Control of HIV infection is associated with enhanced CD8 T cell functionality during consecutive analytical treatment interruptions

Gabriel Duette

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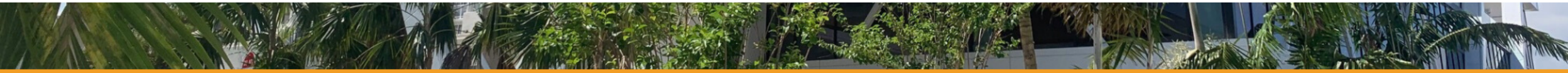
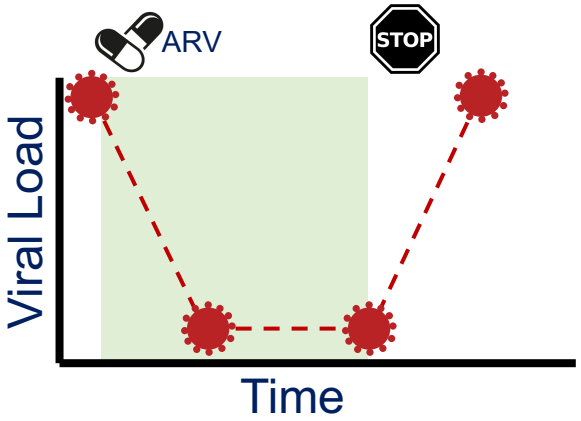


CONFLICTS OF INTEREST

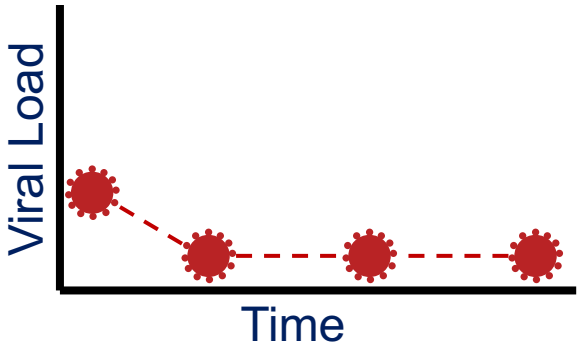
- *No conflicts of interest to declare*

Virological control in People Living with HIV

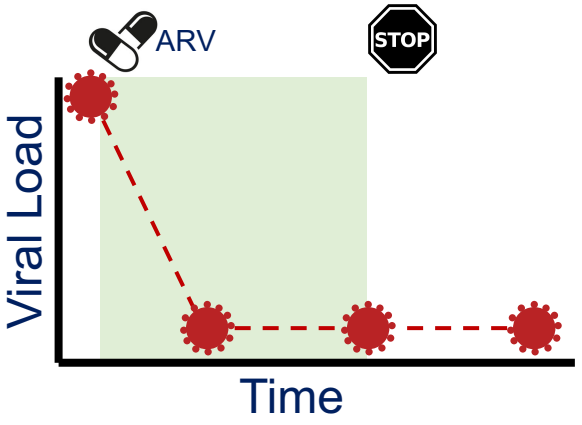
Non-controllers



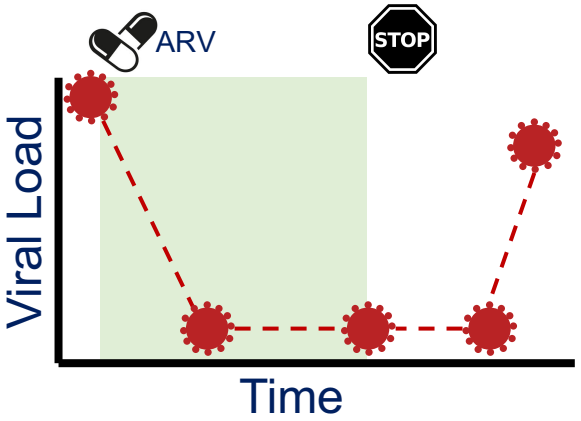
Elite controllers

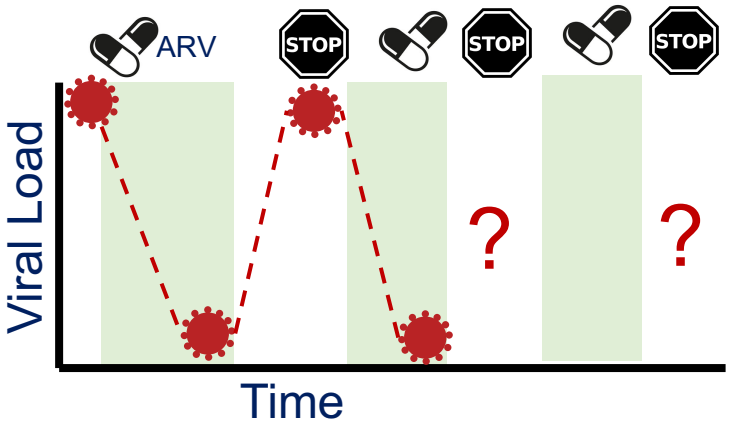


Post-treatment controllers



Transient controllers



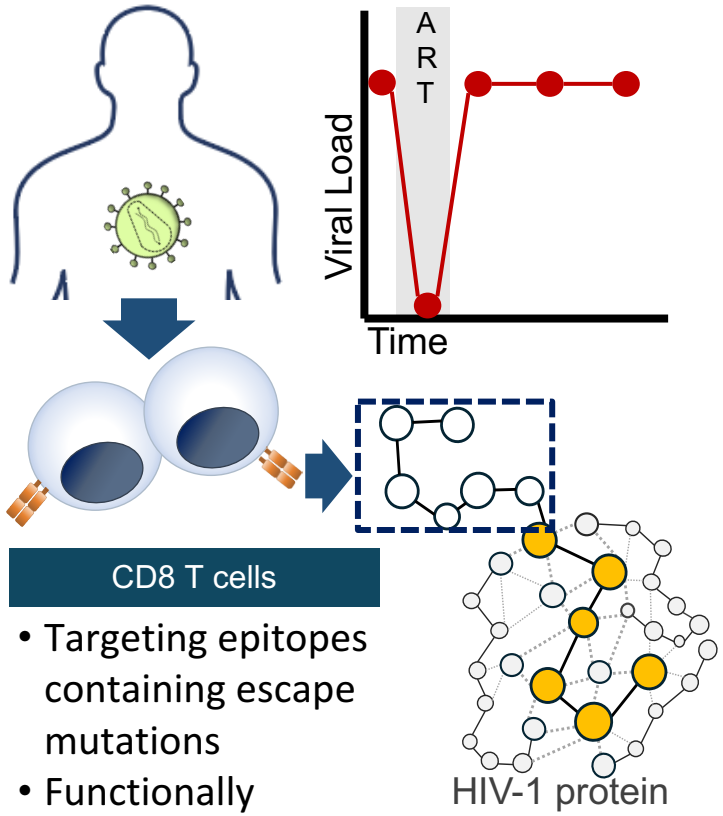


PULSE Study (Samples collected 2006):

- ART during acute/early infection.
- Three consecutive ATIs.
- ART was reinitiated when the viral load reached 5000 copies/ml.
- 10% experienced transient viral control during the second and/or third ATI.

Virological control in People Living with HIV

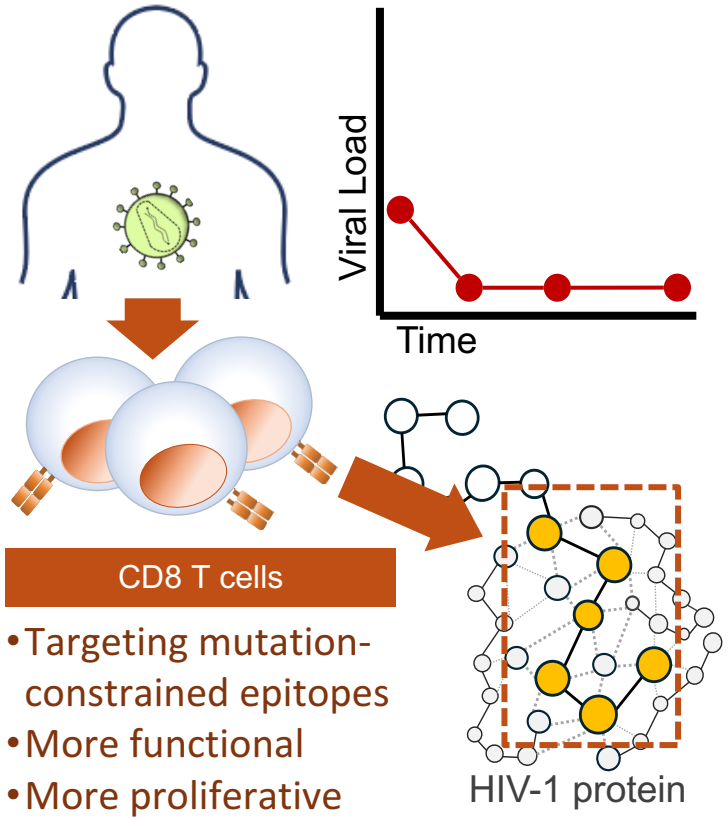
Non-Controller



CD8 T cells

- Targeting epitopes containing escape mutations
- Functionally "exhausted"

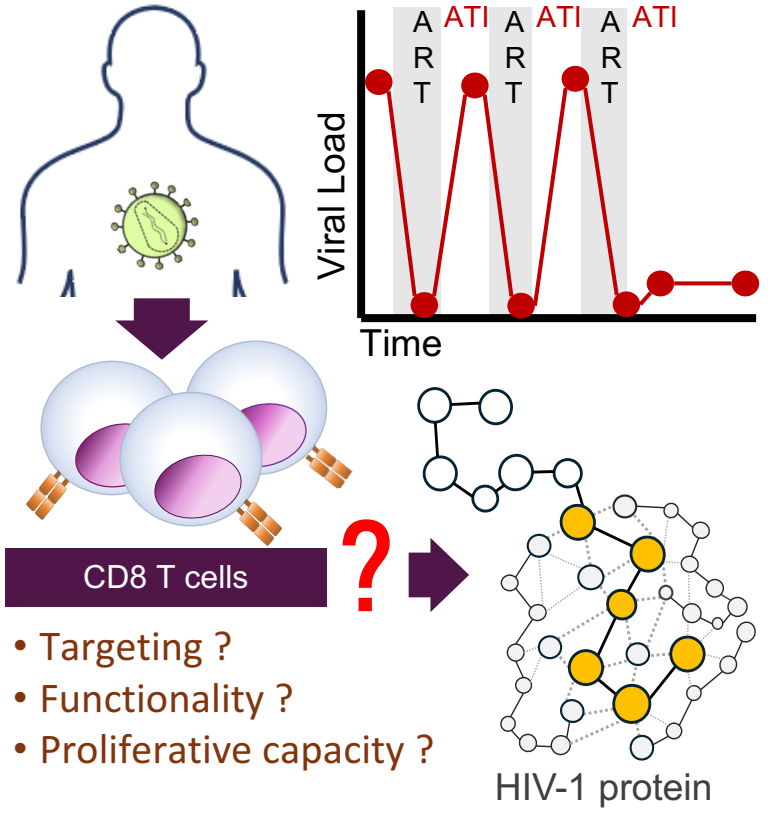
Elite Controller



CD8 T cells

- Targeting mutation-constrained epitopes
- More functional
- More proliferative

ATI Controller

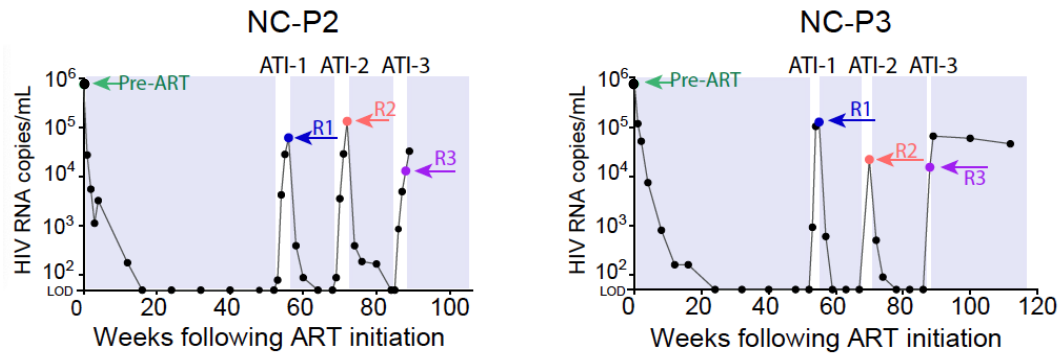


CD8 T cells

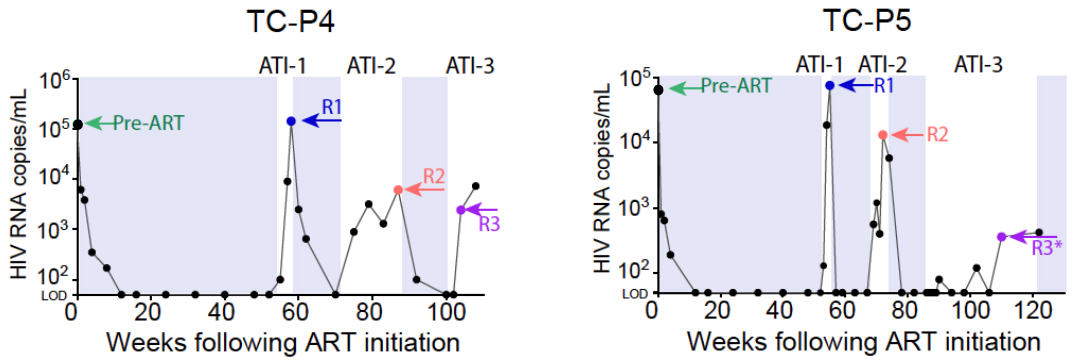
- Targeting ?
- Functionality ?
- Proliferative capacity ?

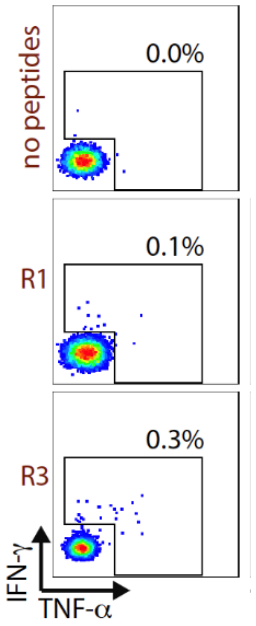
CD8 T cells exhibit lower immune activation during transient viral control

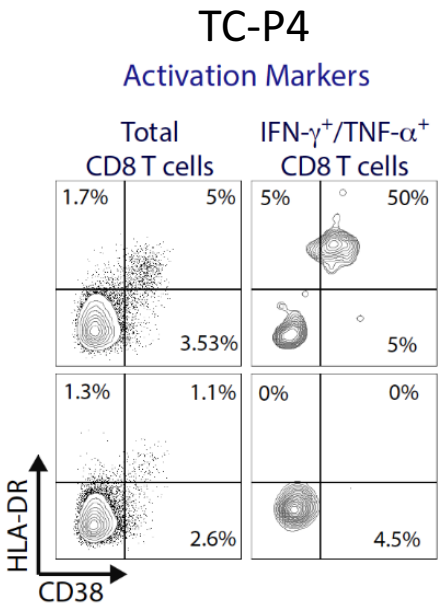
Non-controller

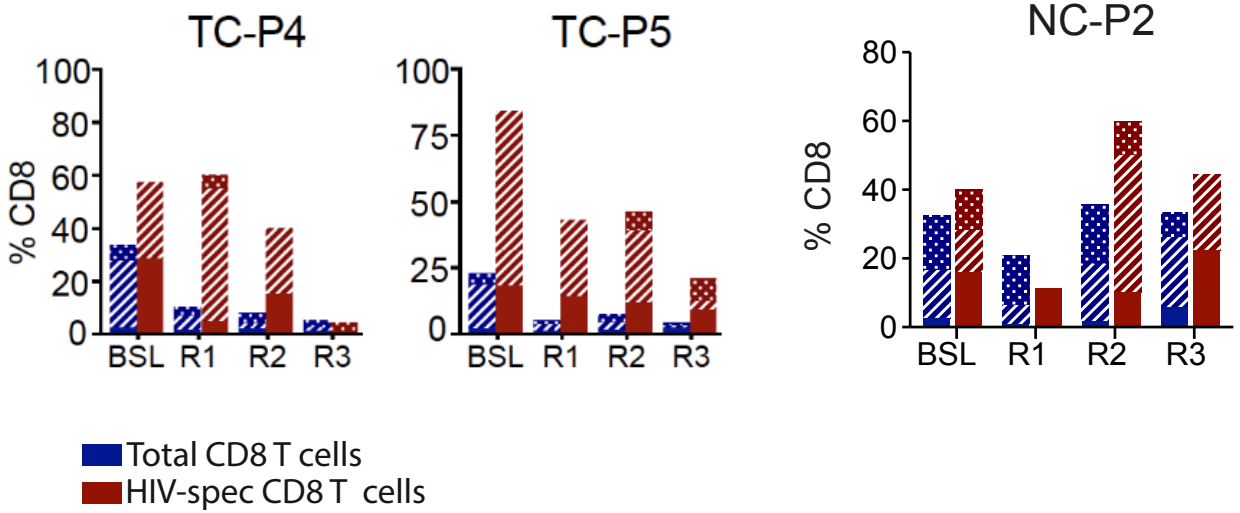


Transient-controller



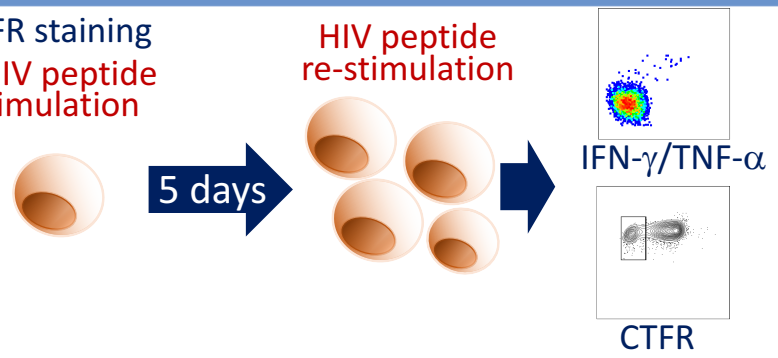




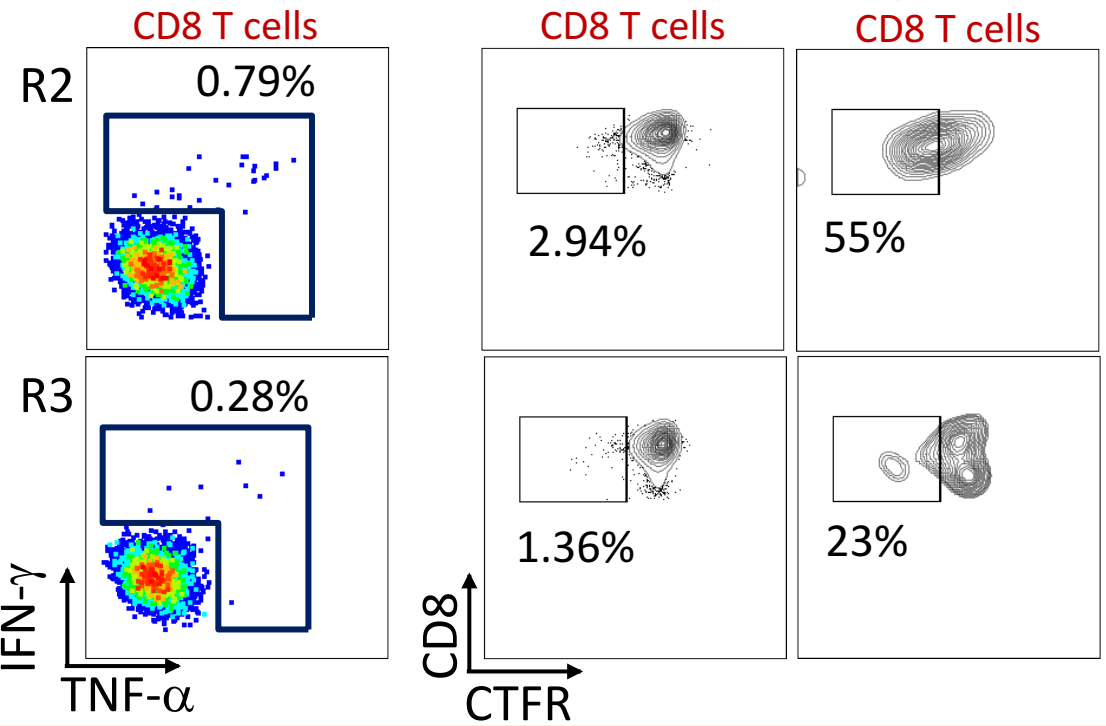


CD8 T cells exhibit higher proliferation capacity during transient viral control

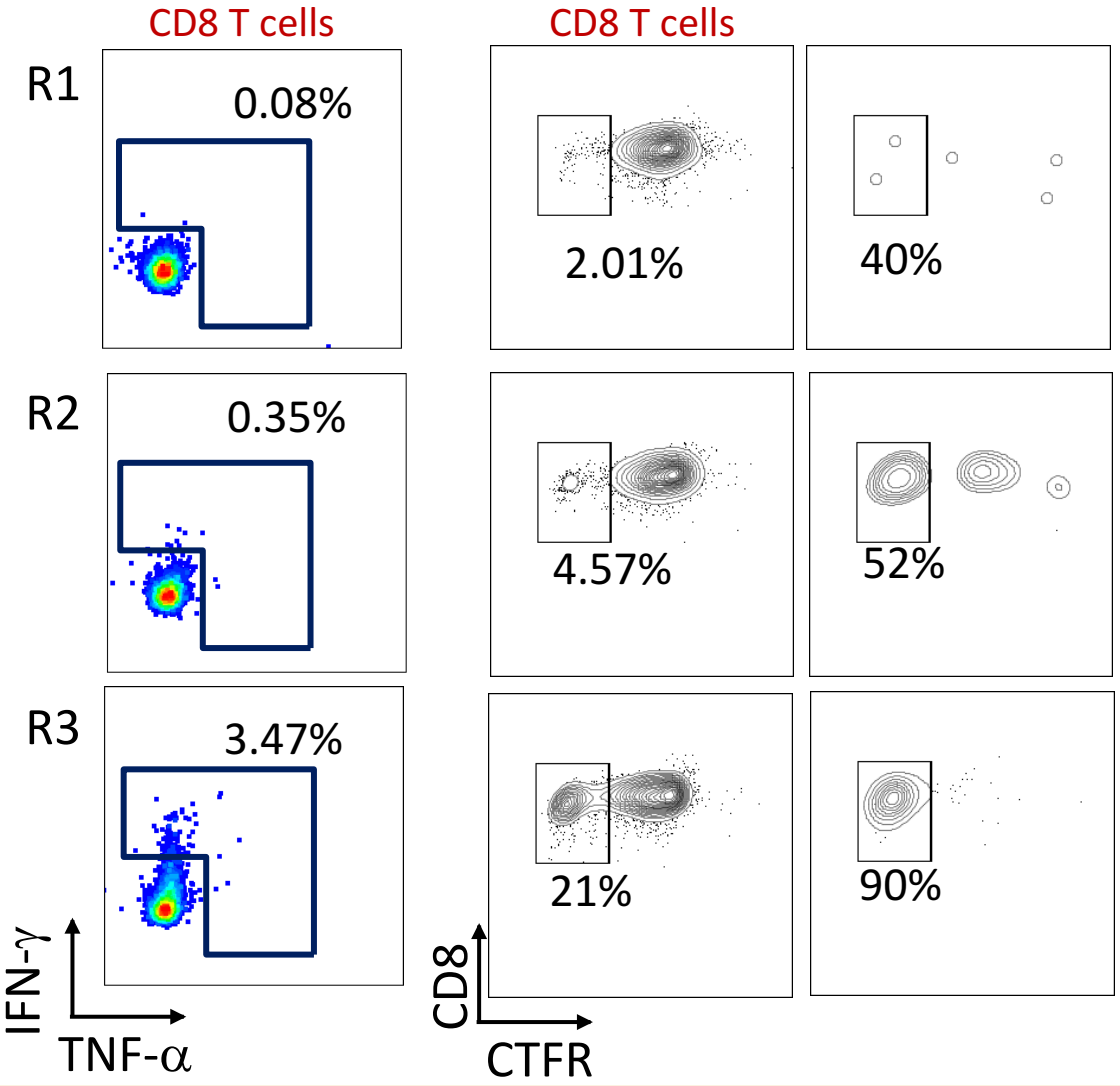
CD8+ T cell proliferation



Non-controller

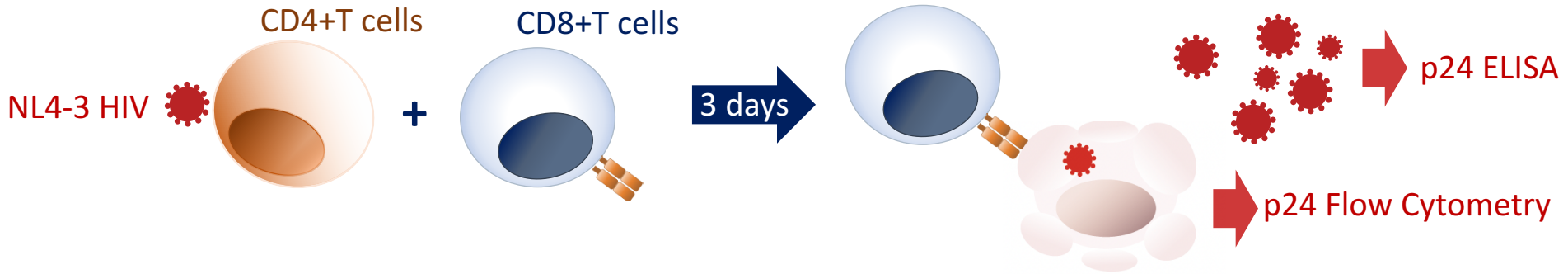


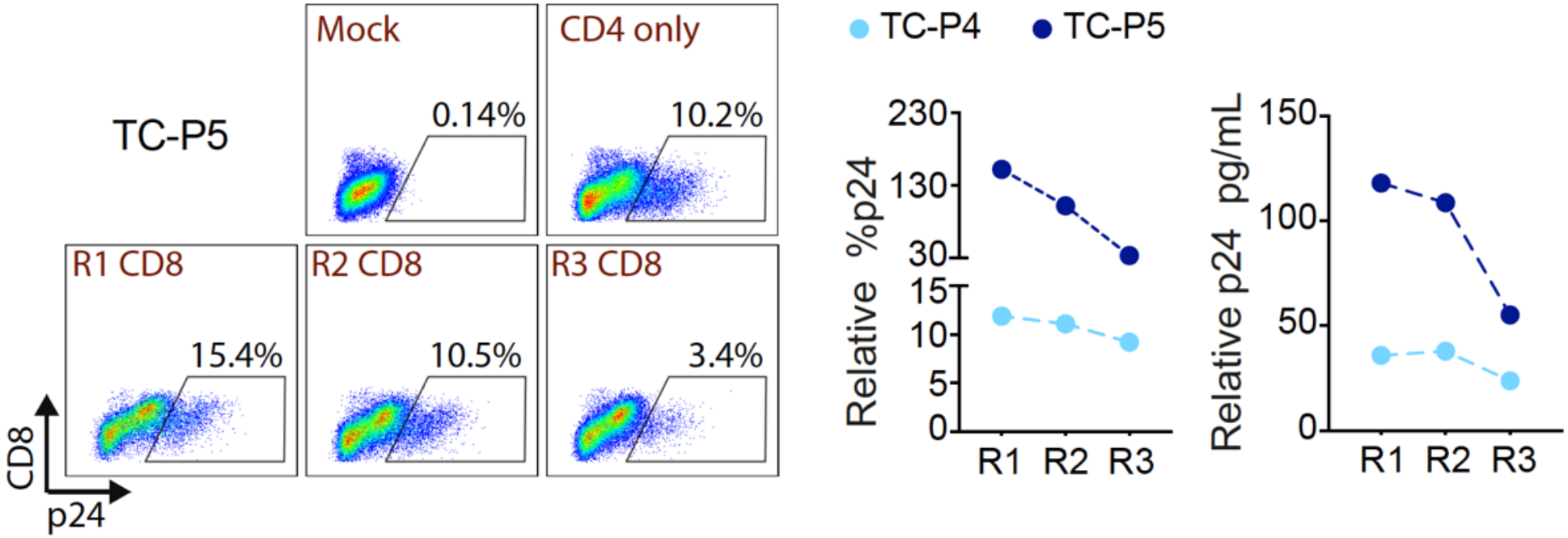
Transient-controller



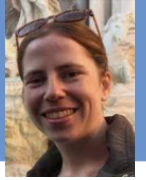
CD8 T cells exhibit higher cytotoxic capacity during transient viral control

Ex vivo T cell–based HIV suppression assay





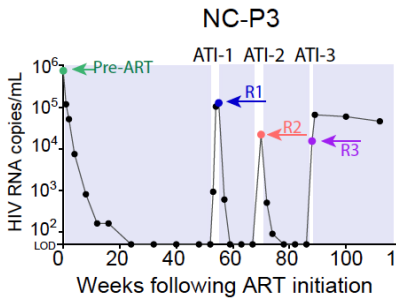
Genetically-distinct HIV-1 populations are associated with transient virological control

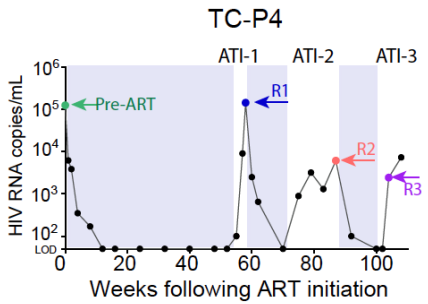


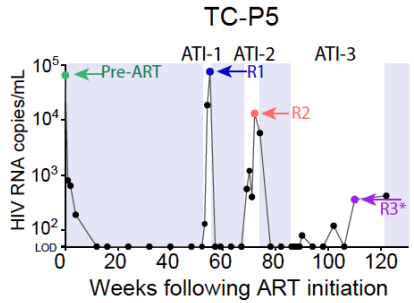
Dr. Katie Fisher

Non-controller (NC)

Transient-controller (TC)

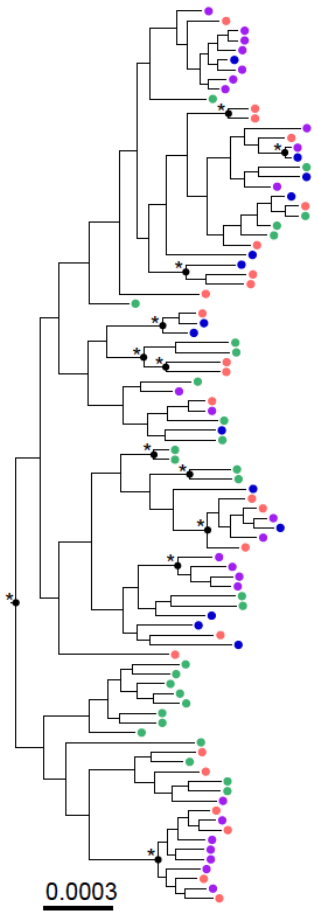


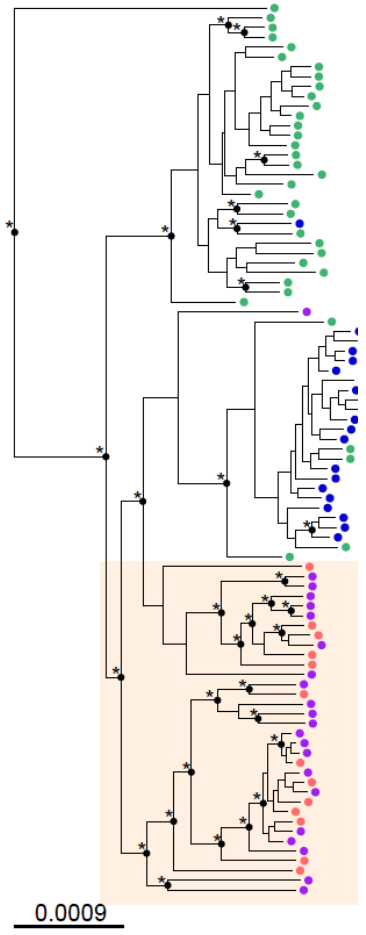


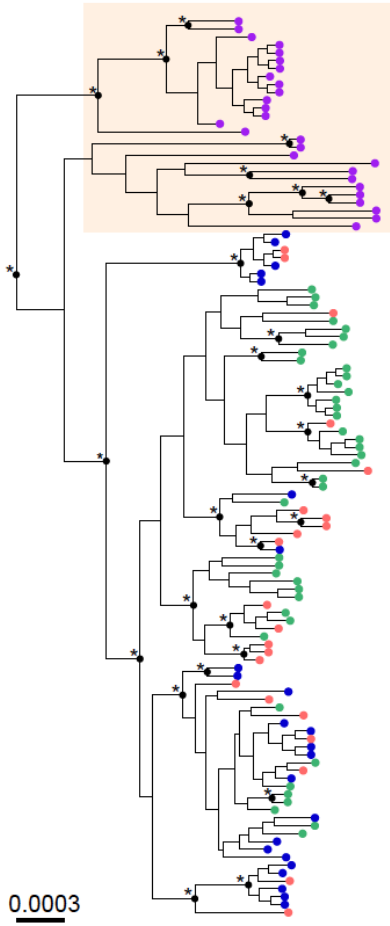


- Pre-ART Plasma
- R1 Plasma
- R2 Plasma
- R3 Plasma

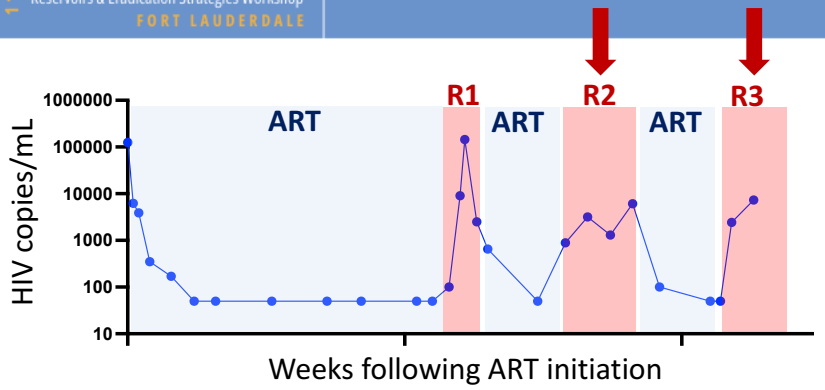
(genetically-intact sequences only)

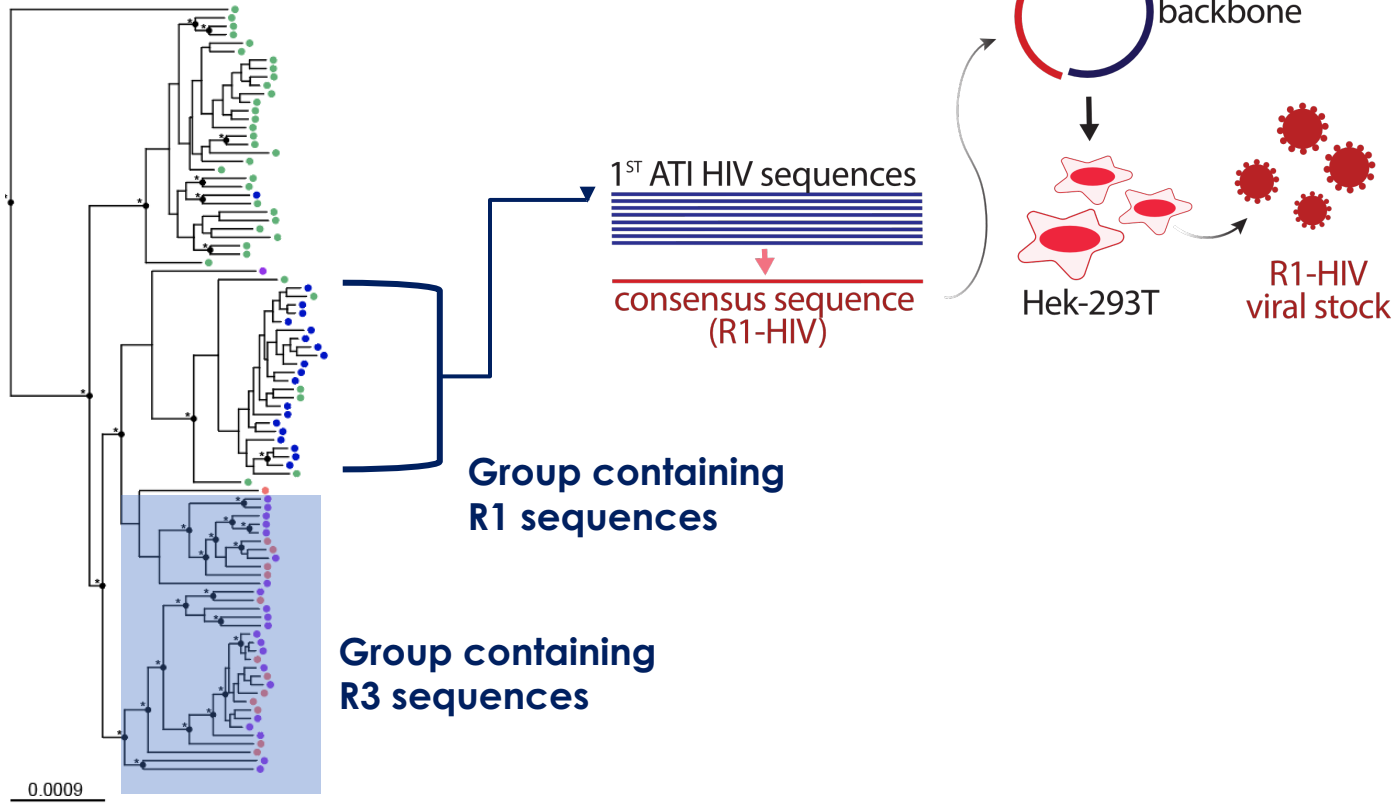


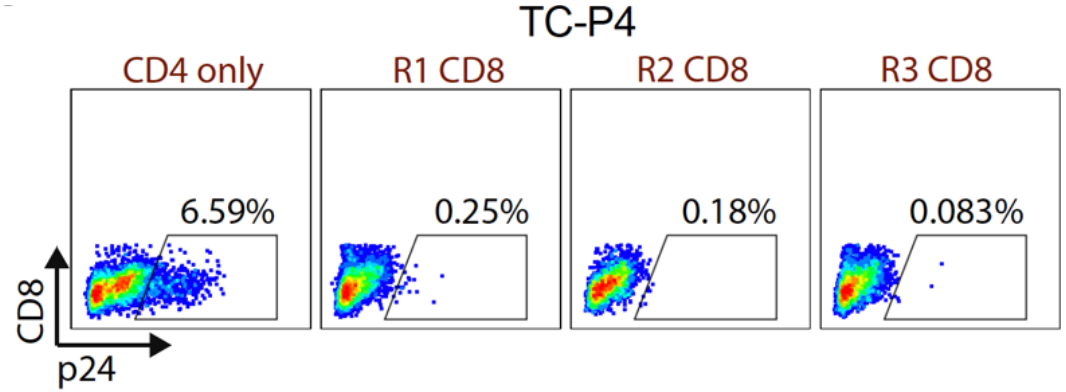


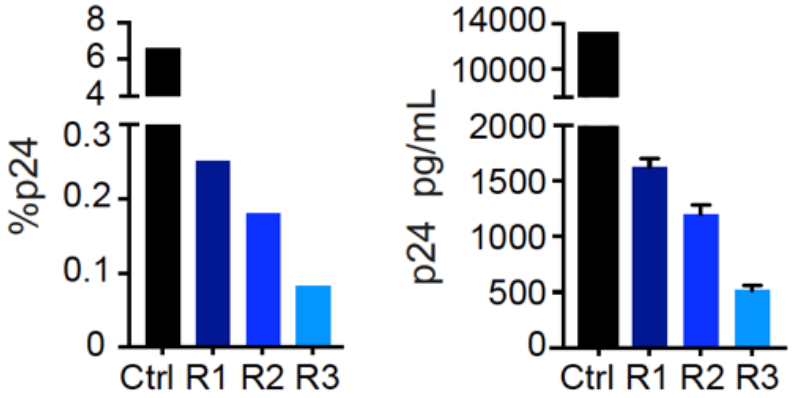


CD8 T cells exhibit higher cytotoxic capacity during transient viral control

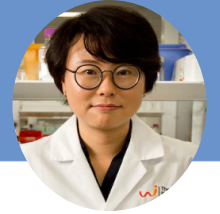








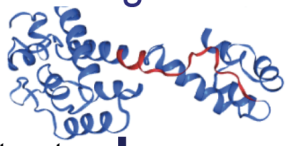
Immunoinformatics Analysis Pipeline (IMAP)



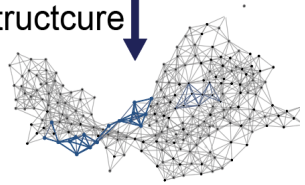
Dr. Eunok Lee

Step 1:

HIV Gag



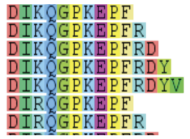
Translate protein structure as network structcure



Calculate network score for individual amino acid residues

Step 2:

Calculate network score for 8-14mers peptides



Step3:

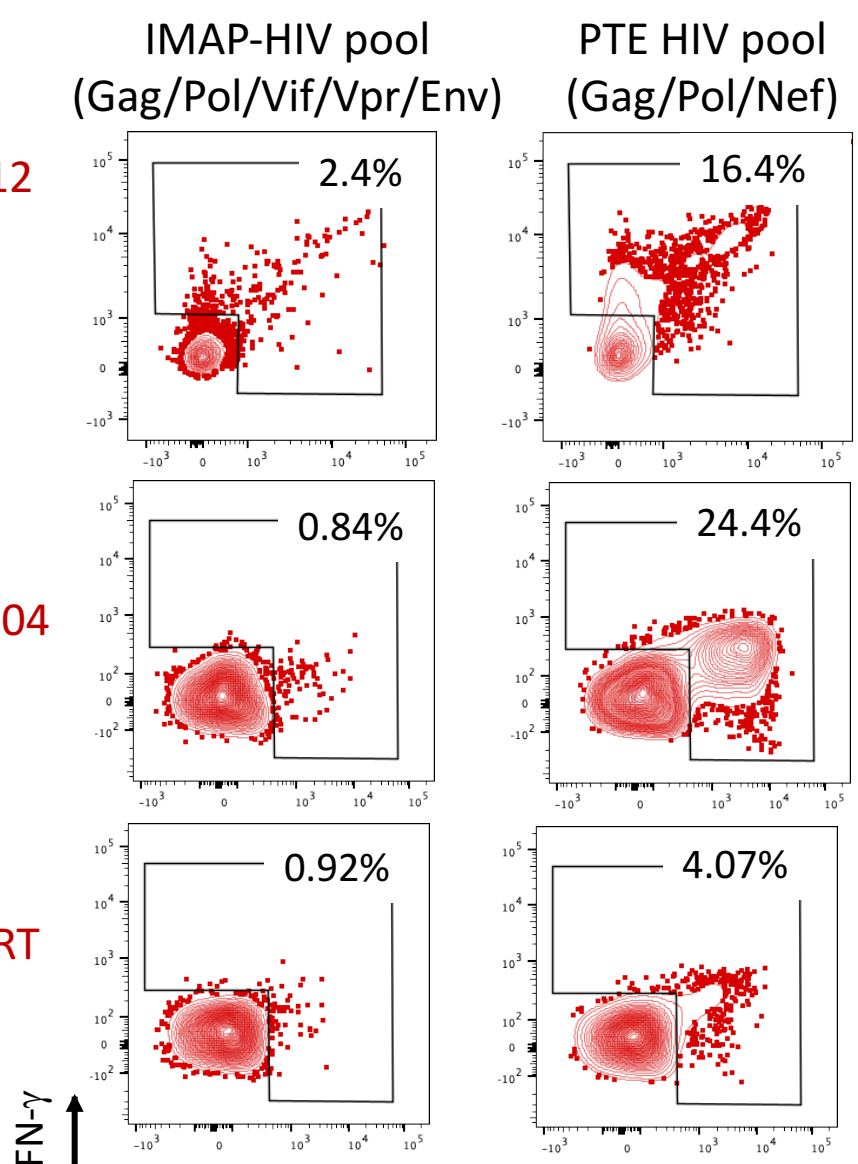
Select highly networked peptides and map them to HIV reference sequence

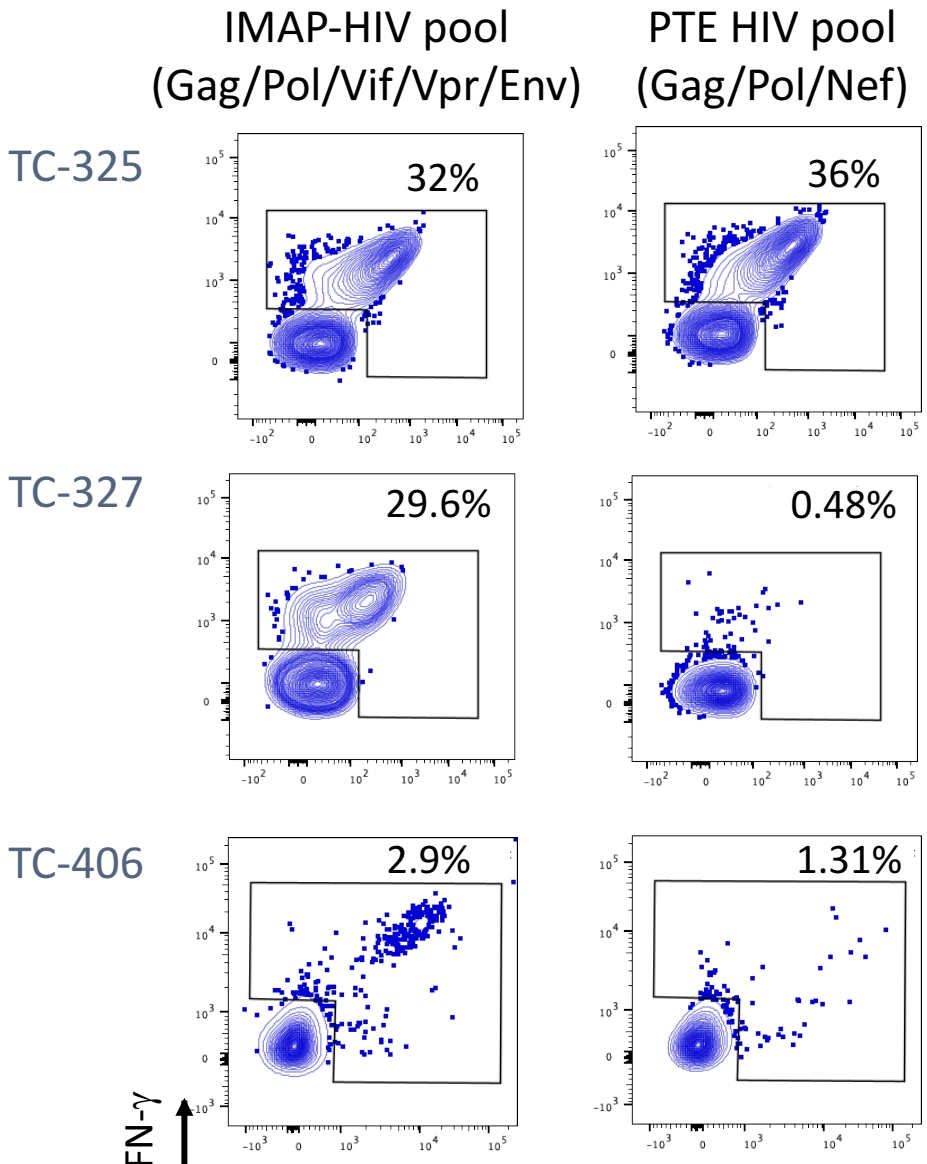
HIV peptide pools:

Gag
Pol
Vif
Vpr
Env

Transient controllers exhibit a higher CTL response to IMAP-HIV peptides

Dr. Josefina Marin





CONCLUSIONS

- Consecutive ATIs results in a potential “vaccinal effect” improving CD8 T cell proliferation, cytokine production and cytotoxicity during the delayed HIV-1 rebound.

- The viral variants emerging during transient virological control are genetically distinct to those derived from the earlier timepoints.

- Our results indicate that the immune system can be effectively primed to control the dominant variants contributing to virological failure.

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Institute for Infectious Diseases

amfAR

ARCHE
amfAR Research Consortium on HIV Eradication

Australian Government
National Health and Medical Research Council

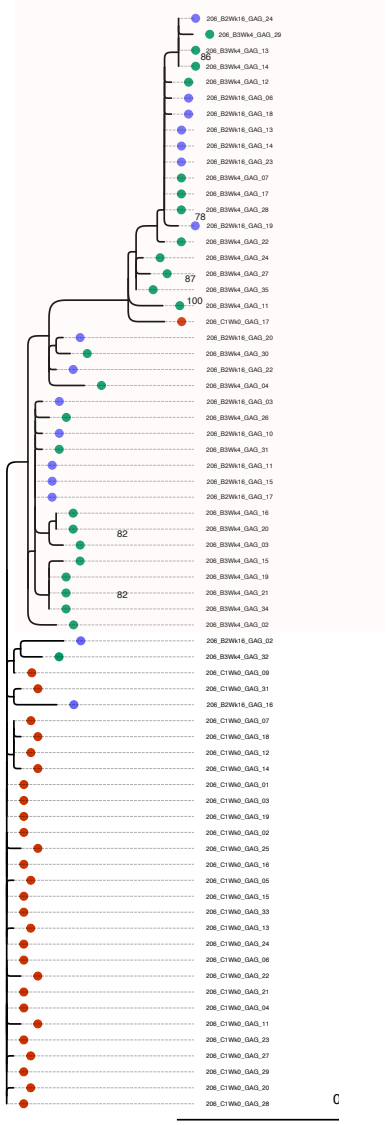
NIH National Institute of Allergy and Infectious Diseases

DARE

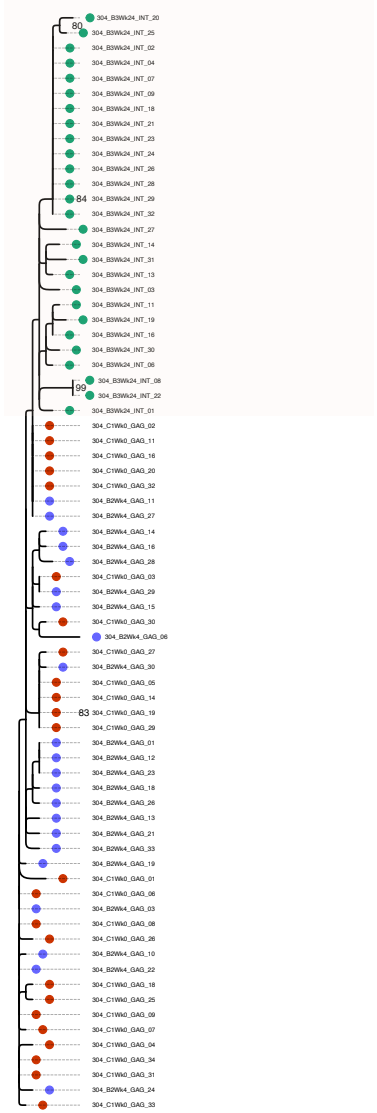
Sandra and David Ansley

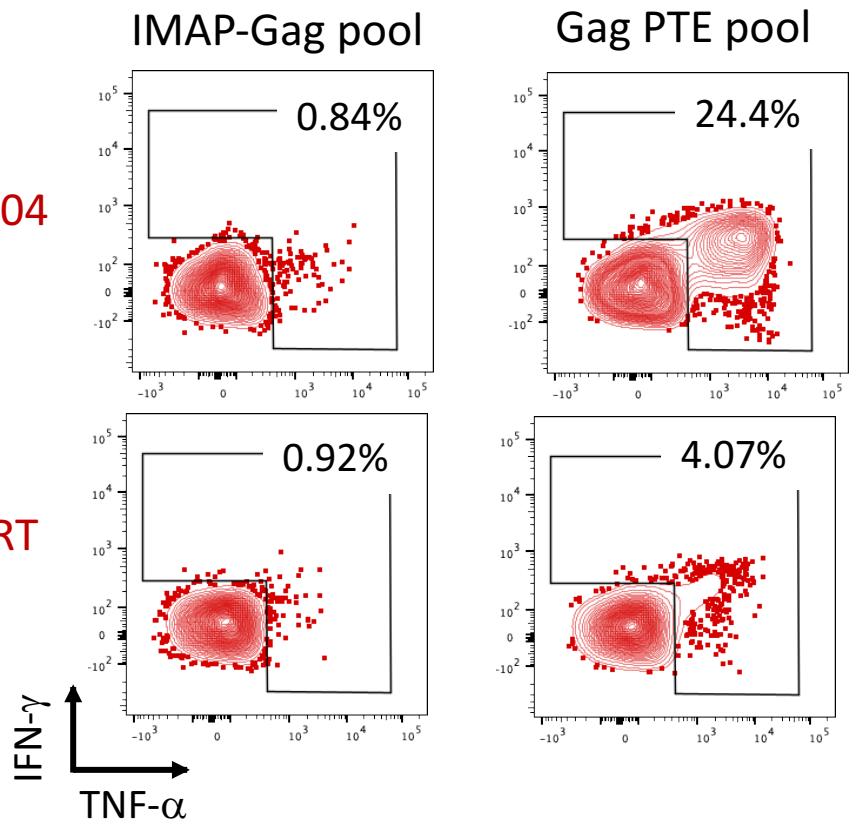
We acknowledge with gratitude the people living with HIV who participated in these studies

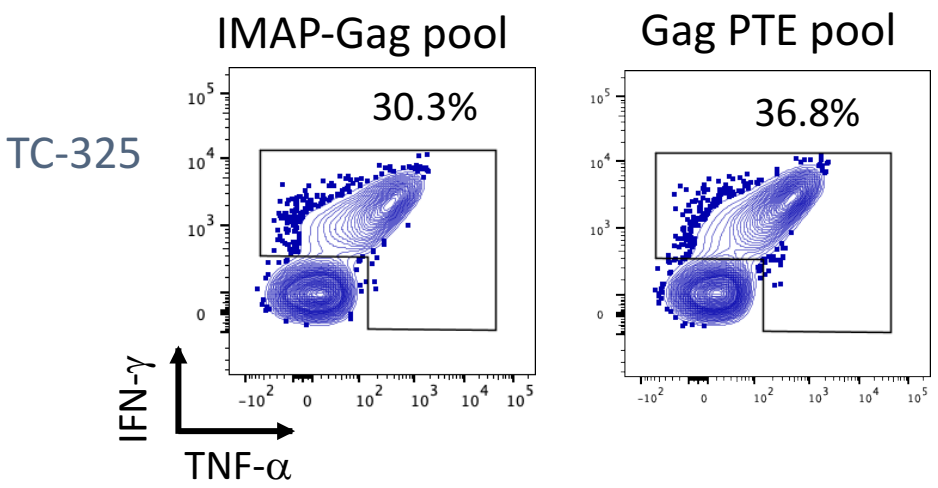
TC-P4
Env



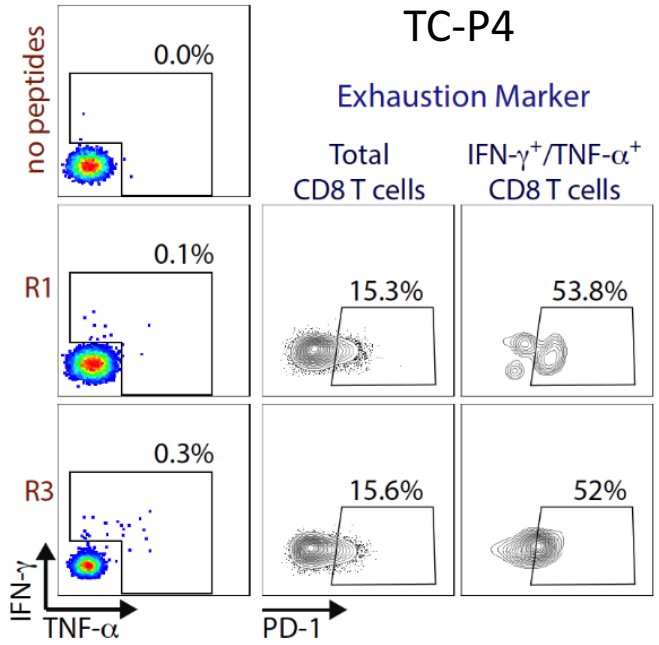
TC-P5
Env

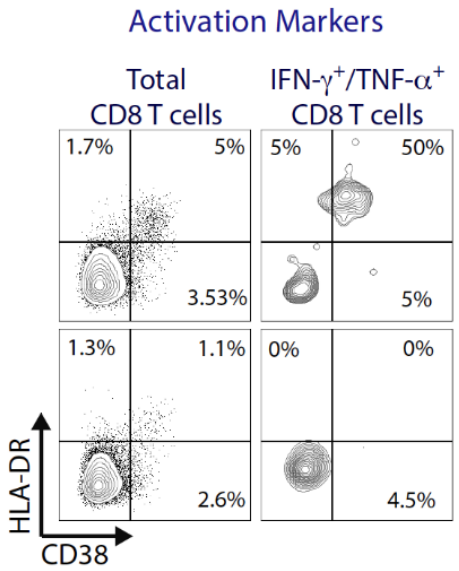


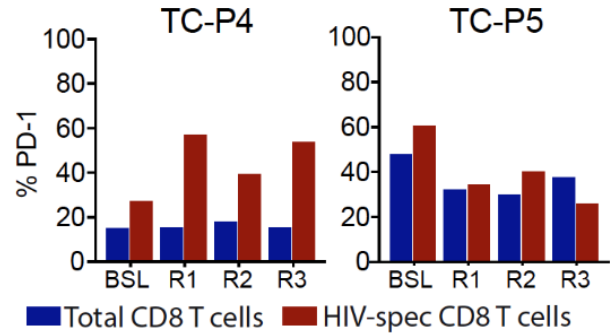

IMAP-Gag pool
Gag PTE pool
NC-104
ART
0.84%
24.4%
0.92%
4.07%
IFN-γ
TNF-α

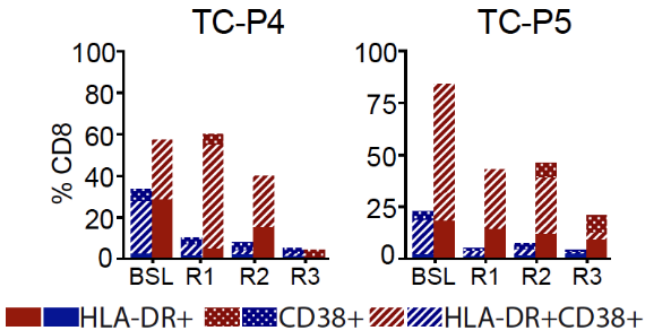

IMAP-Gag pool
Gag PTE pool
TC-325
30.3%
36.8%
IFN-γ
TNF-α

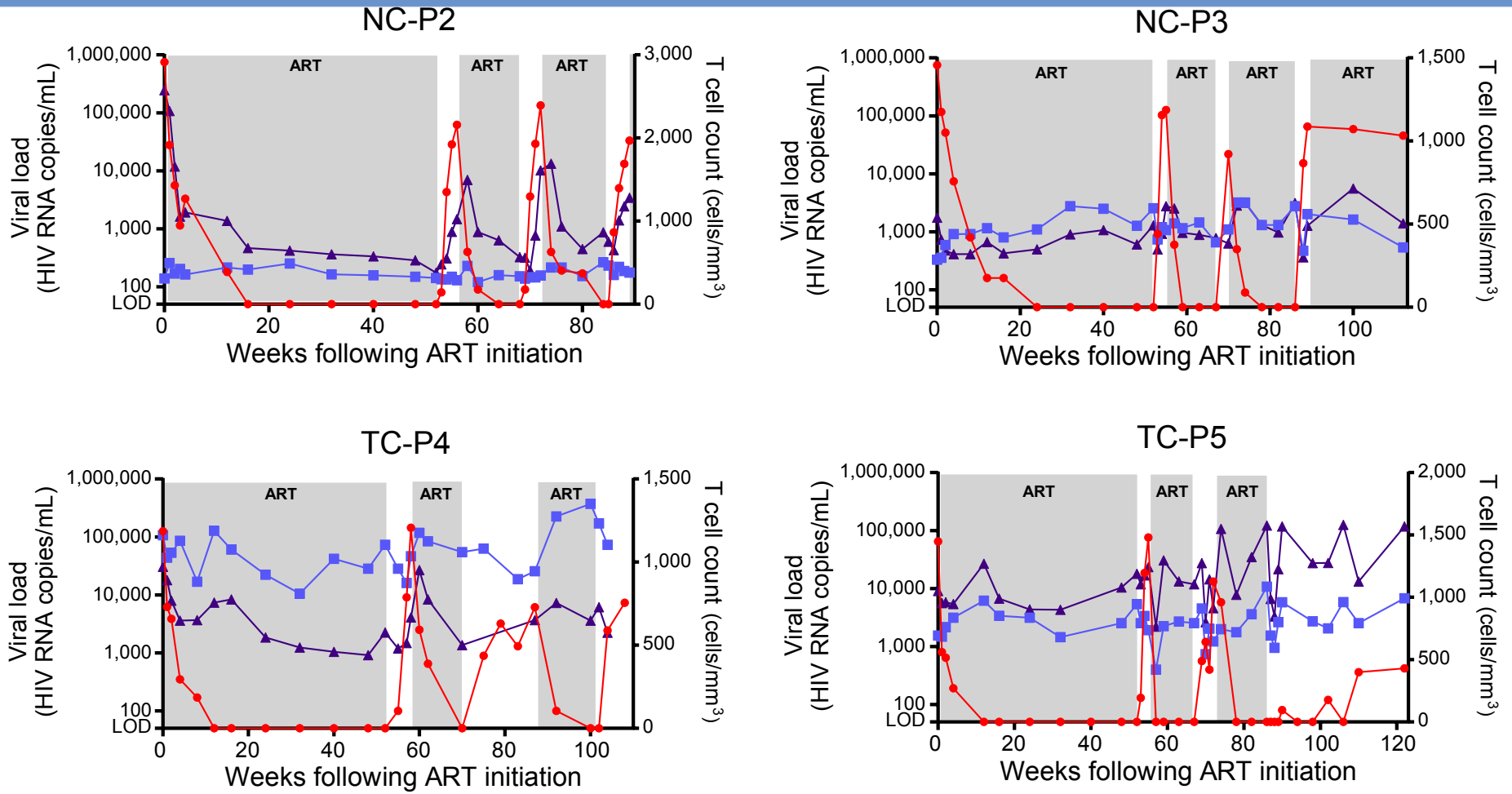
CD8 T cells exhibit lower immune activation during transient viral control

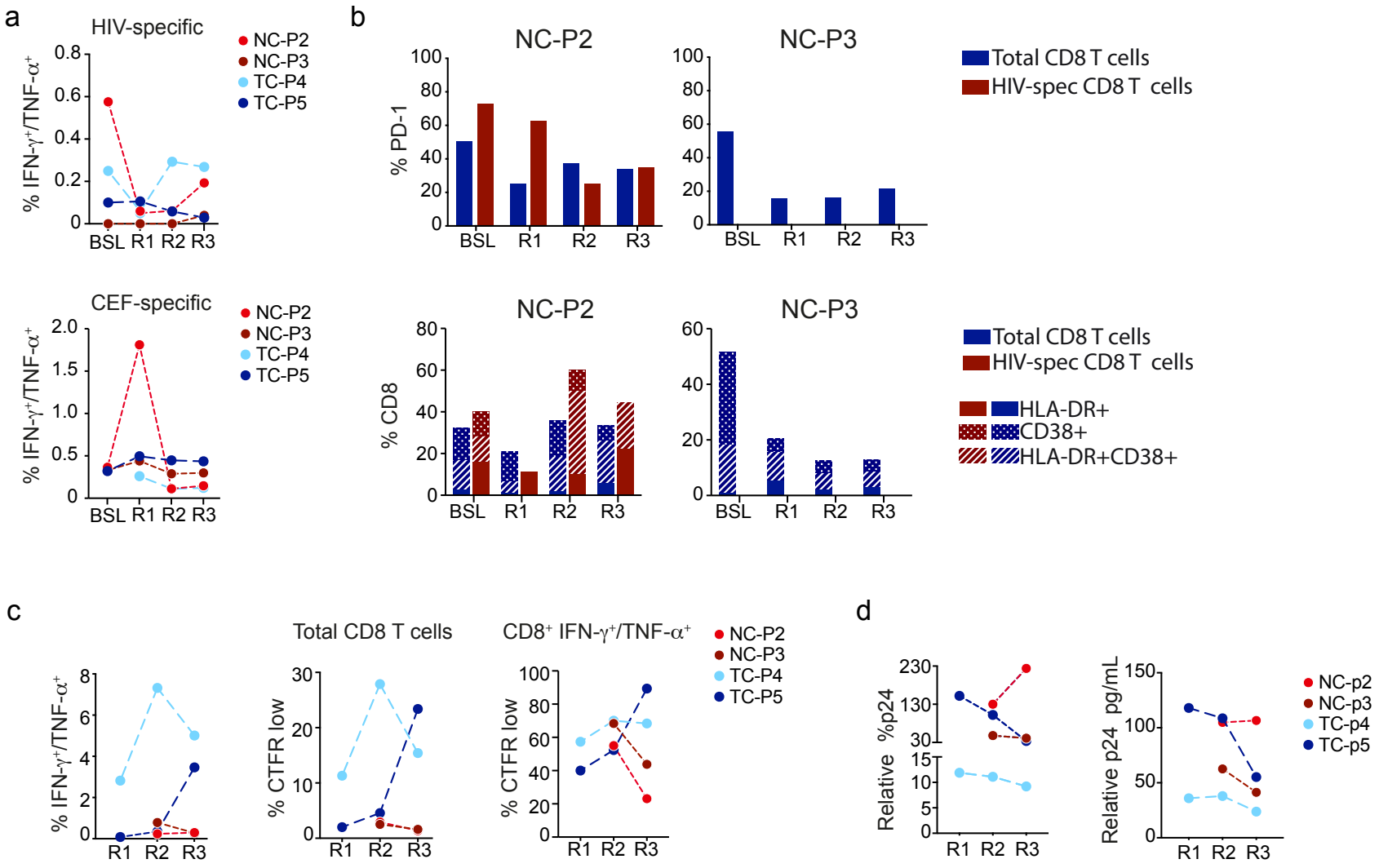









NC-P2
NC-P3
TC-P4
TC-P5
ART
Viral load (HIV RNA copies/mL)
T cell count (cells/mm3)
Weeks following ART initiation
LOD
HIV plasma viral load
CD4+ T cell count
CD8+ T cell count


a
HIV-specific
% IFN-γ+/TNF-α+
NC-P2
NC-P3
TC-P4
TC-P5
BSL R1 R2 R3
CEF-specific
b
NC-P2
NC-P3
% PD-1
% CD8
Total CD8 T cells
HIV-spec CD8 T cells
HLA-DR+
CD38+
HLA-DR+CD38+
c
Total CD8 T cells
CD8+ IFN-γ+/TNF-α+
% CTFR low
d
Relative %p24
Relative p24 pg/mL
NC-p2
NC-p3
TC-p4
TC-p5