

Results: Phylogenetic trees showed that there was no specific clustering between PR's env gene versus those in SPs. In V3 region, GPGQ motifs were found in all SPs and predicted phenotype of SPs were all NSI, while V3 region of PRs evolved more rapidly. There was deglycosylation of env V3 sequence of HIV-1 subtype CRF01_AE infected PRs, whereas it was conserved in SPs. Positive selective pressure operated only on env V3 region in PRs and this reflected nonsynonymous substitution accumulation on env V3 region in PRs.

Conclusions: These findings showed that the host immune responses may be one selective pressure driving sequence changes in V3 region in PRs.

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FOUNDATIONS FOR A PHASE III HUMAN IMMUNODEFICIENCY VIRUS VACCINE TRIAL: A DECADE OF THAI-U.S. ARMY COLLABORATIVE RESEARCH

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As part of the response of the Royal Thai Army to the outbreak of human immunodeficiency virus (HIV) in Thailand, a collaboration was established with the U.S. Army to jointly work toward the development of vaccines for the prevention of HIV infection. During the first decade of this collaboration, studies have been carried out in the diverse disciplines that are crucial to providing the foundations for efficacy trials of candidate HIV vaccines. Studies of host, pathogen, and vaccine interventions included studies of viral diversity, epidemiology, disease course, potential vaccine cohorts, and Phase I/II clinical trials. Collaborations were expanded to other Thai institutions and to overseas partners, resulting in the Thai AIDS Vaccine Evaluation Group. The efforts of these collaborations resulted in the development of candidate vaccines specifically designed for use in Thailand, and sequential evaluations that have led to the threshold of the world's next and largest efficacy trial of HIV vaccines.

Mil Med. 2004; 169(8): 588-93.

HLA CLASS I SEROTYPES AND CYTOTOXIC T-LYMPHOCYTE RESPONSES AMONG HUMAN IMMUNODEFICIENCY VIRUS-1-UNINFECTED THAI VOLUNTEERS IMMUNIZED WITH ALVAC-HIV IN COMBINATION WITH MONOMERIC GP120 OR OLIGOMERIC GP160 PROTEIN BOOSTING

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Antigen-induced cellular immunogenicity may vary between populations due to differences in human leukocyte antigen (HLA) diversity and, hence, may play a critical role in the protection

afforded by vaccines. In the setting of two, phase I/II human immunodeficiency virus-1 vaccine trials of a recombinant canarypox prime, and boosting with either recombinant monomeric gp120 or oligomeric gp160, we assessed the association between specific human leukocyte antigen (HLA) class I serotypes and the presence of cytotoxic T-lymphocyte response measured by ^{51}Cr -release assay. HLA class I serotypes A11, A24, A33, B46, and B75 were the most common, present in 10% or more of 245 individuals studied. Forty of 187 (21.4%) Thai adults who received either ALVAC-HIV with gp120 or oligomeric gp160 or ALVAC alone had a precursor cytolytic CD8 T-cell response (pCTL). HLA-B44 was positively and significantly associated with a pCTL response (odds ratio 7.6, 95% CI: 2.7-21.2), whereas B46 was negatively associated but not robust when adjusted for multiple comparisons. Responses to Env proteins accounted for the majority (nine of 11) of pCTL activity among those persons with B44. This HLA class I serotype occurred in 9.4% of participants overall (including the placebo group), less commonly than what is reported from populations of European ancestry. These results strengthen the importance of assessing HLA class I distributions in conjunction with studies of vaccines designed to elicit cellular immunity in different populations.

Tissue Antigens. 2004; 64(3): 251-6.

IMMUNE RECONSTITUTION FOLLOWING AUTOLOGOUS TRANSFERS OF CD3/CD28 STIMULATED CD4⁺ T CELLS TO HIV-INFECTED PERSONS

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We have previously shown that adoptive transfer of in vitro CD3/CD28 activated autologous CD4⁺T cells results in increased CD4 counts and CD4/CD8 ratios in HIV+ subjects. In this report, analysis of variable beta (Vbeta) chain T cell receptor (TCR) repertoire showed that CD3/CD28 stimulation was able to increase polyclonality within skewed spectra types in vitro. In vivo, two of eight subjects showed increase in TCR diversity and importantly, in no subject did a highly skewed in vivo repertoire emerge. Measurement of proliferative response to alloantigen showed increases following infusions. Response to pharmacological stimulus and lectin via Interferon- γ ELISpot assay showed increases in a subset of subjects following infusions. However, interferon- γ response to HIV antigens and peptides declined concurrent with stable or diminishing latent infectious viral load in CD4⁺T cells. These data provide further evidence that adoptive transfer of activated autologous CD4⁺ T cells can augment the immune system.

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