

P10 GENETIC POLYMORPHISM OF THIOPURINE S-METHYLTRANSFERASE IN A NORTHEASTERN THAI POPULATION

Somrudee Srimartpirom¹, Wongwiwat Tassaneeyakul², Veerapol Kukongwiriyapan¹, Wichittra Tassaneeyakul¹

¹*Department of Pharmacology, Faculty of Medicine, ²Department of Toxicology, Faculty of Pharmaceutical Sciences, Khon Kaen University, Khon Kaen 40002, Thailand.*

ABSTRACT

Genetic polymorphism of Thiopurine S-methyltransferase (TPMT) is a cytosolic enzyme that preferentially catalyzes the S-methylation of thiopurine drugs including azathioprine, 6-mercaptopurine and thioguanine. TPMT activity exhibits autosomal codominant genetic polymorphism and patient inheriting TPMT deficiency are at high risk of potentially fatal hematopoietic toxicity. To date, more than eight mutant alleles have been reported, with TPMT*2, TPMT*3A and TPMT*3C being the most common mutant alleles. These variant alleles results from point mutations in the TPMT open reading frame leading to decrease in enzymatic activity. Ethnic differences in the frequency of mutant alleles are now recognized. TPMT*3A is the most prevalent mutant allele in Caucasians, with TPMT*3C and TPMT*2 being rare allele whereas TPMT*3C is the most prevalent mutant allele in East Asians. The aims of the present study were to elucidate the genetic basis for the TPMT polymorphism in a Northeastern Thai population. TPMT*1 to TPMT*3 were analyzed using the polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) and allele specific PCR. Among the 200 Northeastern healthy Thai subjects genotyped, 181 subjects (90.5%) were homozygous wild type allele (TPMT*1/TPMT*1), 18 subjects (9.0%) were heterozygotes (TPMT*1/TPMT*3C) and 1 subject (0.5%) was homozygous mutant (TPMT*3C/ TPMT*3C). Only TPMT*3C variant allele was found in this population and the frequency of this mutant allele accounts for 5%. This study confirms ethnic differences in TPMT allele frequency and about 9.5% of a Northeastern Thai population have an increased risk for thiopurine-induced toxicity.

Key words: Thiopurine S-methyltransferase, TPMT, Thai, genetic polymorphism