Retrovirology

Poster presentation

P16-43. A hierarchy of antiviral activity between different epitope-specific CD8+ T cells can be attributed to early elimination of HIV-infected cells

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from AIDS Vaccine 2009
Paris, France. 19–22 October 2009

Published: 22 October 2009

Retrovirology 2009, **6**(Suppl 3):P272 doi:10.1186/1742-4690-6-S3-P272

This abstract is available from: http://www.retrovirology.com/content/6/S3/P272

Background

It has been hypothesised that the slow progression to AIDS exhibited by HLA-B*2705+ HIV-infected individuals is due to the immunodominant B*27-restricted response towards the p24 Gag epitope KK10 (Gag residues 263–272). This study aims to discern the contributing correlates of immune protection in HLA-B*2705+ HIV-infected individuals by comparing CD8+ T cell epitope specificity, cytokine profile, granzyme production and the kinetics of epitope presentation.

Methods

HLA-B*2705 MHC-I tetramers were used to enrich CD8+ T cell lines (>98% specific), specific for the Gag epitope KK10, the Vpr epitope VL9, and Pol epitope KY9. We compared the polyfunctionality, proliferation, granzyme production and specific killing capacity of these epitope-specific CD8+ T cells. We also compared the polyfunctionality and granzyme production of epitope-specific CD8+ T cells directly from ex vivo PBMCs. We then compared the ability of the different B*2705-restricted epitope specific CD8+ T cell lines (>98% specific) to suppress viral replication in vitro. HIV-permissive cells expressing B*2705 were infected and cocultured with the CD8+ T cells, firstly by synchronized magnetofection™ and monitored over 24 hours and secondly by 'natural' infection and monitored over 5–10 days.

Results

The Gag KK10- and Pol KY9-specific CD8+ T cells could elicit antiviral activity by 6 hours post-infection whereas the Vpr VL9-specific CD8+ T cells didn't elicit antiviral activity until 18 hours post-infection. We observed a clear hierarchy of antiviral potency dictated by epitope or HIV protein specificity (Gag KK10>Pol KY9>Vpr VL9). Antiviral activity did not correlate with polyfunctionality, proliferation, granzyme production or killing capacity.

Conclusion

The potent antiviral activity displayed by Gag KK10-specific CD8+ T cells may be due to early presentation of Gag epitopes on HIV-infected cells. A vaccine which promotes CD8+ T cells which can elicit early antiviral activity may help prevent viral dissemination during HIV infection and is a rational approach to vaccine design.