Retrovirology



Poster presentation

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P05-03. The use of immune complexes to enhance antibody responses against neutralizing epitopes on HIV envelope

CE Hioe*, M Visciano, R Kumar, J Liu and M Tuen

Address: Pathology, New York University School of Medicine, New York, USA

* Corresponding author

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

Published: 22 October 2009

Retrovirology 2009, 6(Suppl 3):P79 doi:10.1186/1742-4690-6-S3-P79

This abstract is available from: http://www.retrovirology.com/content/6/S3/P79

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Background

The capacity of immune complexes to augment antibody (Ab) responses is well established. The enhancing effects of immune complexes have been attributed mainly to Fcmediated adjuvant activity. On the other hand, antigenic alterations of specific epitopes as a result of immune complex formation have been less well studied.

Methods

We probed for alterations in the antigenicity of HIV gp120/Ab complexes using ELISA with monoclonal Abs specific for different gp120 regions. The immunogenicity of the gp120/Ab complexes was evaluated in mice immunized with the complexes.

Results

The data show that gp120/Ab complexes display higher reactivity with mAbs to the neutralizing epitopes on the V3 loop. Enhanced Ab responses to the V3 loop were detected in mice immunized with thegp120/Ab complexes. Importantly, potent neutralizing activity was observed in the sera immunized with the complexes, but not in the sera of mice immunized with uncomplexed gp120. However, the neutralization was highly restricted to the homologous HIV-1LAI strain. When the immune complexes were prepared using gp120 from a more representative subtype B HIV-1 strain (JRFL), high titers of Ab responses with distinct fine specificity were induced in the sera of immunized mice, but the breadth of serum neutralizing activity was still limited.

Conclusion

The binding of Abs to gp120 alters the antigenicity and immunogenicity of gp120, leading to enhanced potency of Ab responses against the neutralizing V3 epitopes. However, further studies are necessary to improve the breadth of the neutralizing Ab responses.