Retrovirology

Poster presentation

P04-55 LB. Anti-V3 monoclonal antibodies display broad neutralizing activities against multiple HIV-1 subtypes

S Zolla-Pazner[4], T Wrin[1], MS Seaman[2], X Yu[3], B Wood[3], S Self[3] and CE Hioe*[4]

Address: [1]Monogram Biosciences Inc., South San Francisco, USA, [2]Beth Israel Deaconess Medical Center, Boston, USA, [3]SCHARP, Seattle, USA and [4]New York University School of Medicine, New York, USA

* Corresponding author

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Background

The V3 loop of gp120 was identified as the "principle neutralizing domain" of HIV-1, but because of its high sequence variability, V3 has been considered an inappropriate target for vaccines. However, V3 is a part of the Env that interacts with the chemokine receptors and therefore, despite its sequence variation, must retain conserved structural features. Nevertheless, the ability of anti-V3 antibodies to neutralize diverse HIV-1 isolates from different subtypes has remained in question.

Methods

HIV neutralization experiments were conducted in two independent labs to test seven anti-V3 monoclonal antibodies (mAbs) against a total of 98 pseudoviruses (psVs) expressing Env of HIV-1 subtypes A, B, C, D, and AG from acute and chronic patients. MAbs against parvovirus or anthrax antigens were used as negative controls. Statistically significant neutralization was determined based on evaluation of the area under the titration curve (AUC).

Results

Statistically significant neutralization ($p < 0.001$) was detected with each anti-V3 mAb against 26-35% of psVs but not with the irrelevant mAb controls. For many mAb/psV combinations, 50% neutralization was not attained at the highest mAb concentration tested (50 μg/ml), although dose-response relationships were demonstrated by the neutralization curves, and the AUC values were significantly above background. All seven mAbs showed statistically significant neutralizing activities against psVs carrying Envs of all subtypes tested. As many as 63% and 45% of psVs with subtypes B and C Envs had significant neutralization activity, respectively, by at least one anti-V3 mAb, although among psVs with Env of subtypes A and D, only one or two in each subtype (10-20%) were sensitive to the anti-V3 mAbs. Overall, 52 (53%) of 98 psVs showed significant neutralization activity against one or more anti-V3 mAbs.

Conclusion

While the neutralization potency of individual anti-V3 mAbs is generally low, anti-V3 mAbs display both intra- and inter-subtype neutralizing activities.