Retrovirology

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Oral presentation

Characterization of gp120 and Its Single-chain Derivatives, gp120-CD4 and gp120-M9: Implications for Targeting the CD4i Epitope in HIV-1 Vaccine Design

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Single-chain derivatives of gp120 linked to the first two domains of CD4 (gp120-$CD4_{D12}$) or to the CD4 analogue CD4M9 were assessed for their abilities to elicit CD4-induced neutralizing antibodies. Both complexes showed binding to a CD4i epitope as defined by the mAb 17b. Addition of exogenous CD4 did not increase 17b binding to gp120-$CD4_{D12}$ but augmented binding to gp120-M9 perhaps reflecting the lower binding affinity of M9 to gp120 compared to $CD4_{D12}$ or suggesting that M9 does not completely fill the CD4 binding site of gp120. Vaccination of guinea pigs and rhesus monkeys with recombinant protein or DNA prime followed by protein boosting generated broadly neutralizing antibodies only for sera generated against gp120-$CD4_{D12}$. Passage of these sera over a $CD4_{D12}$ affinity column removed neutralizing activities. Rhesus monkeys were also immunized with gp120-human CD4 or gp120-rhesus CD4 complex. Virus-neutralizing antisera were observed for each of these groups, but titers were much greater for the gp120-human CD4 complex. Neutralizing antibody titers showed a significant correlation to CD4 antibody titer for both vaccine groups. These data suggest that most neutralizing antibodies generated by gp120-CD4 complexes are directed against CD4.