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Cross-clade CTL recognitions for clade B and A/E viruses in A/E virus-infected Japanese individuals

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Background

Cytotoxic T lymphocytes (CTLs) play an important role in the control of HIV-1. CTL responses to HIV-1 have been well studied in HIV-1 clade B-infected and clade C-infected individuals. However cross-clade CTL recognitions have not been well analyzed. In this study, we analyzed cross-clade CTL recognition for clade B and A/E viruses in A/E virus-infected Japanese individuals.

Methods

PBMC samples were collected from chronically HIV-1 infected Japanese cohort in NCGM. Twenty-six clade A/E-infected individuals were analyzed by ELISPOT assay using the 11-mer overlapping peptides and then the responses of CTLs to these peptides was compared to those from 402 clade B-infected Japanese individuals. Thereafter CTL responses to each single peptide and to truncated peptides were evaluated by ELISPOT assay and intracellular cytokine staining (ICC) assay, respectively.

Results

Similar level of CTL responses to Gag, Pol and Nef were found in clade A/E-infected individuals as compared to that in clade B-infected ones. We identified 15 cross-clade CTL epitopes from 14 cocktails where the frequency of responders was high in clade A/E infected samples. The sequences of 7 epitopes were conserved between clade B and clade A/E viruses, whereas 8 epitopes showed different amino acid sequences between two viruses. In these 8 epitope regions, we confirmed cross-clade CTL recognition by ICC assay using clade A/E consensus sequence peptide.

Conclusion

Cross-clade CTLs were predominantly induced in clade A/E-infected individuals by clade B consensus sequence peptides in this study. Moreover, CTL responses were induced not only in conserved region but also in different sequence region between the 2 viruses, indicating that polymorphic sequence epitopes among clades can be also candidate for the target of CTL-based vaccines. Further analysis of cross-clade CTL recognition is needed for the widely applicable vaccine development.

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