

UGT1A1 PROMOTER GENE POLYMORPHISM (TA REPEATS) ASSAY

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TriCore Reference Laboratories now offers testing for *UGT1A1* gene polymorphism. This assay identifies the number of TA repeats in the 5' promoter region of the *UGT1A1* gene that predict toxicity from irinotecan therapy which is widely used in metastatic colorectal carcinoma and other solid tumors. It can also identify the *UGT1A1* variant commonly present in Gilbert's syndrome.

The *UGT1A1* enzyme is solely responsible for metabolism of many endogenous and exogenous pharmacologic compounds including irinotecan. Therefore, the polymorphic variants of this gene have been associated with adverse effects of irinotecan such as severe diarrhea and neutropenia.

Among many variants described in the literature, a few have shown significant impact on metabolism of irinotecan and its toxicity. The wild type *UGT1A1* gene contains homozygous 6 TA sequence repeats in the 5' untranslated region of the gene and is associated with normal levels of *UGT1A1* enzyme expression. Presence of 7T repeats is known as *UGT1A1*28*. Individuals with heterozygous 7 TA (6/7) repeats or homozygous 7 TA (7/7) repeats show significantly reduced expression of *UTG1A1* enzyme. Compared to the wild type genotype, patients carrying the 7/7 genotype demonstrate approximately 70% reduction in enzyme expression and are therefore significantly predisposed to irinotecan toxicity. The homozygous *UGT1A1*28* (7/7) is seen in approximately 10% of the US population. This common polymorphism is also associated with Gilbert's syndrome. Other less common genotypes include *UGT1A1*36* (5 TA repeats) that may increase *UGT1A1* enzyme level and *UGT1A1*37* (8 TA repeats) that decrease enzyme levels lower than those with *UGT1A1*28*. Other uncommon variants in the promoter region and mutations in the coding region of the *UGT1A1* gene that may influence glucuronidation will not be detected by this assay.

For additional information, please contact:

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REFERENCES

- ¹ Schulz C, Heinemann V, Schalhorn A, et al. *UGT1A1* gene polymorphism: Impact on toxicity and efficacy of irinotecan-based regimens in metastatic colorectal cancer. *World J Gastroenterol*. 2009 Oct 28; 15(40): 5058–5066.
- ² Innocenti F, Undevia SD, Iyer L, et al. Genetic variants in the UDP-glucuronosyltransferase *1A1* gene predict the risk of severe neutropenia of irinotecan. *J Clin Oncol*. 2004;22:1382-1388.

Ordering instructions are on the reverse side.

ORDERING INFORMATION

UGT1A1 PROMOTER GENE POLYMORPHISM (TA REPEATS) ASSAY

UDP GLUCURONOSYLTRANSFERASE 1A1 (UGT1A1) GENOTYPING

Test Code.....MDUGT	Testing Performed.....Friday
CPT Code.....81350, G0452-26	Reported.....Reported in 7 days
Methodology.....Polymerase Chain Reaction (PCR) and Fragment Analysis	Related Document.....Hematopathology Requisition

COLLECTION

Specimen	Preferred: Whole Blood Acceptable: Bone Marrow
Collection Container	Preferred: EDTA - Lavender Acceptable: EDTA - Pink ACD - Yellow
Collection Amount	Preferred.....4.0 mL Minimum.....1.0 mL

PROCESSING

Specimen Processing Instructions	CRITICAL: Do not open or share tube.
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SHIPPING/TRANSPORT AND STORAGE

Stabilities/Storage (Collection to initiation of testing)	Temperature	Stability
	Ambient	5 days
	Refrigerated	5 days
	Frozen	Unacceptable
Shipping Instructions	Ship ambient and overnight for Monday-Saturday receipt.	