Retrovirology

Poster presentation

P19-42. Engineering, expression and antigenic and immunogenic characterization of novel soluble clade A/B heterotrimeric gp140-envelope glycoproteins

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Background

The functional HIV-1 Env exists on the surface of infectious virions as a non-covalently associated trimer of heterodimers (gp120 and gp41). The protomers of the trimer are identical in composition and glycosylation and form a structure on which conserved neutralization epitopes are not readily exposed and are poorly immunogenic. We are investigating the possibility that conserved neutralization epitopes are less occluded and are more immunogenic on trimers that are composed of distinct protomers. We engineered, expressed and purified stable heterotrimers formed from Envs derived from SF162 (clade B primary isolate) and four clade A primary isolates (Q168a2, Q259d17, Q461e2 & Q769h5) and determined their antigenic and immunogenic properties.

Methods

Heterotrimeric gp140s were produced by transient transfection and purified using affinity, tag-based and size exclusion chromatography. Epitope exposure was determined by ELISA using mAbs. Rabbits were immunized with heterotrimeric Env SF162gp140His/Q461e2gp140FLAG) or with a mixture of the corresponding homotrimers, using PEI as an adjuvant. Antibody titers were determined using ELISA and Luminex.

Results

The CD4-binding site (and potentially the MPER) is better exposed on the heterotrimer compared to the corresponding homotrimers. Anti-Env antibody titers were elicited by both the heterotimer and mixed homotrimers, but distinct epitope specificities were evident. The heterotrimer elicited high titers of anti-4E10 antibodies, while such antibodies were not elicited by the corresponding mix of homotrimers. All animals immunized with the heterotrimer also elicited anti-2F5 antibodies. Thus, it appears that the MPER is highly immunogenic on the clade A/B heterotrimer.

Conclusion

The exposure and immunogenicity of specific epitopes differs between the gp140 heterotrimer and mixed homotrimers. The fact that the heterotrimer elicited high titers of anti-4E10 and anti-2F5 antibodies suggests that such constructs could be optimized to elicit neutralizing antibodies against these conserved neutralization epitopes.

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