

## ENHANCED SENSITIVITY OF DETECTION OF CYTOTOXIC T LYMPHOCYTE RESPONSES TO HIV TYPE 1 PROTEINS USING AN EXTENDED *IN VITRO* STIMULATION PERIOD FOR MEASURING EFFECTOR FUNCTION IN VOLUNTEERS ENROLLED IN AN ALVAC-HIV PHASE I/II PRIME BOOST VACCINE TRIAL IN THAILAND

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A phase I/II prime-boost vaccine trial in HIV-1-seronegative adults was conducted in Thailand using ALVAC-HIV (vCP1521) as a prime, boosting with either oligomeric gp160 TH023/LAI or Chiron HIV Thai subtype E (CM235) plus U.S. subtype B (SF2) gp120. Cytotoxic T lymphocyte (CTL) assays were conducted at one of the vaccine trial sites (Siriraj Hospital) at a single time point following the completion of immunization demonstrated that 8 of 50 (16%) vaccine recipients showed HIV-specific CTL by standard chromium release assay (CRA) after *in vitro* stimulation (IVS) for 2 weeks. Five additional vaccinees (13/50 = 26%) showed CTL responses after IVS for up to 4 weeks. Moreover, one volunteer with a positive CTL response to a single HIV antigen at Day 14 demonstrated a response to an additional HIV-1 antigen(s) after the longer IVS period. CTL activity was CD8<sup>+</sup> restricted. Despite extension of the IVS up to 4 weeks, no CTL responses were detected in placebo recipients. These results imply that extension of the IVS period may increase the sensitivity of the CRA when measuring HIV-specific CTL in ALVAC-HIV prime-boost recipients without compromising specificity.

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## EVOLUTION OF ENVELOPE SEQUENCES IN HIV-1 SUBTYPE CRF01\_AE INFECTED THAI PATIENTS WITH DIFFERENT RATES OF DISEASE PROGRESSION

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**Background:** To understand the relationship between disease progression and amino acid variations of envelope region of HIV-1 subtype CRF01\_AE and to determine whether sequence changes on env due to selective immune pressure.

**Methods:** We obtained and analyzed sequences of the V1-V5 region of the HIV-1 env gene from nine HIV-1 subtype CRF01\_AE (E) infected Thais. Five are progressors (PRs; follow-up CD4<sup>+</sup> cells < 200/mm<sup>3</sup> and progression to AIDS) and four are slower progressors (SPs; asymptomatic and/or follow-up CD4<sup>+</sup> cells > 350/mm<sup>3</sup> at the end of follow-up). HIV-1 DNA from two time points per individual were directly sequenced. They were followed at least 16 months. Selective pressure at the amino acid level was measured by using the synonymous/nonsynonymous base substitutions (ds/dn) ratio and ds/dn ratio of PRs and SPs were compared between early and late time points.