**UDP Glucuronosyltransferase 1A1 (UGT1A1) Genotyping**

**ARUP test code 0051332**

**UGT1A1 Genotyping Specimen**
Whole Blood

**UGT1A1 Genotyping Allele 1**
(TA)6 or *1

**UGT1A1 Genotyping Allele 2**
(TA)7 or *28 *

**UGT1A1 Genotyping Interpretation**

See Note

Indications for ordering:
- Determine sensitivity to irinotecan or related compounds.
- Confirm a diagnosis of Gilbert Syndrome.

Heterozygous UGT1A1 (TA)6/(TA)7: One copy of *1 (TA)6 and one copy of *28 (TA)7 were detected. Partially decreased UGT1A1 enzyme levels are anticipated. Dosing should be based on clinical findings. Heterozygosity for the *28 allele has not been associated with Gilbert's syndrome (benign familial hyperbilirubinemia).

This result has been reviewed and approved by Rong Mao, M.D.

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**H=High, L=Low, *=Abnormal, C=Critical**
BACKGROUND INFORMATION: UDP Glucuronosyltransferase 1A1 (UGT1A1) Genotyping

CHARACTERISTICS: UGT1A1 is responsible for the clearance of drugs (e.g., irinotecan) and endobiotic compounds (e.g., bilirubin). Irinotecan's major active and toxic metabolite (SN-38) is inactivated by the UGT1A1 enzyme and then eliminated via the bile. UGT1A1 gene mutations cause accumulation of SN-38, which may lead to irinotecan-related toxicities (neutropenia, diarrhea).

CAUSE: Variations in TA repeat number in the TATAAA element of the 5' UGT1A1-promoter affects transcription efficiency. The common number of repeats is six [(TA)6, *1 allele], while seven repeats [(TA)7, *28 allele] is associated with reduced transcription activity. Homozygosity for the (TA)7 allele is also associated with Gilbert Syndrome (benign familial hyperbilirubinemia).

ALLELES TESTED: *36 allele, (TA)5; *1 allele, (TA)6; *28 allele, (TA)7 and *37 allele, (TA)8.

- 6/6 (*1/*1): diarrhea 17 percent; neutropenia 15 percent
- 6/7 (*1/*28): diarrhea 33 percent; neutropenia 27 percent
- 7/7 (*28/*28): diarrhea 70 percent; neutropenia 40 percent

ALLELE FREQUENCY:
- *1(TA)6: Caucasians 0.61, Asians 0.84, African Americans 0.47
- *28(TA)7: Caucasians 0.39, Asians 0.16, African Americans 0.43

METHODOLOGY: Polymerase chain reaction followed by size analysis using capillary electrophoresis.

LIMITATIONS: Variations in the UGT1A1 gene, other than those targeted, will not be detected. Clinical significance of the rare *36, (TA)5 and *37, (TA)8 alleles in predicting irinotecan toxicities is not well established. Genetic and non-genetic factors other than UGT1A1 may contribute to irinotecan toxicity and efficacy. Diagnostic errors can occur due to rare sequence variations.

Test developed and characteristics determined by ARUP Laboratories. See Compliance Statement C: aruplab.com/CS
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