Retrovirology

Poster presentation

P16-24. Crucial contribution of sub-dominant HLA-C allele restricted CTL responses to the control of HIV

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Background

HLA-A and -B alleles have been associated with relative control of HIV disease and specific HLA-B restricted CTL responses have been implicated with effective antiviral activity. Despite recent reports finding genomic associations between the C locus and relative HIV control, little is know regarding HLA-C restricted CTL responses to HIV and their ability to facilitate viral control.

Methods

In a cohort of 248 HIV infected individuals from Peru, we determined the breath, magnitude and specificity of dominant and sub-dominant HLA-C restricted immune responses using an overlapping peptide set spanning the entire viral clade B HIV proteome.

Results

After correction for linkage disequilibrium with other HLA class I alleles, HLA-C alleles showed a wide range of relative protection from HIV disease progression, with HLA-C07, C08 and C17 alleles being associated with relative viral control while HLA-C04 was associated with high viral loads and low CD4 counts independently of HLA-B35 co-expression. Assessing "break-through" individuals, i.e. subjects who failed to control in vivo viral replication despite expressing one of the protective HLA-C alleles, indicate that relative control is in at least some cases mediated by sub-dominant T cell responses to HLA-C restricted epitopes.

Conclusion

These analyses strongly suggest that HLA-C restricted immune responses should be considered for HIV vaccine immunogen design, particularly also in the light of recent data indicating potentially synergistic effects of HLA-C restricted epitopes and recognition by NK cells.