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P17-06. Development of a replication-defective Herpes Simplex virus 1 recombinant expressing HIV-1 clade A envelope protein

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Background

The HSV-1 d106 mutant virus is a promising viral vector because it allows robust expression of the foreign antigen, induces a balanced cellular and humoral immune response and is efficacious in HSV-immune animals. It has deletions in immediate-early genes ICP4, ICP22, ICP27 and ICP47 that render it absolutely replication-deficient in normal cells, thus making it safe for use as a vaccine vector. Recently, in a prime-boost regimen, d106 recombinants expressing SIV proteins have shown significant protection in the SIVmac239 challenge model in rhesus macaques (Kaur et al., 2007 and unpublished results).

Methods

Using homologous recombination we have engineered an HSV-1 d106 recombinant vector that expresses a codon-optimized envelope glycoprotein (env) of Clade A HIV-1. Western blotting and immunofluorescence analysis indicate that robust expression of env continues for as long as 48 hours post infection in infected cells in culture, and that the env expression cassette is completely stable in the vector for at least 8–10 passages of the recombinant virus in culture. Viral yields of 250 pfu/cell are observed; thus, production should be feasible. Quantitative real-time PCR enumerates viral preparations as having particle: PFU ratios of 10–80, documenting the high specific infectivity of the preparations.

Results

These results support the development of d106-EnvA as a lead vector for clinical trials and our studies strengthen the potential of these recombinant vectors as promising clinical products.

Conclusion

This work is part of an effort to generate a panel of replication-deficient HSV-1 vectors expressing HIV antigens from various clades, which will allow a comparison of other viral vaccine vectors and development of potential combined vaccine regimens in the search for an effective HIV vaccine.