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The C5 region of HIV-1 gp120 binds specific

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Background

The C5 region of HIV-1 gp120 has sequence homology with both HLA class I and class II molecules. We have previously shown by UV cross linking that some peptides can bind gp120. In this study, using gp120 mutants and envelopes from a number of different HIV-1 and HIV-2 isolates, we report the specificity of this finding and explore the implications of these results for treatment.

Methods

We used mass spectrometry to determine the specific binding of selected peptides to gp120 preparations, one of which has the C5 region deleted. We also looked at the three dimensional binding of a number of HIV-1 and HIV-2 isolates.

Results

We show that HIV gp120 can bind peptides in a similar manner to HLA molecules and that this property is confined to the C5 region as the C5 deleted mutant has no binding ability. Moreover, we show this as a property of all HIV-1 isolates but not of HIV-2 isolates. Moreover, an antibody to the C5 region is able to inhibit mixed lymphocytic reactions in keeping with the structural similarity between this region and HLA.

Conclusion

The ability of the C5 region to bind peptides suggest that its similarity with HLA could drive a chronic activation process in certain HLA backgrounds. This property could also explain the antigen specific anergy which is reported prior to the decline in CD4 levels. We have previously reported that exposed but non infected individuals have high titre antibodies to this region and more recently it has been reported that long term non progressors also have high titre antibodies to this region. Although these antibodies are non neutralising in standard virus neutralization assays the antibodies may be able to neutralize the activation and hence the pathogenesis of disease. Therefore peptides from the C5 region could provide the basis of a more effective therapeutic vaccine.