Mutation-Constrained Regions of HIV-1 Proteins Elicit Antigen-Specific Effector CD8 T-Cell Responses

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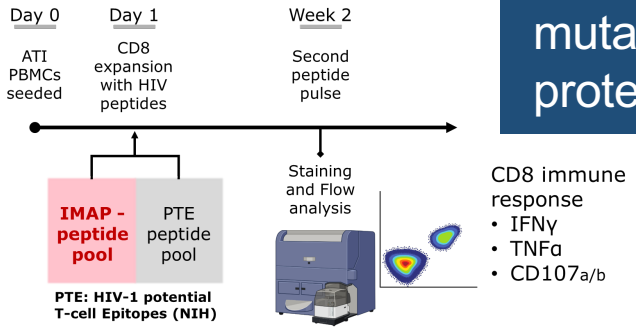
BACKGROUND

We developed the **Im**munoinformatics **A**nalysis **Pi**peline (**IMAP**) to identify 182 peptides (**IMAP-peptides**) from 5 HIV-1 protein regions (**Gag, Pol, Vif, Vpr, and Env**) which are mutation-constrained, genetically-conserved across global HIV-1 subtypes, and predicted to bind common HLA-1 alleles providing 99% worldwide coverage.

To validate the predicted immunogenicity of these IMAP-peptides, we assessed the CD8 T cell responses to the total HIV-1 IMAP peptide pool (182 peptides) and IMAP-peptides pooled by HIV-1 protein.

Therapeutic strategies using the IMAP-peptides have the potential to expand the number of CD8 T cells and redirect their response to these highly conserved and mutation-constrained HIV-1 protein regions.

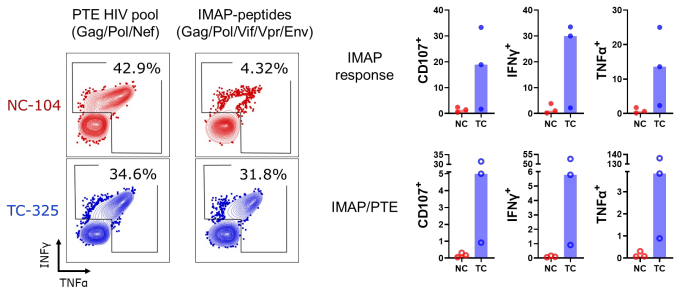
METHODS



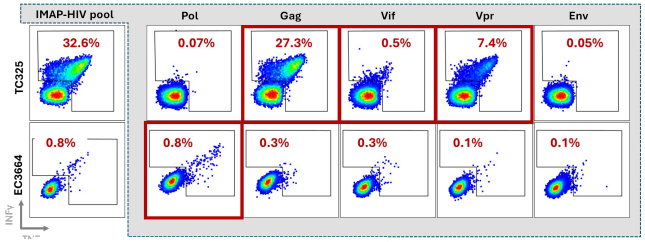
Experimental design for immunogenicity validation of IMAP-peptides.

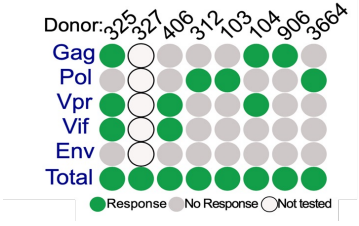
We collected peripheral blood mononuclear cells (PBMCs) from 8 participants, including: transient-controllers (TCs) who controlled viral rebound after antiretroviral therapy (ART) was stopped (n=3); non-controllers who experienced viral rebound in the absence of ART (n=3); one participant on ART, and one elite controller.

RESULTS: Transient controllers exhibit a higher CD8 response to HIV-1 IMAP-peptides



RESULTS: The response to the individual IMAP-HIV protein pools is donor dependent.

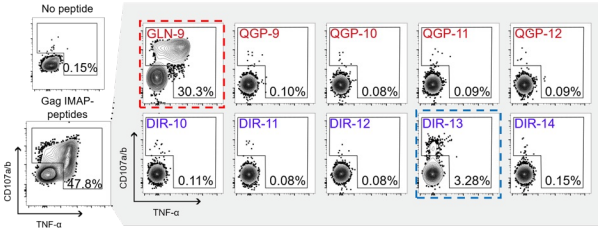




TC: 325, 327, 406
NC: 312, 103, 104
On ART: 906
elite controller (EC): 3664

8 out of 8 donors showed response to our IMAP-HIV pool

RESULTS: Two out of the 33 Gag IMAP-peptides are driving the immune response in this sample (TC:325).



CONCLUSIONS: **Our results reveal that the IMAP-peptides from four HIV-1 proteins (Gag, Pol, Vif and Vpr) and the total HIV-1 IMAP-peptide pool elicited a CD8 T cell effector response.**

The higher potential of CD8 T cells from TCs to recognize and respond to these mutation-constrained HIV epitopes may contribute to their virological control.

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