VIKAS 54183096207 PID NO: P11180389918 Age: 18 Year(s) Sex: Male	**Reference: Dr.KOS LAB** Sample Collected At: METROPOLIS HEALTHCARE LTD DELHI F-2, Block -B1 (Ground Floor) Mohan Co-oprative Industrial Estate Mathura Road, New Delhi -110044 **Zone: OUT-01(OS)110044**	**VID: 11187319798** Registered On: 10/07/2018 07:23 PM Collected On: 08/07/2018 Reported On: 19/07/2018 06:37 PM	

Test Name : **UGT1A1 Gene Polymorphism (TA Repeat)**

Specimen : Whole Blood

Results

TA Repeats	UGT1A1 Genotype
7/7	**UGT1A1 *28/*28**

Method : PCR-Sequencing

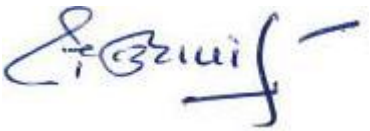
UGT1A1 Gene Polymorphism test detects the four polymorphisms [*36(TA5), *1(TA6), *28(TA7) and *37(TA8)] in the promoter region of the UDP glucuronosyl transferase gene (UGT1A1).

Interpretation

- Individuals who are homozygous for *UGT1A1**28 allele with 7 TA repeats may have a benign, congenital condition, Gilbert's syndrome, in the absence of cancer.
- Patients who are homozygous for 6 TA repeats (UGT1A1*1/*1) demonstrate full enzyme activity and is associated with minimal toxicity with standard irinotecan dosage.
- Patients with one 6 TA allele and one 7 TA allele (6/7 heterozygous/ UGT1A1*1/*28) demonstrate reduced glucuronidation activity, with about 12.5% risk of neutopenia toxicity.
- Patients with 2 alleles each with 7 TA repeat (7/7 homozygous/ UGT1A1*28/*28) demonstrate severely reduced glucuronidation activity, with about 50 % risk of severe toxicity and significant risk for grade 4 neutropenia or severe diarrhea following irinotecan treatment.

Clinical Significance and Utility:

- Irinotecan is an anti-cancer agent that is used for the treatment of metastatic carcinoma of the colon or rectum and may also be used for lung, brain, and breast tumors.
- Although it prolongs survival, it causes severe (grade 3-4) diarrhea and neutropenia in approximately 20-35% of patients treated.
- UDP-glucuronosyltransferase (UGT1A1) is responsible for the clearance, by glucuronidation, of drugs (e.g., irinotecan) and endogenous substances (e.g., bilirubin).
- Variations of the TA repeat length in the UGT1A1 promoter TATA element may lead to decreased gene expression and accumulation of toxin metabolite SN-38.
- UGT1A1 genotyping test result will provide valuable information to physicians prior to initiating or modifying treatment or supplementing treatment with additional drugs.



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- UGT1A1 variants may also be associated with Gilbert syndrome (a benign familial hyperbilirubinemia) and Crigler-Najjar syndrome (a rare form of non-hemolytic jaundice which may lead to brain damage).
- Individuals with Gilbert syndrome have a reduced level of hepatic bilirubin UGT1A1 enzyme necessary for the conjugation of bilirubin. A A(TA)7TAA polymorphism in the promoter region of the UGT1A1 gene has been identified in the majority of Caucasian individuals with Gilbert syndrome (80-100%).
- In India about 10% of the (TA)7TAA homozygotes carry the 'CAT' insertion and the insertion significantly elevate the bilirubin level and has a functional impact (Farheen 2006).

Indications for Testing:

- Patients being considered for treatment with irinotecan
- Individuals with suspected Gilbert's syndrome

Note:

This test has been developed and its performance is validated at Metropolis Healthcare Ltd.

Limitation of the Assay:

- The current test will only test the TATA box polymorphism of the UGT1A1 gene. The other variations of this gene will not be detected.
- Presence of PCR inhibitors in the sample may prevent DNA amplification. Paradoxical results may arise due selection of inappropriate specimens and contamination during specimen collection.

Reference:

- Glimelius et al., 2011. The Pharmacogenomics Journal, 11, 61–71
- Farheen et al., 2006. World J Gastroenterol; 12(14): 2269-2275
- Palomaki et al., 2009. IN Medicine, Vol. 11, No. 1, p21-34

-- End of Report --

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