Impact of ART initiation on HIV-1 soluble gp120 levels and CD4 counts in PLWH

352

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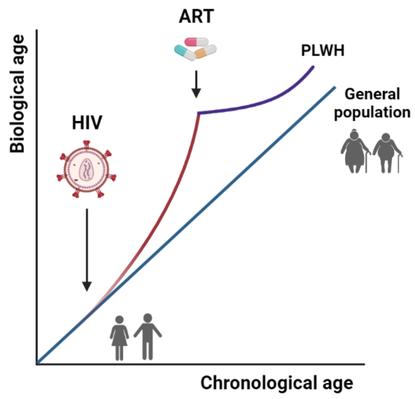
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BACKGROUND

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

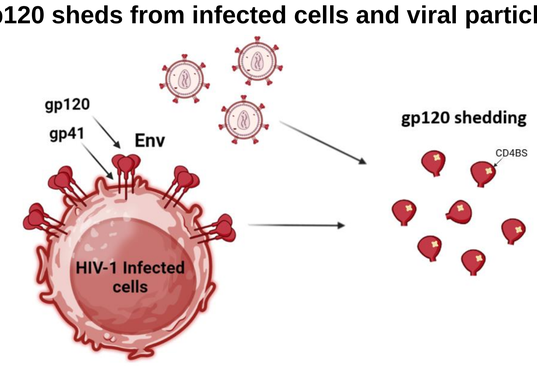
PLWH have higher incidence of :

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

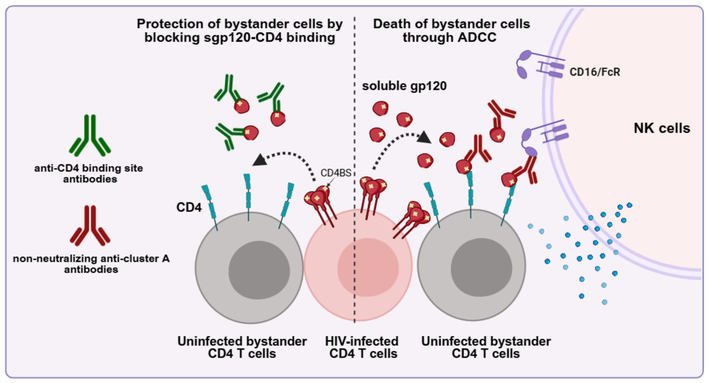


Modified from Rodés et al., 2022, eBioMedicine

gp120 sheds from infected cells and viral particles

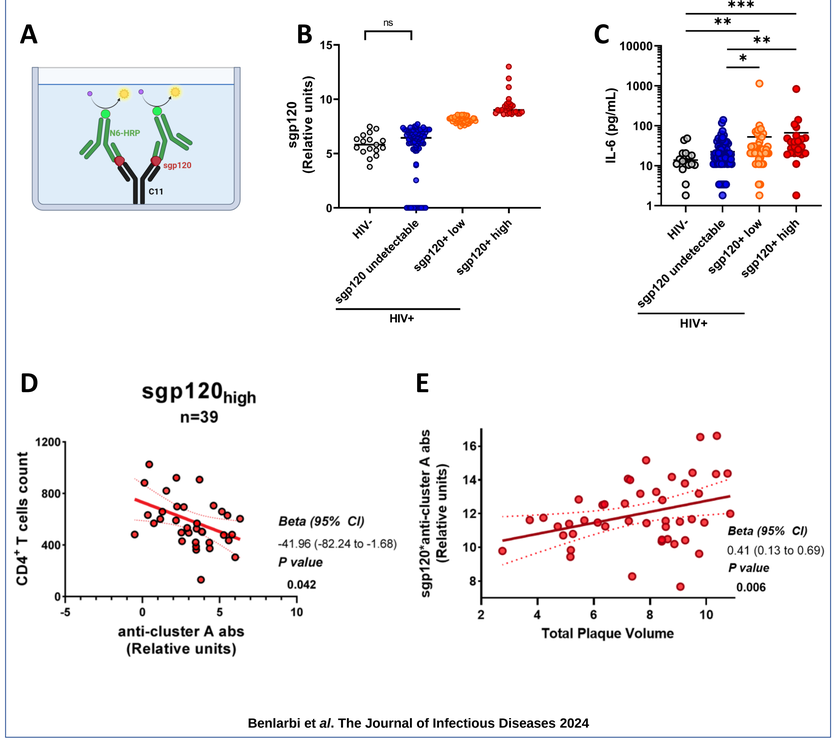


Soluble gp120 has immunomodulatory properties *in vitro*



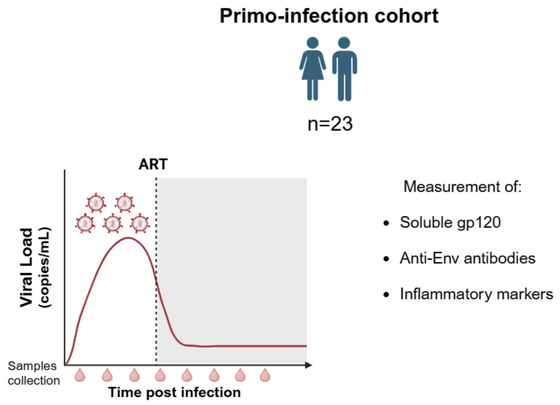
Richard *et al*. eBioMedicine 2016; Richard *et al.* Cell Chemical Biology 2023; Benlarbi et *al.* MedRxiv 2025

Soluble gp120 is immunomodulatory in PLWH with undetectable viral load



Benlarbi et *al*. The Journal of Infectious Diseases 2024

RESULTS



Age, mean (IQR), years	36.78 (22-56)
Male sex, (%)	22 (95.6)
Absolute CD4 counts, mean (SD), cells/mL	557.4 (207)
Absolute CD8 counts, mean (SD), cells/mL	1119 (580)
CD4/CD8 ratio, mean (SD)	0.64 (0.54)
Time before ART initiation, mean (IQR), years	1.41 (0.05-4.02)
Time on ART, mean (IQR), years	4.15 (2.7-4.9)
Viral Load, mean (SD), copies/mL	5 679 323 (26 848 285)

Table 1. Baseline characteristics of longitudinal samples from primo-infection cohort.

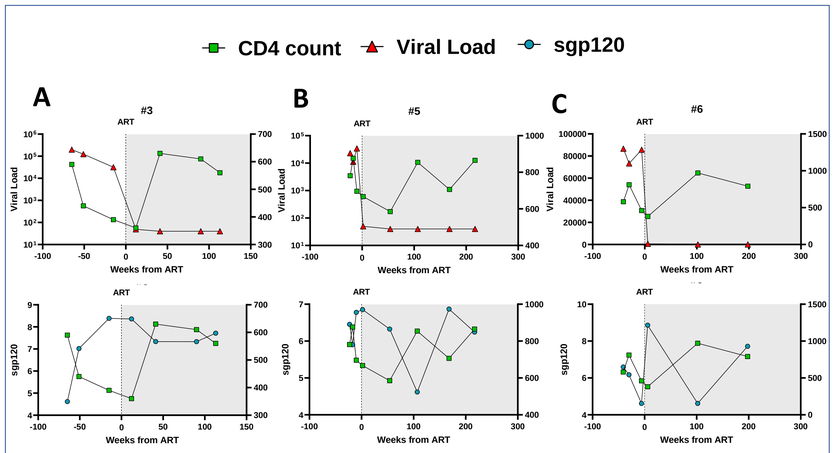


Figure 1. Longitudinal evaluation of CD4 count, viremia and sgp120 in three participants.

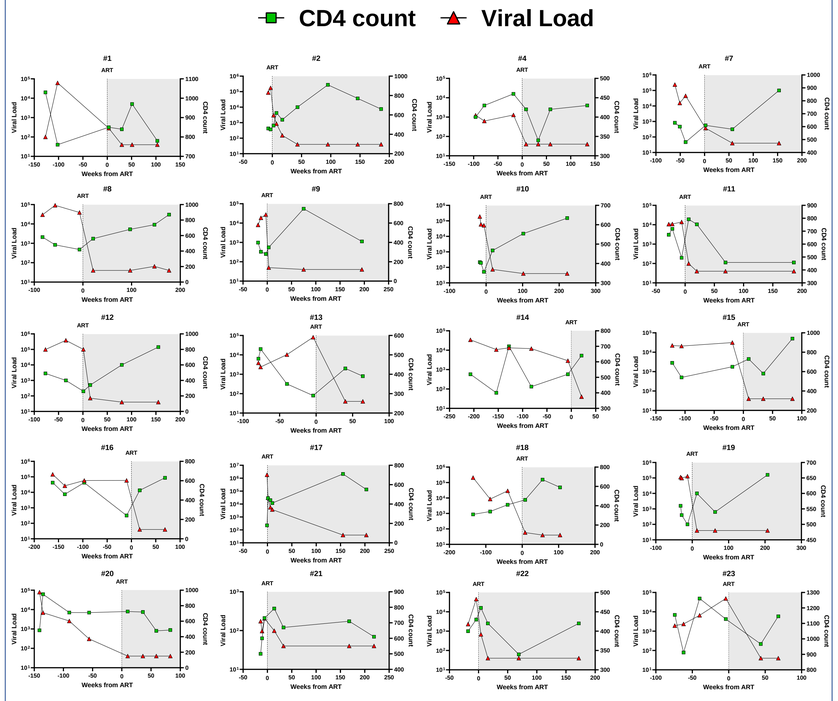


Figure 2. Viral Load and CD4⁺ T cells before and after ART initiation in 20 PLWH.

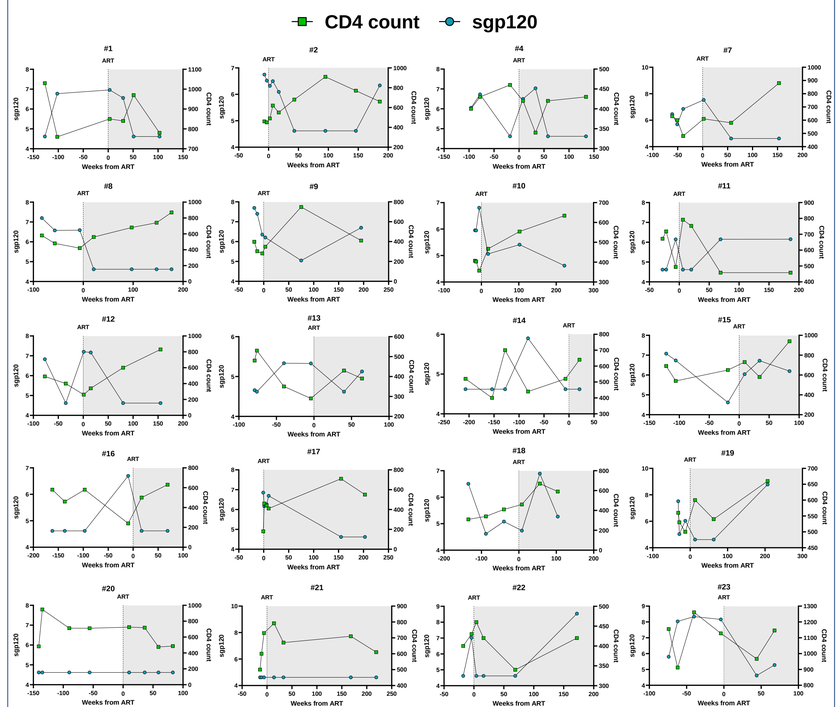


Figure 3. Levels of sgp120 and CD4⁺ T cells before and after ART initiation in 20 PLWH.

	Beta	P-value	P-value for interaction
CD4 count[a]	-46.91 (-75.17 to -18.65)	**0.001**	NA
Stratified by absence/presence of anti-CD4 binding site Abs			
Without anti-CD4BS Abs CD4 count[b]	- 57.38 (-89.63 to -25.13)	**<0.001**	0.18
With anti-CD4BS Abs CD4 count[c]	-14.86 (-69.34 to 39.62)	0.59	
Stratified by ART status			
Pre ART visits CD4 count	-27.10 (-73.93 to 17.94)	0.23	0.38
Post ART visits CD4 count	- 52.17 (-84.64 to -19.70)	**0.002**	

[a]predicted change for CD4 levels is presented for each 100 unit increase in levels of sgp120 (measured in relative units)
[b]absence of anti-CD4BS Abs were noted in 117 samples from 22 participants
[c]anti-CD4BS Abs were present in 32 samples from 8 distinct individuals

Table 2. Association between sgp120 and CD4⁺ T cells count stratified by the absence or presence of anti-CD4BS Abs and before or after ART initiation in PLWH.

CONCLUSIONS

- **sgp120 can be detected after ART initiation, despite viral load suppression.**
- **In Post ART visits, sgp120 is negatively associated with CD4 counts.**
- **CD4 counts in participants with anti-CD4BS antibodies were not affected by sgp120.**

➢ **Altogether, our results raise the intriguing possibility that therapeutic approaches targeting sgp120 could provide immune benefits and mitigate HIV-associated immune dysfunction in PLWH.**

ACKNOWLEDGEMENTS

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Schematics prepared with BioRender (Biorender.com)