

4037854 MBMG/M : MAJOR: MOLECULAR GENETICS-GENETIC ENGINEERING; M.SC. (MOLECULAR GENETICS-GENETIC ENGINEERING)

KEY WORDS : HIV-1 SUBTYPE E / HIV PROTEASE / PROTEASE INHIBITOR / DRUG RESISTANCE/ REVERSE TRANSCRIPTASE INHIBITOR

RERNGWIT BOONYOM: IN VIVO VARIABILITY OF VIRAL PROTEASE FROM HIV-1 SUBTYPE E INFECTED THAI PATIENTS TREATED WITH REVERSE TRANSCRIPTASE INHIBITORS. THESIS ADVISORS: SAKOL PANYIM, Ph.D., WICHET LEELAMANIT, Ph.D. 118 p. ISBN 974-663-046-6

Human immunodeficiency virus type 1 (HIV-1) protease (PR), an aspartic enzyme, cleaves viral precursor proteins to become mature proteins. This proteolytic process is required to complete the viral life cycle, thus generating infectious particles. Therefore, many investigators have intensively studied genetic diversity, enzymatic behavior, and inhibitor susceptibility of HIV-1 PR.

For example, studies of HIV-1 PR coding domain from zidovudine treated patients infected with HIV-1 subtype B showed the appearance of resistance mutations to protease inhibitors. In this project, we analyzed the variability of viral protease from HIV-1 subtype E epidemically in Thailand. Our analysis of 100 protease coding domains from 10 patients who had received RT inhibitors but no protease inhibitor indicated that many amino acid substitutions associated with protease inhibitor resistance were detected. The amino acid substitutions including M36I and V82A which have been proven to be associated with drug resistance were found in subtype E PR variants. The consensus sequence of the PR variants showed similarity with the CM240 reference sequence from subtype E, but it was clearly different from other subtypes. In addition, much variability appeared in the P6/PR cleavage site, while sequences of the PR/RT cleavage site were absolutely conserved.