ANTIBODY PROFILING IDENTIFIES ANTIBODY TARGETS ASSOCIATED WITH NATURAL HIV CONTROL

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Disclosure: None

Background

- HIV viral suppression is associated with delayed disease progression and reduced transmission.

- HIV controllers suppress HIV viral load (VL) to low levels without antiretroviral treatment (ART).

- We compared antibody profiles in HIV controllers, viremic non-controllers, and non-controllers who were virally suppressed on ART.

# **Methods**

- We used a massively parallel antibody profiling system (VirScan) to quantify antibody binding to 3,384 peptides spanning the HIV genome.

- Peptides with different antibody reactivities between controllers and non-controllers were identified using moderated t-tests and q-values for multiple testing correction.

- Comparison of these peptides was assessed in the validation cohort using one-sided moderated t-tests and Fisher's inverse chi-squared test.

- Using linear regression, we examined the relationship between median antibody reactivity to each of the identified peptides and VL set point.

Study Cohort	Sample source	Participant status	Viral load (copies/mL)	# persons	# samples
Discovery Cohort	SCOPE Study	Elite controllers	<40	13	13
		Viremic controllers	40-2,000	27	27
		Non-controllers suppressed on ART	<40	21	21
		Viremic non-controllers	>2,000	12	12
Validation Cohort	JH Medicine Elite Controller Cohort	Elite controllers	<50	29	29
	JH HIV Clinic	Non-controllers suppressed on ART	<400	37	37
Analysis of viral load set point and antibody reactivity	RV217 Study	Longitudinal samples collected prior to ART initiation	Various	53	298
	GS Cohort	Longitudinal samples collected prior to ART initiation	Various	54	231

Results

- In the Discovery Cohort, we identified 62 peptides that were preferentially targeted in HIV controllers compared to non-controllers.

- In the Validation Cohort, combined antibody reactivity to these peptides was also higher in elite controllers compared to non-controllers who were virally suppressed on ART. Reactivity of antibodies to the 62 peptides was similar among HIV controllers who did or did not have the protective HLA-B*57 allele.

- Higher antibody reactivity to a subset of the peptides in the p17 cluster was significantly associated with lower viral load set points in ~~the group of~~ longitudinally-followed non-controllers.

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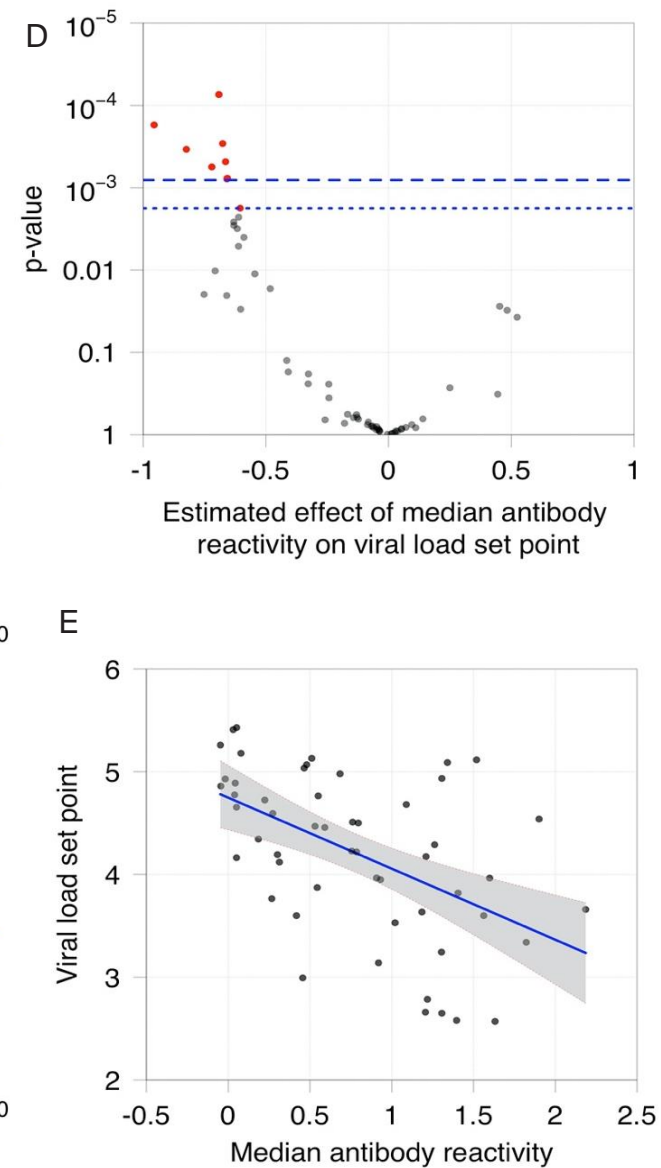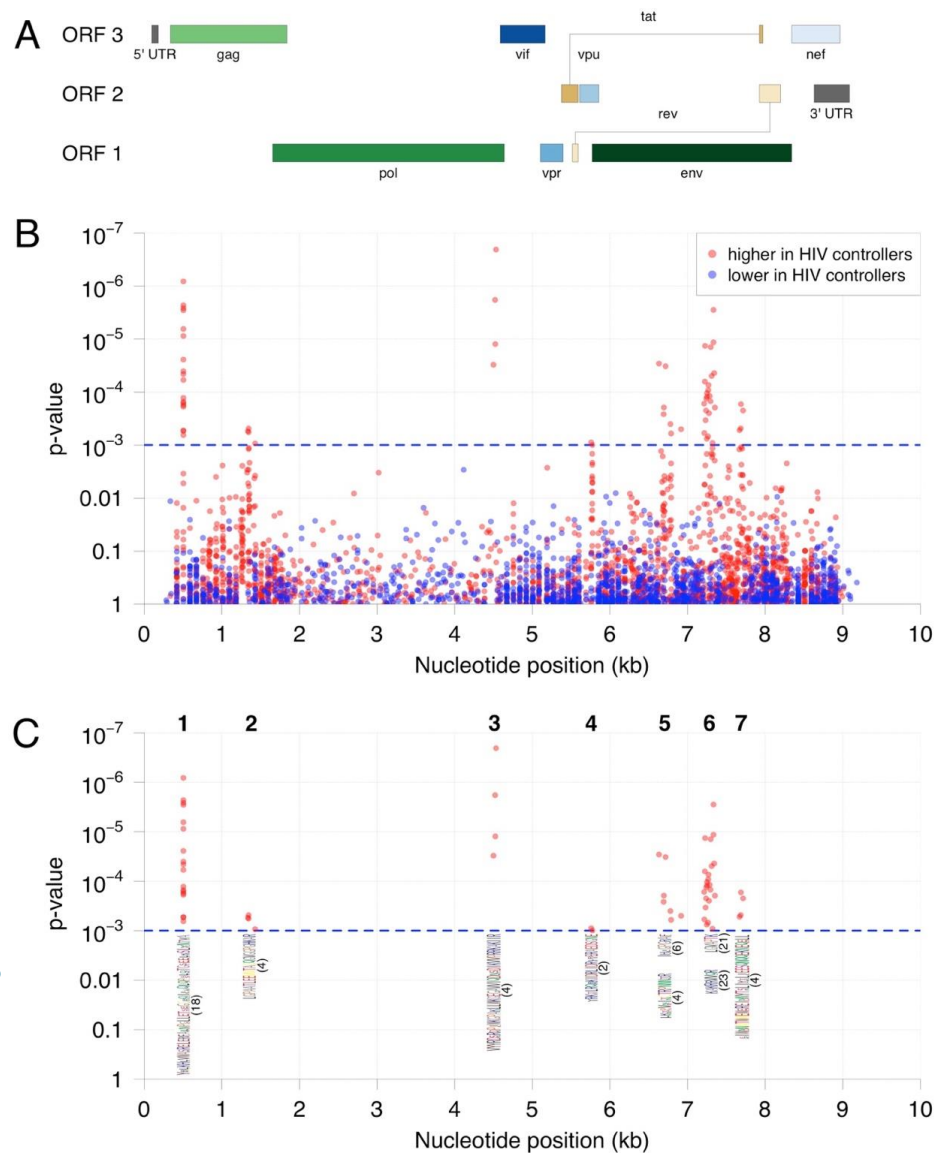
Conclusions

- A comprehensive, unbiased assessment of antibody reactivity to HIV peptides spanning the viral genome identified clusters of homologous peptides that were preferentially targeted in HIV controllers and in non-controllers who had lower viral load set points.

- This research provides new insights into natural control of HIV infection and may inform research on immune-based interventions for HIV prevention and treatment.

- Further research is needed to characterize antibodies that target these peptides and to evaluate T- cell targeting of these epitopes.

Acknowledgements

/HIVptn