CANCER PHARMACOGENOMICS: THE RELEVANCE OF GENETIC PROFILE IN OPTIMIZATION DRUG THERAPY FOR AZATHIOPURINE AND 5-FLUOROURACIL

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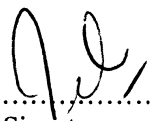

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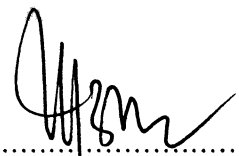

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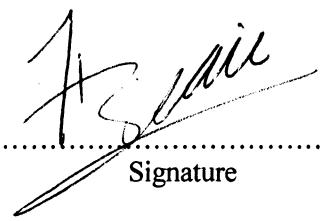

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ABSTRACT

Title:

Introduction: Pharmacogenomic studies contribute to genetic information in preventing severe side effects of drugs. Genetic polymorphisms in drug metabolizing enzymes such as dihydropyrimidine dehydrogenase (DPD) had been associated with variable clinical outcomes in many commonly prescribed chemotherapy drugs including 5-Fluorouracil and irinotecan.

Objectives: The review of literature had shed lights to the importance and possible impact of genetic polymorphism of *DPYD* and *TPMT* in individualization of drug therapy for 5-FU and thiopurines. However, there were no data reported for Malaysian. Current study thus aimed to explore the role of pharmacogenetics in personalized medicine in our own population.

Materials and methods: Genotyping methods for *DPYD* and *TPMT* were developed using dHPLC and allele specific PCR respectively. 5-FU levels were measured in colorectal cancer patients using developed method. DNA from healthy volunteers and patients were screened.

Results: Genotyping of *DPYD* had detected one reported mutation *DPYD*5*, two new mutations in exon 14 1823 T>C and 1827 G>A and one intronic reagion of exon 13, 13 IVS-11G>A with allele frequencies of 14.5%, .9.1%, 9.1% and 0.9% respectively. Genotyping for *TPMT* revealed 7 (7%) to be heterozygous for *TPMT* variant alleles. The predominant allele detected is TPMT*3C and is in concordance with previous studies done on Southeast Asian populations.

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