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Poster presentation

P05-10. Sequential immunization with a subtype B HIV-1 envelope quasispecies elicits broader neutralization than vaccination with a single envelope clone

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Background

HIV-1 evolves rapidly within the host, resulting in the development of diverse HIV-1 variants called a viral "quasispecies" population. Envelope (Env) is the only target of neutralizing antibodies (NAbs), which can prevent infection of target cells. NAbs develop over time as the Envelope diverges. A major goal of HIV-1 vaccine efforts, so far elusive, is the design of Env-based immunogens effective at eliciting broad NAbs. We hypothesized that programming the B cell response could be achieved by exposing the host to a collection of env variants representing the viral quasispecies members.

Methods

Fifteen sequences were selected as representatives of the Env quasispecies in a macaque that developed broad NAbs following infection with $SHIV_{SF162P4}$. The exact sequences were created by site-directed mutagenesis in a codon-optimized expression plasmid. Rabbits were immunized via gp160 DNA prime (gene gun) and gp140 protein boost. Three vaccine strategies were compared: sequential env clones (Sequential), cocktail of env clones (Mixture), or single env variant (Clonal). Purified IgG was tested for binding and neutralizing antibodies.

Results

All strategies induced similar levels of Env-specific binding antibodies regardless of vaccine approach. All groups developed autologous NAbs, with better neutralization obtained in the clonal and sequential groups and with weaker responses to variants with increased number of potential N-glycosylation sites. The NAb response was partially directed against the V3 loop. Heterologous neutralization was observed in the sequential group.

Conclusion

This study is the first to explore the use of multiple native HIV-1 Env variants as immunogens. Immunization with a collection of env quasispecies variants resulted in the development of broader NAbs than immunization with a single *env* gene alone, suggesting that it is possible to educate the immune system by exposing it to a native HIV-1 quasispecies derived from an individual with a broadened NAb response.