MOPE0045

Deficient class-switched IgG antibody response to the HIV CD4 binding site and neutralizing IgG synthesis induced by covalent immunization

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ABSTRACT

Background: Adaptive immune responses against HIV gp120 is mostly directed to the highly immunogenic and immunodominant variable domain of gp120 (V3 loop), and part of the gp120-superantigen determinant is poorly immunogenic.

Methods: HIV infected subjects sera were from the San Francisco Health Study for analysis. Subjects were divided into two groups, with gp120 and eneptidergic gp120 (E416-433) ovalbumin immunogen, or ovalbumin immunogen. gp120 and eneptidergic gp120 were further purified by affinity purification using immobilized ovalbumin or Pretein G columns.

Results: Affinity purified IgG and IgM from HIV infected subjects were tested for binding to immobilized E416-433 by ELISA. E416-433 binding IgG, but not IgM immunogen, displayed robust and specific binding to the CD4BS. CD4BS binding by IgM from E416-433-immunized mice was also detected. E416-433 binding IgM and IgG from the sera of gp120 immunized mice. Shown are the results of 3 immunizations using pooled sera from gp120 immunized mice. Shown are the results of 3 immunizations using pooled sera from gp120 immunized mice. Shown are the results of 3 immunizations using pooled sera from gp120 immunized mice.

Conclusions: This is the first direct evidence of IgG downregulation by gp120. gp120 induced IgM responses are characterized by a conventional adaptive maturation of the CD4BS during HIV infection and IgG immunization in antibody class shift a deficient IgG to IgM class switching of CD4BS specific IgG. Covalent immunization with E416-433 allows the IgM to IgG class switching to the poorly immunogenic CD4BS region.

INTRODUCTION

- Evaluation of human immunodeficiency virus (HIV) will require an effective approach to the vaccine problem.
- There is no consensus gp120 determinant necessary for binding the primary test cell or mediator (CD8+ T, the CD4 binding site (CD4BS), is poorly immunogenic.
- Antigens that neutralize HIV remain a key area for development.
- E416-433 is a highly conserved sequence present at the gp120 outer domain.
- E416-433 displayed robust and specific binding to the CD4BS, which is the critical determinant of HIV immunogenicity.
- Affinity purified IgM and IgG from HIV infected subjects were tested for binding to immobilized E416-433 by ELISA.
- Binding of IgM and IgG to immobilized E416-433 is specific and robust.
- IgM but not IgG from E416-433 immunization displayed robust and specific binding to the CD4BS.
- CD4BS binding by IgM from E416-433 immunization was also detected.
- E416-433 binding IgM and IgG from the sera of gp120 immunized mice.

METHODS

- E416-433 of phi (a T cell superantigen) contains six cysteine residues, which form the core immunogenic determinant of gp120.
- gp120 is a critical component of the HIV envelope.
- gp120 contains a highly conserved sequence located at the gp120 outer domain.
- The gp120 outer domain is highly conserved sequence at the gp120 outer domain.
- E416-433 displayed robust and specific binding to the CD4BS.
- Affinity purified IgM and IgG from HIV infected subjects were tested for binding to immobilized E416-433 by ELISA.
- Binding of IgM and IgG to immobilized E416-433 is specific and robust.
- IgM but not IgG from E416-433 immunization displayed robust and specific binding to the CD4BS.
- CD4BS binding by IgM from E416-433 immunization was also detected.
- E416-433 binding IgM and IgG from the sera of gp120 immunized mice.

RESULTS

- IgG from E416-433 immunization displayed weak class switching at levels of 120x
- IgM but not IgG from E416-433 immunization displayed robust and specific binding to the CD4BS.
- CD4BS binding by IgM from E416-433 immunization was also detected.
- E416-433 binding IgM and IgG from the sera of gp120 immunized mice.

CONCLUSIONS

- This is the first direct evidence of IgG downregulation by gp120.
- gp120 induced IgM responses are characterized by a conventional adaptive maturation of the CD4BS during HIV infection and IgG immunization in antibody class shift a deficient IgG to IgM class switching of CD4BS specific IgG. Covalent immunization with E416-433 allows the IgM to IgG class switching to the poorly immunogenic CD4BS region.

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