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The roles of HIV-1 specific CD8+ T cell responses and HLA class I alleles on viral control and viral escape in HIV-1 infected Thai individuals

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Background

Knowledge about the role of specific HLA class I alleles, CD8+ T cell responses, and viral escape on viral control have not been well characterized in clade CRF01_AE and Asian ethnics.

Methods

195 naïve HIV-1 CRF01_AE infected Thai individuals were screened for HIV-1 specific CD8+ T cell responses with a set of 413 OLPs of the HIV-1 proteome by IFN-gamma ELISpot assay. Novel epitopes were characterized by HLA restriction and fine epitope mapping. The association of epitopes and/or HLA alleles with low VL level and/or viral escape was analyzed.

Results

Thirty-three OLPs were identified as potential novel epitopes. A viral control epitope, RI10 (HIV-protease, previously described in HIV-1 B clade as -B*13 restricted) was found restricted by HLA-A*0203 in Thais. Interestingly, HLA-A*0203+ve patients with RI10 responders had a significantly lower VL than non-responders ($p = 0.0167$). This data may support the low VL from loss of viral fitness of RI10. Moreover, the patients exhibiting mutations in RI10 showed no ELISpot responses. Another known HLA-A*1101 epitope, AK11 (in Gag-p24) was also identified as a viral control epitope in this study. Of note, there was no significant mutation found in patients expressing A*1101. We also found a novel immunodominant epitope (29% response rate) restricted by HLA-Cw*0102: YI9 (in Gag-p24) which was associated with viral escape. Mutations at P2 (S278X), P4 (V280X) and P5 (S281G) impaired the Elispot responses, however the P2 anchor S278K mutation had the highest negative impact ($p = 0.0002$).

Conclusion

In HIV-1 CRF01_AE infected Thais we characterized three CD8 epitopes (RI10, AK11 and YI9) restricted by HLA-A*0203, -A*1101 and -Cw*0102, respectively. RI10 and AK11, but not YI9, were associated with lower VL and possible control of HIV. Further characterization of those possible novel epitopes is warranted.

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