Retrovirology

Poster presentation

P12-01. Construction and characterization of recombinant envelope glycoproteins derived from HIV-1 pre-seroconversion strains as potential vaccine immunogens

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Background

The search for novel immunogens capable of eliciting neutralizing antibodies (NAbs) against HIV-1 is complicated by its high mutation rate which modifies envelope glycoproteins (Env) during the course of HIV-1 infection and drives NAb escape. However Env from transmission strains due to absence of NAb selection pressure could be antigenically distinct from late stage Env and hence profiling them would help identify novel vaccine immunogens capable of eliciting NAbs.

Methods

Blood samples were collected from 36 HIV-1 patients of pre-seroconversion (PSC) cohort based on p24 antigen, viral load, ELISA and western blot assays. Five samples (within Fiebig stage IV) were chosen to generate a panel of 28 gp160 clones. These were genotyped for amino acid changes in potential N-linked glycosylation (PNG) sites, length of variable loops (VL) and binding sites of receptors and neutralizing monoclonal antibodies (mAbs). These were phenotyped for Env mediated entry utilizing CD4, CCR5 and CXCR4. Recombinant gp140 clones were constructed to produce soluble gp140. Purified gp140 Env were assessed by ELISA for binding affinities to CD4, b12, 2G12, 2F5 and 17b+sCD4.

Results

The number of PNG sites and length of V4 VL were lower, with fewer changes in CD4, co-receptors and mAbs binding sites compared with AD8 and pNL4.3 reference sequences. 10(36%) PSC Env clones mediated entry using all 3 receptors. Recombinant gp140 Env clones were constructed, stably expressed and soluble oligomers purified. Affinities studies by ELISA for 5 selected Env in comparison with AD8, showed 4 Env to possess high binding affinities to CD4, b12, 2F5, 2G12, 17b+sCD4 and 2 Env to 2G12.

Conclusion

Characterization studies of PSC Env indicates that early Env have fewer modifications unlike late stage Env, signifying better exposure of conserved functional domains and neutralization sensitive epitopes required to elicit NAbs. The immunogenicity of PSC Env are currently being assessed in animal models.