

## O1: FREQUENT CO-OCCURRENCE OF POLYMORPHISMS IN UDP-GLUCURONOSYLTRANSFERASE 1A1 AND 1A6 IN THAI $\beta$ -THALASSEMIA/HbE AND AFRICAN AMERICAN SICKLE CELL ANEMIA PATIENTS

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### ABSTRACT

UDP-glucuronosyltransferases (UGTs) are important Phase II metabolizing enzymes. This enzymes can conjugate with a wide variety of endogenous and exogenous compounds. The UGT 1A family contains many isoforms. The polymorphism or variant of different isoforms may involve with many diseases and abnormal drug metabolism. Polymorphism of UGT1A1 (UGT1A1\*28) is associated with Gilbert's syndrome, a deficiency in glucuronidation of bilirubin leading to mild hyperbilirubinemia. While two missense mutations on one allele of UGT1A6 (UGT1A6\*2) results in the lower glucuronidation rates of several drugs. Previous studies revealed that there is strong association of hyperbilirubinemia and gallstone formation in  $\beta$ -thalassemia/Hb E and sickle cell anemia patients with the number TA repeats in the promoter of the UGT 1A1 gene. This communication is a report of our preliminary data of genetic polymorphism of UGT 1A in 260 Thai  $\beta$ -thalassemia/Hb E and 163 African American sickle cell anemia patients. Genomic DNA was obtained by standard methods from peripheral blood leucocytes. The promoter region of UGT 1A1 and coding region of UGT 1A6 were sequenced by automated sequencing. The frequencies of the TA repeats 6/6, 6/7 and 7/7 at the promoter of UGT1A1 gene in  $\beta$ -thalassemia/Hb E and sickle cell anemia patients were 0.711, 0.277, 0.011 and 0.251, 0.313, 0.135, respectively. However none of the  $\beta$ -thalassemia/Hb E cases have the following genotypes; 5/6, 5/7, 5/8, 6/8 and 7/8, while it was found in 28.8% of sickle cell anemia cases. Co-occurrence of UGT1A1\*28 and UGT1A6\*2 was found in both groups. Sixteen haplotypes were revealed including a haplotype consisting of allelic variants of all two isoforms.

This preliminary data suggest that the polymorphism of drug metabolism enzyme gene may involve in the drug use, individualized medicine in Thai patients.

**Key words:** UDP-glucuronosyltransferases (UGTs),  $\beta$ -thalassemia/Hb E, sickle cell anemia