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P03-01. The relationship of envelope evolution to lentiviral persistence and vaccine efficacy

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Background

We recently reported a direct, inverse, significant linear correlation of Env divergence from our live-attenuated vaccine strain (EIAVD9) and protection from disease. This marked effect of Env variation or viral evolution on vaccine efficacy begged the current questions: what is the relationship of Env variation and viral evolution to vaccine efficacy and does the evolution of virus in inapparent carriers differ from the evolution of attenuated vaccine viruses? Hence we further examined this relationship of Env divergence, evolution, and vaccine efficacy via investigations into Env evolution during inapparent infections, the elimination of ancestral viral species in infected ponies, and EIAVD9 day of challenge (DOC) evolution association with vaccine protection.

Methods

To implement this study we first examined Env populations from an experimentally infected long-term inapparent-carrier treated with dexamethasone to abrogate immune control of infection and enhance replication of viral quasispecies from reservoir tissues. Second, DOC Env populations were examined from 24 outbred ponies that were vaccinated with EIAVD9 and subsequently challenged with three challenge strains of increasing Env divergence from the vaccine strain.

Results

Characterization of the inapparent-carrier populations revealed only novel quasispecies distinct from all previous populations. Comprehensive analysis of tissue and

plasma samples from immune suppressed carriers indicated that the original infectious inoculum and early viral populations were evidently eliminated. DOC sequence analysis of EIAVD9 vaccinates demonstrated viral evolution, although at lower levels than observed with virulent EIAV strains at 7 months post-infection. EIAVD9 evolution revealed a significant association with vaccine protection from disease.

Conclusion

Env evolution is a double-edged sword: in the context of a live-attenuated vaccine strain it is associated with increased protection from disease upon challenge. Conversely, while the host immune system is able to eliminate a diverse array of variants, viral persistence is maintained by a relentless evolution of new Env populations from tissue reservoirs.