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Refined identification of neutralization-resistant CRF02_AG viruses and their sensitivity to anti-MPER neutralizing antibodies

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Background

The first antibody-inducing HIV-1 vaccines are unlikely to protect against all HIV-1 isolates. There is thus a danger that a vaccine will select for HIV-1 viruses that are highly resistant to antibody-mediated neutralization. We sought to identify and characterize such viruses.

Methods

A diverse panel of 24 HIV-1 pseudoviruses was tested for neutralization resistance using two sets of samples from ARV-naive HIV-1-infected individuals selected for good neutralizers: sera from South Africa donors (n=68, infected >1 year, subtype C predominant area) and CRF02_AG-infected plasma samples from Cameroon donors (n=12, good neutralizers selected from 22 samples).

Results

Sensitivity to South Africa sera by subtype was C>B≈CRF02_AG>A. Importantly, and in contrast to previous reports, CRF02_AG plasma neutralized CRF02_AG viruses better than other panel viruses ("within-subtype neutralization"). This included three (257-31, 251-18 and 33-7) of five CRF02_AG viruses previously designated as tier 3 (most resistant). This within-subtype neutralization testing showed that the other two tier 3 CRF02_AG panel viruses, 253-11 and 278-50 were highly resistant. Most CRF02_AG viruses, including 253-11 and 278-50 were sensitive to two membrane proximal external region (MPER)-specific monoclonal antibodies and soluble CD4 (sCD4), suggesting targets for neutralization of even these highly resistant viruses. This information may help design a global HIV-1 vaccine. We also propose testing viruses with within-subtype samples selected for good neutralizers in order to evaluate their neutralization resistance.

Conclusion

Some but not all CRF02_AG viruses are sensitive to neutralisation by CRF02_AG-derived plasma, even though most are previously reported as highly resistant (Tier 3). Further work is necessary to properly characterize such Tier 3 viruses. If research focus is not placed on such resistant viruses, a future partially effective HIV-1 vaccine may select for them.

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