Immunogenicity testing of multi-gene HIV-1 (CRF02_AG) DNA vaccine constructs

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Background: We developed an AIDS vaccine for West Africa based on a DNA plasmid vector expressing CRF02_AG gag, pol, tat, rev, vpu, and env genes. To optimize the production of HIV-like particles (VLP) and potentially improve the effectiveness of the vaccine, we generated two vaccine constructs: a non-mature (unprocessed Gag Pr55 comprises the core) VLP expressing construct (IC25) and a mature (processed capsid p24 comprises the core) VLP expressing construct (IC48). To determine whether there is improved immunogenicity from mature VLPs, immunization trials were initiated.

Methods: Young adult rhesus macaques (n=16) were immunized with 0.6 mg of either IC25 or IC48 DNA intramuscularly (IM) at 0, 8, and 24 weeks. DNA priming will be followed by a modified vaccinia virus Ankara (MVA) IM boost expressing Gag, Pol and Env CRF02_AG proteins. Serologic responses and peak cellular responses, evaluated with peptide pools made from the vaccine construct CRF02_AG sequence, will be measured for all animals. We are also evaluating the extent of immunologic cross-recognition for diverse HIV-1 subtypes by using peptide pools from Kenyan A, U.S. B, and Thai A/E sequences.

Results: While IC25 expressed predominantly immature VLPs when transfected in vitro, the IC48 construct (encoding an attenuated protease) produced mature VLPs in vitro and could fuse and enter cells analogous to wild-type HIV. As anticipated, no serologic responses were detected following DNA prime immunizations in non-human primates. 4 of 8 animals from each construct group had detectable T-cell responses using IFN-γ ELISPOT analyses following DNA priming, although no difference between groups was observed. Peak MVA-induced serologic and cellular responses are anticipated by late summer, 2003.

Conclusions: While both vaccine constructs are projected to prime significant cellular responses reminiscent of DNA vaccines, production of mature VLPs in vivo may still hold yet unappreciated immunologic advantages.