ABSTRACT

The synergistic effect of gene polymorphisms on drug induced side-effects among patients with pulmonary tuberculosis

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Background: Polymorphisms may decrease detoxification gene activities and cause illness in affected individuals. This study investigates the relationships between detoxification protein gene polymorphisms and drug induced side-effects of anti-tuberculosis (TB) disease drugs among patients with pulmonary tuberculosis.

Materials and Methods: 64 TB-infected cases (23 cases and 41 controls) were included in analysis. We designed the natural or mutagenesis primers to detect the variant genotypes found in the study subjects. The polymerase chain reaction (PCR) products were digested with appropriate restriction enzymes and the restriction fragment length polymorphism (RFLP) patterns were analyzed to determine nucleotide variations.

Results: The synergistic effects were found between UGT1A7 and CYP2E1 in the study. The odds ratio of 2.25 (95% CI = 1.12-6.32) was found when patients with both UGT1A7*3 and CYP2E1*c1 genotype. This study indicated that the UGT1A7 and CYP2E1 polymorphisms may correlate the drug induced side-effects among TB patients in Taiwan. Checking liver enzymes and detoxification genotype before treatment and regular monitoring liver enzymes during treatment are highly recommended.

Discussion: Application of pharmacogenetics or pharmacogenomics, such as assessing UGT and CYP genetic polymorphism, may help prevent this hepatotoxicity. The results from these investigations will prove to be helpful for understanding the side-effects of TB and provide novel insights in controlling mycobacterial infection in our population.