Retrovirology

Poster presentation

P04-03. Cross-clade neutralization analysis of plasmas from clade B, C and CRF01_AE HIV-infected donors

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Background

The genetic diversity of HIV-1, particularly in Env, is considered a major challenge for vaccine researchers, especially those attempting to elicit broadly neutralizing antibodies. Categorizing HIV strains into neutralization serotypes may help determine the requirements for maximal vaccine immune coverage. HIV is divided into clades, based on genetic relatedness, principally in Env. Investigations as to whether these clades might help to define neutralizing serotypes have so far mostly been confined to small studies, and have been hampered by the challenges of traditional PBMC-blast neutralization assays. The observation that some HIV+ plasmas neutralize viruses from several major clades hints of an undercurrent of conserved neutralization, but its potency relative to any clade-restricted activity is unknown. High throughput pseudovirus neutralization assays provide a way to investigate.

Methods

Here, we measured neutralization of 45 primary viruses from clades B, C and CRF_01 AE by 12 broad plasmas from the same 3 clades.

Results

Significant cross-neutralization was observed, and well-defined neutralizing serotypes was absent. However, each plasma exhibited a unique pattern against the spectrum of viruses. Increased intraclade neutralization titers was observed in many cases. These were most pronounced for clade B-E viruses that were neutralized 2–10 fold more potently by clade-matched plasmas in several cases. We also investigated binding serotypes by gp120 ELISA, where we observed greater intraclade binding titers for B-E plasmas, mirroring the intraclade neutralization. Mapping analyses suggested that in some cases, the cross-neutralizing activity is mostly directed to gp120 and overlaps the CD4 binding site.

Conclusion

The generally broad neutralization observed suggests that an immunogen based on one or a few Envs could, in principle, provide worldwide HIV-1 protection. Clade C Envs may be worth special attention, considering the particularly broad plasma neutralizing activities. The challenge remains to better define the cross-neutralizing specificities and moreover, to find immunogens able to induce them.