Retrovirology

Poster presentation

P19-14. Recombinant alphavirus replicon particles as a platform to evaluate immunogenicity of early transmitted clade C virus envelopes

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Background

The primary objective of our current HIV vaccine research program is to develop and evaluate novel recombinant alphavirus replicon and Env protein-based vaccine formulations against HIV that may offer improved immunogenicity and protective efficacy over other HIV vaccine approaches tested. Our approach described here is to employ diverse HIV Env antigens from transmitted HIV strains as substrates for the development of vaccine immunogens with enhanced exposure to the immune system of the conserved epitopes involved in virus binding/entry. Previously, we showed that full protection of macaques from mucosal homologous SHIV challenge was achieved using recombinant VEE/SIN alphavirus Env prime Env protein boost. The aim of the present work is to build upon this work to identify novel Env immunogens.

Methods

22 early transmitted HIV-1 clade C envelopes were selected following specific criteria. For each envelope, gp140 uncleaved and gp140 uncleaved ΔV1V2 codon optimized genes were cloned and expressed in plasmid and alphavirus (VEE/SIN)-based vectors. In addition, the corresponding gp160 gene was used to produce molecularly matched infectious pseudoparticles for virus neutralization studies.

Results

All envelopes showed high levels of expression in 293T cells and 50% showed substantial levels of secretion into the cell culture medium. For each envelope, the expressed proteins were characterized for sCD4 and MAb binding to establish their integrity as well as their antigenic properties. The neutralization sensitivities of corresponding pseudoviruses are also under evaluation, and infectious recombinant alphavirus replicon particles expressing these Envs are in preparation.

Conclusion

We produced and characterized new vaccine candidates for preclinical evaluations based on 22 clade C HIV envelopes from early transmitted viruses. Immunizations using alphavirus prime plus Env protein boost will be initiated to elucidate the *in vivo* epitope recognition of these Env by animal hosts, and the relative abilities of these new antigens to induce virus neutralizing responses.