HIV POST-TREATMENT CONTROLLERS SHOW ENHANCED CD8+ T CELL PROLIFERATIVE CAPACITY AFTER ART CESSATION

447

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BACKGROUND

HIV post-treatment controllers (PTCs) present a natural model of functional cure in which control of viral load is established after interruption of ART. Unlike spontaneous ("elite") controllers, where the contribution of CD8+ T cells to viral control is well-established, CD8+ T cell function in PTCs remains understudied.

Similarly to spontaneous controllers, prior cohort studies of PTCs have shown similar or reduced *ex vivo* HIV-specific CD8+ T cell responses in PTCs when compared to post-treatment non-controllers (NCs). However, highly proliferative HIV-specific CD8+ T cell responses have been shown to be greatly enhanced in spontaneous controllers compared to viremic progressors. In the present study, we investigated **if HIV post-treatment controllers also have more highly proliferative, functional CD8+ T cells compared to non-controllers?**

METHODS

Figure 1: Phenotypic definitions

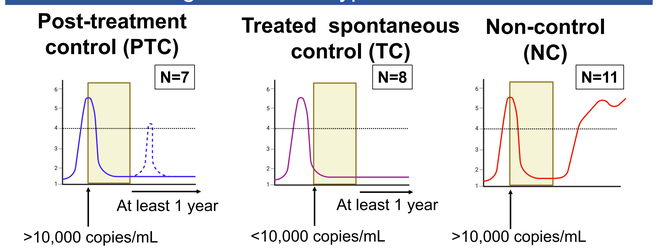
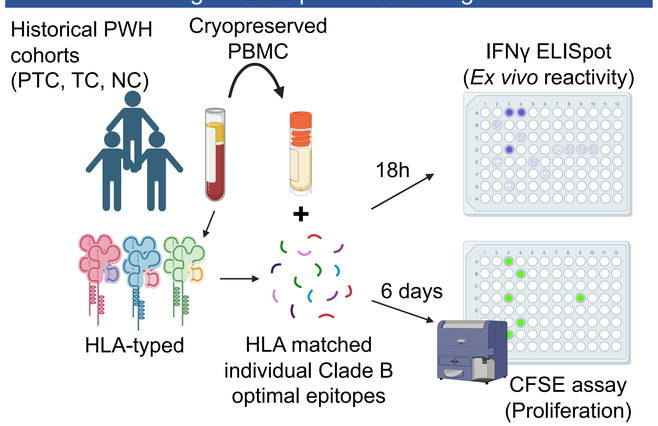


Figure 2: Experimental design



RESULTS

- Our PTC cohort is mostly early-treated **(Table 1)**
- *Ex vivo* T cell reactivity towards CD8+ epitopes is lower in PTCs compared to TCs (P<0.01), and the same between TCs and NCs **(Figure 4)**
- Proliferative responses towards CD8+ epitopes are stronger in PTCs and TCs (P<0.01 and P<0.05, respectively, **Figure 5**)
- We calculated proliferative capacity by normalizing %CFSElow cells to *ex vivo* ELISpot magnitude for the same epitope
- Greater proliferative capacity is displayed by PTCs and TCs compared to NCs (P<0.001 and P<0.05, respectively, **Figure 6**)

Table 1: Cohort Overview

	PTC	TC	NC
N	**7**	**8**	**11**
Treatment Timing			
Early	6	5	5
Chronic	1	3	6
Pre-ART VL (log10)			
Median	**4.42**	**3.11**	**4.98**
Q1	*4.34*	*2.99*	*4.33*
Q3	*5.84*	*3.29*	*5.30*
Weeks on ART			
Median	**141**	**120**	**164**
Q1	*73*	*65*	*69*
Q3	*265*	*262*	*310*
Weeks post-TI sampled			
Median	**58**	**179**	**68**
Q1	*22*	*82*	*28*
Q3	*607*	*222*	*101*
VL (log10) at sample date			
Median	**1.70**	**2.80**	**4.56**
Q1	*1.30*	*2.52*	*4.12*
Q3	*2.60*	*3.43*	*5.02*
Protective HLA	**3**	**2**	**0**
B*14:01	2	-	-
B*27:05	-	2	-
B*57:01	1	1	-

Figure 3: Cohort viral loads

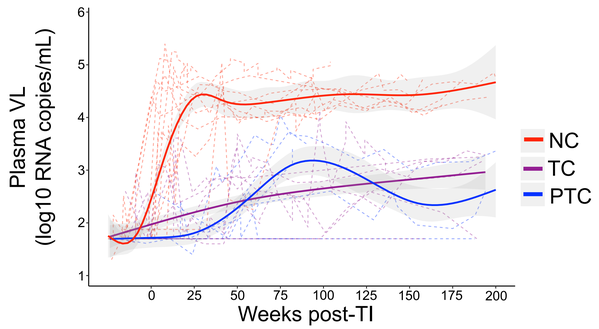


Figure 4: PTCs have reduced *ex-vivo* CD8+ T cell reactivity

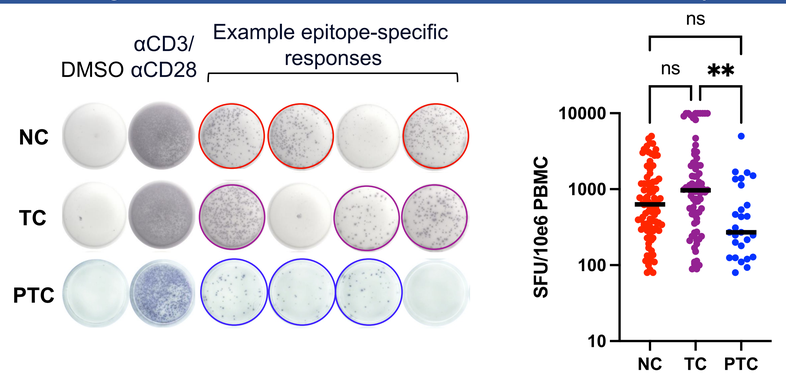


Figure 5: PTCs and TCs both show strong HIV-specific CD8+ T cell proliferation

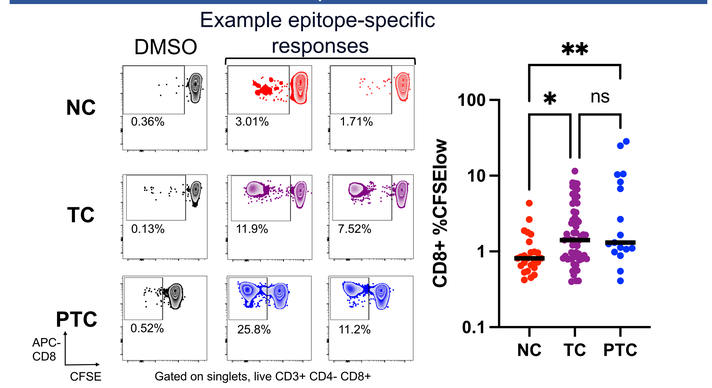
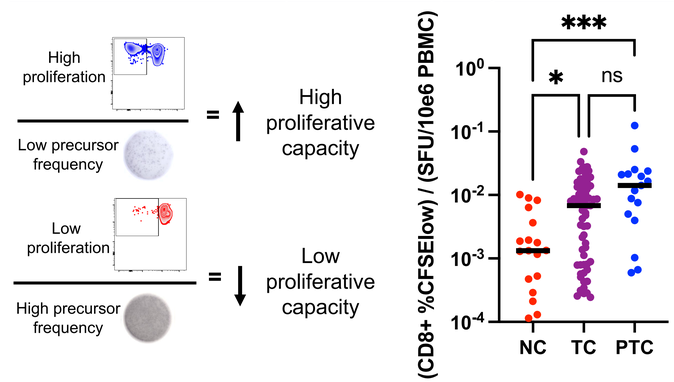


Figure 6: PTCs and TCs have markedly increased CD8+ proliferative capacity



CONCLUSIONS AND IMPLICATIONS

- Despite lower *ex-vivo* reactivity, **HIV-specific CD8+ T cells in PTCs had enhanced proliferative strength and capacity** relative to NCs
- **<u>Functional</u> CD8+ T cell responses likely play a key role in post-treatment control of HIV infection**
- Induction of highly proliferative CD8+ T cell responses by therapeutic vaccination could lead to drug-free HIV remission
- Evaluation of T cell proliferation, rather than *ex vivo* reactivity, is critical in immune monitoring of therapeutic interventions

ACKNOWLEDGEMENTS

This work was supported by the Bill and Melinda Gates Foundation and the DARE HIV Cure Collaboratory (UM1AI164560). We'd like to thank the Ragon Institute Flow Cytometry Core and Processing Lab for their technical support. We thank all of the study participants.