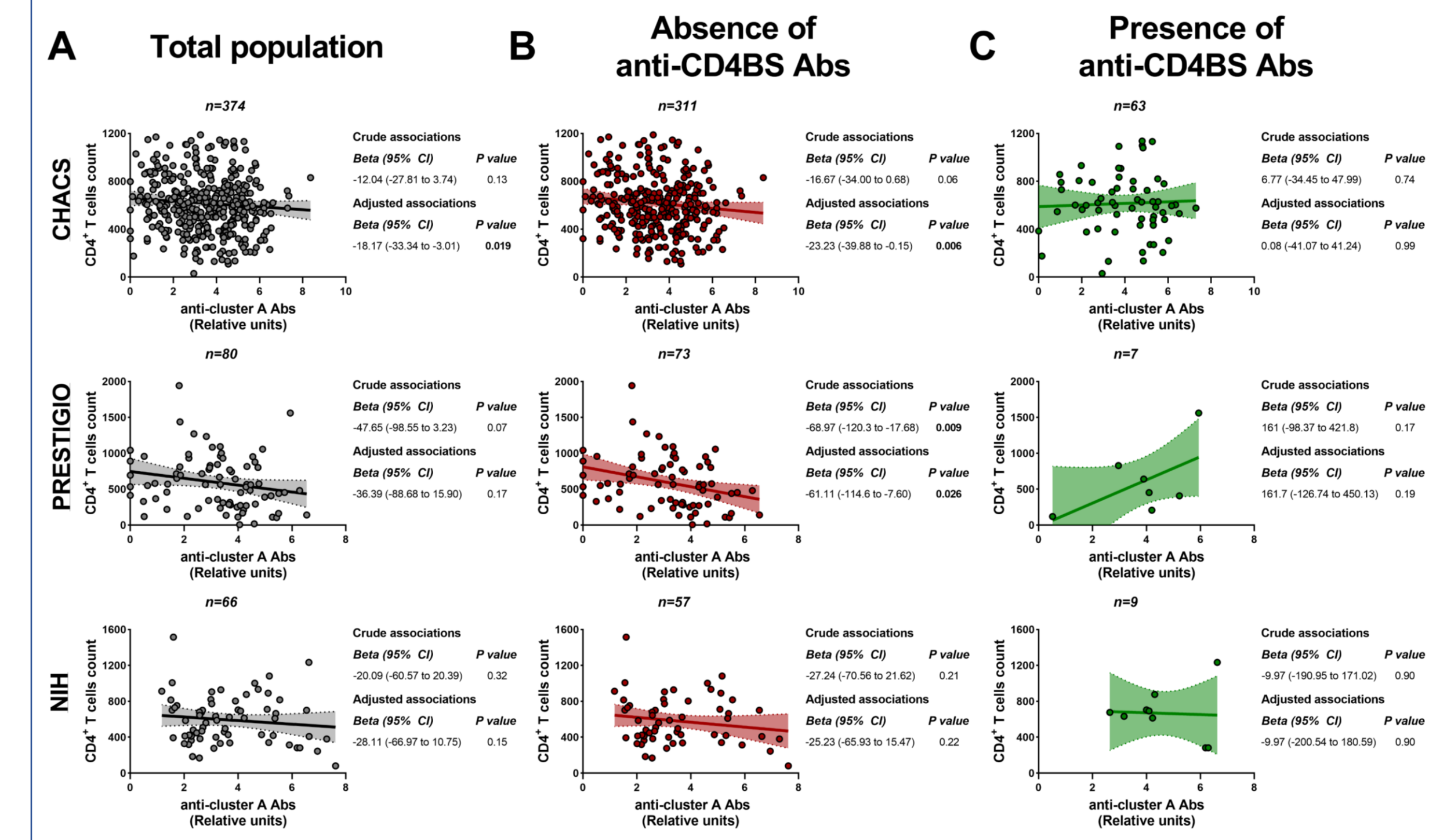


Figure 3. Association between CD4⁺ T cells count and anti-cluster A abs in the absence or presence of anti-CD4BS Abs in PLWH.

	n	Beta*, 95% CI	P-value
Overall**	520	-23.85 [-37.75 to -9.95]	0.001
Absence of anti-CD4BS Abs	441	-31.91 [-46.97 to -16.84]	<0.001
Presence of anti-CD4BS Abs	79	13.10 [-26.35 to 52.55]	0.51

*beta coefficients represent the predicted change in CD4 count for each increase of 1-log₂ in levels of anti-cluster A antibodies
 **12 participants did not have information on CD4 counts and were excluded from the analysis
 All models are adjusted for age, sex, duration of antiretroviral therapy and nadir CD4

Table 2. Pooled adjusted associations between anti-cluster A Abs and CD4 count, overall and stratified by the absence or presence of anti-CD4BS Abs.

CONCLUSION

- Anti-cluster A Abs are associated with lower CD4 counts in PLWH
- The presence of anti-CD4BS Abs in PLWH plasma abrogates this association
- Anti-CD4BS Abs block sgp120-mediated CD4 T+ cell killing

Our results suggest that blocking gp120-CD4 interaction, beyond the benefit of blocking viral entry, could lead to novel therapeutic approaches to tackle residual immune dysfunction in ART-treated PLWH.

ACKNOWLEDGEMENTS

