RAPID SCREENING FOR C3435T POLYMORPHISM IN EXON 26 OF THE MULTI-DRUG RESISTANCE (MDR1) GENE IN MALAY PATIENTS WITH ACUTE LEUKEMIA

Y. Badrul Hisham[1], H. Rosline [2], W. M. Wan Maziah [3], S. Mohammad Ros [1], B. Abdul Aziz [1], B. Norsa'adah [4] M. Y. Narazah[5]

[1]Human Genome Center, [2]Department of Hematology, [3]Department of Pediatrics, [4]Unit of Biostatistics & Research Methodology, School of Medical Sciences, Health Campus, Universiti Sains Malaysia, [5]Advanced Medical and Dental Institute (AMDI), Universiti Sains Malaysia

Introduction: The over expression of P-glycoprotein has been found to be associated with therapy resistance in hematological malignancies including acute leukemias. Recently, a single nucleotide polymorphism (SNP) in exon 26 (C3435T) in the MDR1 gene has shown to have functional consequences with altered expression of P-gp. Denaturing HPLC has been established as a rapid method for screening SNP in the form of heteroduplex of the DNA samples under partially denaturing condition.

Objective: To develop a rapid denaturing HPLC technique for screening a C3435T polymorphism in exon 26 of the multi-drug resistance (MDR1) gene in Malay patients with acute leukemia.

Methodology: The SNP C3435T was determined by using dHPLC technique in 83 Malay patients diagnosed as acute leukemia; 35 (34.0%) were acute myeloid leukemia (AML) and 48 (46.6%) were acute lymphoblastic leukemia (ALL) from HUSM. The profiles of dHPLC analysis were compared with wild type samples as a control.

Results: The optimum temperature for detection of C3435T mutation was empirically optimized at 61^{o}C. Of 48 sample of ALL subjects, 19 (39.58%) were single peak for homozygous wild-type CC, 20 (41.67%) were heterozygous peaks for heterozygous CT mutation while 9 (18.75%) were homozygous TT mutation. Of 35 sample of AML subjects, 9 (25.72%) were single peak for homozygous wild-type CC, 23 (65.71%) were heterozygous peaks for heterozygous CT mutation while 3 (8.57%) were homozygous TT mutation.

Conclusion: The use of denaturing HPLC in mutation detection was reliable because of its sensitivity and specificity. Thus, denaturing HPLC is a good candidate for routine screening and detection of mutations in medical as well as research settings.