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# P08-05. Does increased expression of HLA-C allow better control of HIV-1 viral load?

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## Background

A polymorphism ~35 kb upstream of the HLA-C gene (the "-35 SNP") correlates with host control of HIV-1 in Caucasians: the minor allele (C) associates with lower set point viral loads than the major allele (T). A link between viral load and HLA-C is suggested by linkage of the two SNP alleles with different HLA-C alleles, and by the fact that HLA-C is not down-regulated by nef.

## Methods

We are investigating whether the -35 SNP correlates with the surface level of HLA-C using the antibody DT9, which recognises both HLA-C and HLA-E. The contribution of HLA-E to this staining is being assessed with the HLA-E-specific antibody MEM-E/06, and saturation-binding experiments are being used to measure the relative levels of HLA-E and HLA-C. We are also investigating functional differences individuals homozygous for the protective (C/C) and non-protective (T/T) -35 alleles.

## Results

DT9 staining of lymphocytes is significantly lower for T/T subjects compared with C/C subjects ($p = 0.046$), but this is due to HLA-Cw7. Staining of T/T individuals who are homozygous for Cw7 is significantly lower than for both C/C individuals ($p = 0.004$) and T/T individuals who do not have (or who are heterozygous for) Cw7 ($p = 0.007$). We see no difference in the frequency or magnitude of ex vivo T cell responses to HLA-C-restricted peptides between C/C and T/T HIV-infected subjects. Likewise, there is no difference in the ability of NK cells from C/C and T/T subjects to control the replication of HIV *in vitro*. T cell clones specific for HLA-C-restricted peptides are being generated to investigate if the efficiency of peptide presentation by antigen presenting cells correlates with the -35 SNP, and the interactions of NK cells with macrophages and dendritic cells are being addressed.

## Conclusion

DT9 staining suggests that surface levels of HLA-C are only significantly lower for T/T subjects who are homozygous for HLA-Cw7.