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The impact of HLA-Cw*12:02 on control of HIV-1 infection

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Background

Previous studies have demonstrated that higher HLA-C expression, which is determined through a single nucleotide polymorphism 35 kb upstream and the variation within the 3' untranslated region of the HLA-C locus, associate with slow progression of HIV-1-infected disease. Although HLA-C plays important roles in presenting antigens to CTLs or a ligand for inhibitory killer cell Ig-like receptors (KIR), the role of HLA-C-restricted CTL and NK cells in the control of HIV-1 is still unclear. Our recent study of chronically HIV-1 infected Japanese cohort showed that the HLA-B*52:01-Cw*12:02 haplotype was significantly associated with lower viral load. In this study, we investigated whether HLA-Cw*12:02-restricted CTLs or NK cells via KIR have a significant impact on viraemic control.

Methods

We sequenced Pol, Gag and Nef from 400 chronically HIV-1 clade B-infected treatment-naïve Japanese individuals and then analyzed amino acid polymorphisms associated with HLA-B*52:01-Cw*12:02 haplotype using Fisher's exact test. Next we performed intracellular IFNg staining or IFNg ELISPOT assay to detect CTL responses to the peptides including those polymorphisms.

Results

We found 9 amino acid polymorphisms significantly associated with HLA-B*52:01-Cw*12:02 haplotype ($p<0.002$ $q<0.2$). By using ICC assay, we identified 2 Cw*12:02-restricted CTL epitopes and 4 B*52:01-restricted ones. Four Cw*12:02-restricted CTL epitopes including previously reported ones were analyzed to investigate the effect of Cw*12:02-restricted CTLs on control of HIV-1. No significant correlation between the responses to these Cw*12:02-restricted epitopes and viral load was found in chronically HIV-1 infected Cw*12:02 positive Japanese individuals.

Conclusion

Those results showed that HLA-Cw*12:02-restricted CTLs have no effect on control of HIV-1 and suggested that HLA-B*52:01-restricted CTLs or Cw*12:02-resticted NK cells control HIV-1 viraemia in Japanese cohort.

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