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Control of HIV-1 by multiple immunodominant HIV-1-specific CD8+ T cells in HIV-1-infected Japanese individuals

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Background

Previous studies of the comprehensive analysis of HIV-1-specific CTL responses in Caucasian and African cohorts demonstrated the association of the CTL responses to HIV-1 Gag protein with the control of HIV-1 replication. However, such analysis in Asian cohorts has not been reported. In the present study, we performed the comprehensive analysis of $CD8^+$ T cell responses against 11-mer overlapping HIV-1 Nef, Gag, and Pol peptides in 401 chronically HIV-1 clade B-infected treatment-naive Japanese individuals.

Methods

The $CD8^+$ T cell responses to cocktails of the peptides were evaluated by measuring IFN-g-producing $CD8^+$T cells by using ELISPOT assay.

Results

To clarify CTLs which control HIV-1 infection in this cohort, we statistically analyzed differences of viral load and CD4 counts between responders to each peptide cocktail in each HLA^+ individuals and non-responders using two-tailed Mann-Whitney's test. We found that several HLA alleles were significantly correlated with low viral load and high CD4 counts in the responses to 5 Nef, 10 Gag, or 16 Pol cocktails. In these cocktails, we identified 2 Nef, 12 Gag and 7 Pol CTL epitopes restricted by 9 HLA alleles. The breadth of CTL responses to these epitopes was significantly associated with low viral load ($p=1.7x10^{-10}$) and high CD4 counts ($p=4.1x10^{-13}$). The total magnitude of responses to the epitopes was also significantly correlated with low viral load ($r=-0.30$, $p=1.8x10^{-9}$) and high CD4 counts ($r=0.37$, $p=5.0x10^{-14}$).

Conclusion

These results suggest that the CTL responses to these epitopes play an important role in the control of HIV-1 infection in chronically HIV-1-infected Japanese individuals.

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