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JUTHAMAS CHUETHONG : IN VIVO SEQUENCE VARIABILITY OF VIRAL PROTEASE OF HIV-1 SUBTYPE E FROM THERAPY-NAIVE THAI PATIENTS. THESIS ADVISORS : WICHET LEELAMANIT, Ph.D., SAKOL PANYIM, Ph.D. 91 p. ISBN 974-663-048-2

HIV-1 isolates are genetically classified into different subtypes according to *env* and *gag* coding sequences. In Thailand, approximately 90% of infected subjects are infected with HIV-1 subtype E while less than 10% are infected with HIV-1 subtype B, respectively. Since any mutation in HIV-1 protease (PR) may generate protease-resistant strains and also the susceptibility of HIV-1 subtype E to protease inhibitors has not been investigated, information on *in vivo* sequence diversity of subtype E PR will lead us to a better understanding of the sensitivity of HIV-1 subtype E protease to inhibitors. We have analyzed 100 protease-coding sequences from 10 therapy-naive Thai patients collected between 1996-1997. Briefly, polymerarse chain reaction technique was used to amplify protease-coding regions from the proviral DNA isolated from peripheral blood mononuclear cells. The data indicated that the protease sequences of subtype E were unique and clearly different from the HIVHXB2CG, the referent strain for subtype B, at eight positions (V3I, I13V, E35D, M36I, S37N, R41K, H69K, and L89M). Protease variants analyzed from a same subject were nearly homogeneous and different from patient to patient. The frequency of critical drug-resistant substitutions was very low. Only V82I was identified in one clone. The frequency of the secondary drug-resistant substitutions including L10I, M36I, L63P, and N88S was 1.18%. In addition, the upstream and the downstream domains of HIV-1 protease, which are located at the p6*/PR and the PR/RT cleavage sites, respectively, were analyzed. The frequency of amino acid variations of the upstream domain was 45.20%, while the amino acid sequences of the downstream domains were absolutely conserved.