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.

<table>
<thead>
<tr>
<th>Study Cohort</th>
<th>Sample source</th>
<th>Participant status</th>
<th>Viral load (copies/mL)</th>
<th># persons</th>
<th># samples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Discovery Cohort</td>
<td>SCOPE Study</td>
<td>Elite controllers</td>
<td>&lt;40</td>
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<td></td>
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<td>Viremic controllers</td>
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<td></td>
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<td>Non-controllers suppressed on ART</td>
<td>&lt;40</td>
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<tr>
<td></td>
<td></td>
<td>Viremic non-controllers</td>
<td>&gt;2,000</td>
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<td>Validation Cohort</td>
<td>JH Medicine Elite Controller Cohort</td>
<td>Elite controllers</td>
<td>&lt;50</td>
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<td>JH HIV Clinic</td>
<td>Non-controllers suppressed on ART</td>
<td>&lt;400</td>
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<td>RV217 Study</td>
<td>Longitudinal samples collected prior to ART initiation</td>
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<td>GS Cohort</td>
<td>Longitudinal samples collected prior to ART initiation</td>
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</table>
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.
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


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