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Effect of site-specific de-glycosylation on HIV gp120-specific CD4 T cell responses

Hualin Li*[1,2], Michael Tuen[1], Sandra Cohen[1], Maria Luisa Visciano[1] and Catarina Hioe[1]

Address: [1]New York University School of Medicine and Veteran Affairs Medical Center, New York, New York, 10010, USA and [2]Shanghai Medical College of Fudan University, Shanghai, China, 200032

* Corresponding author

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Background

Virus specific CD4+ T helper response is critical for maintenance of effective immunity against chronic viral infections. Vigorous HIV-specific T cell responses were found associated with control of viremia in HIV infected individuals. However, in most of the HIV infected individuals, virus specific CD4+ T cell responses are very low or undetectable. While the virus envelope is a critical target for the immune responses, this antigen is poorly immunogenic, especially for CD4+ T cells. One of the possible reasons is the heavy glycosylation of the envelope glycoproteins. In this study, we examined the effects of site-specific de-glycosylation on the presentation of gp120 antigen to the CD4+ T cells.

Materials and methods

Three potential N-linked glycosylation sites located in or flanking the CD4+ T cell epitope clusters in the C4 region of gp120 IIIB were disrupted by site-directed mutagenesis (N to Q) to generate mutants with single or multiple N-glycan deletions. Recombinant proteins were expressed in CHO cells, purified by affinity chromatography and analyzed for reactivity with soluble CD4 and various anti-gp120 mAbs in ELISA. The wild type and mutated proteins were then tested in 3H-thymidine incorporation assays for recognition by a mouse CD4+ T cell clone and a human CD4+ T cell line with specific C4 epitopes.

Results

The reactivities of all of the mutated gp120 proteins to sCD4 and anti-gp120 mAbs were comparable to the wild type, suggesting that no major conformation changes occurred after removal of the specific glycan(s). However, the removal of one N-linked glycans at the C4 region decreased recognition of CD4+ T cells tested, while the deletion of the two other glycans had either slightly enhancing or no effects. Studies are on-going to assess what steps in antigen processing and presentation are affected by these N-glycan removals. In addition, the effects of these mutations on recognition of CD4 T cell specific for epitopes in other regions (C1, C2 and V3) of gp120 are being analyzed.

Conclusion

Removal of certain glycan(s) near a T cell epitope cluster of gp120 did not alter its reactivity with CD4 and mAbs, but could modulate the recognition of these epitopes by CD4 T cells.