Retrovirology

Poster presentation

P03-10. Induction of neutralizing antibodies in Rhesus macaques following mucosal challenge with R5 tropic SHIV162P3 isolate

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Background

Induction of broadly reactive neutralizing antibodies still remains an elusive goal for HIV vaccine development. Although HIV-1-infected individuals typically develop neutralizing antibodies against Tier 1 isolates, significant breadth in antibody response has been observed only in a few patients. Understanding the mechanism of the induction of broadly neutralizing antibodies in HIV-infected humans may help in designing vaccines capable of eliciting such responses in immunized hosts. SHIV-infected nonhuman primates represent a useful model to understand how such broadly reacting antibodies are induced following infection.

Methods

Macaques were challenged with SHIV isolates encoding R5 HIV-1 Env (SHIV162P3) via rectal route and the serum was tested for neutralizing antibody responses against Tier 1 and Tier 2 viruses and against the challenge virus over time. An escape variant from an infected macaque was isolated and characterized by molecular and immunological methods.

Results

Induction of neutralizing antibodies was observed in SHIV162P3-infected animals within 90 days post challenge. Although sera from these animals easily neutralized Tier 1 isolates with varying titers, neutralization of Tier 2 isolates was noted in a few animals that had higher titers against Tier 1 isolates. Viral replication persisted in these animals despite the presence of broadly neutralizing antibodies thereby resulting in the generation of escape variants. Characterization of one such variant from an infected animal with AIDS revealed significant sequence changes in the V2 region of the envelope. This variant was easily neutralized by sCD4 and CCR5 antagonist but remained resistant to neutralization by anti-gp120 antibody b12 and by sera from SHIV162P3-infected animals.

Conclusion

These results suggest that broadly neutralizing antibody response is generated in SHIV162P3-infected macaques mainly due to the persistence of viral replication. Characterization of one such SHIV variant generated in the infected animals revealed changes in neutralization profile and envelope sequences.