



POSTER PRESENTATION

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The HIV-1 protective -35SNP effect in Caucasians is CD8 T cell mediated

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Background

Previous studies in Caucasians have observed that a single nucleotide polymorphism 35kb upstream of the HLA-C gene (-35SNP) associates with control of HIV-1 viral load set-point and cell surface expression of HLA-C. HIV-1 selectively downregulates HLA-A and HLA-B but not HLA-C, via the action of the Nef protein. Thus it has been speculated that higher cell surface HLA-C expression results in a stronger HLA-C-restricted T cell response which might play a role in the control of HIV-1 replication in individuals with the protective -35C variant. However, HLA-C-restricted CD8 T cell responses are relatively weak and we could find no difference in functional HLA-C-restricted CD8 T cell activity measured by IFN- γ ELISPOT assay, according to -35SNP genotype. Therefore, we aimed to examine if there is any correlation between total CD8 T cell function and the -35SNP.

Methods

The viral suppression assay, which involves directly infecting autologous CD4 T cells with primary HIV-1 strains and co-culturing with autologous CD8 T cells, was used as a surrogate for immune control in vivo. The CD8 T cells from 46 antiretroviral therapy naïve HIV-1 infected Caucasians were assessed using this assay.

Results

When CD8 T cell antiviral activity was grouped according to -35SNP genotype, the -35CC group possessed significantly higher CD8 T cell antiviral activity than the -35TT group ($p=0.0151$; Mann-Whitney). Protective HLA-B alleles were always in linkage disequilibrium with HLA-C alleles that are in linkage disequilibrium with the -35C allele. Similarly risk HLA-B alleles were in linkage

disequilibrium with HLA-C alleles that are in linkage disequilibrium with the -35T allele.

Conclusion

In conclusion, the protective -35SNP effect in HIV-1 disease is mediated through CD8 T cells. However, the -35SNP may simply be a marker for protective and risk HLA-B alleles.

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