UGT1A1-28 Genotyping for Irinotecan Toxicity

Detection of the most common polymorphisms are detected in this assay: (TA)5 UGT1A1*36, The (TA)6 UGT1A1*1, (TA)7 UGT1A1*28 and (TA)8 UGT1A1*37. Additional rare polymorphisms exist but are not assessed with this assay.

Indications for Molecular Testing
- Patient with cancer that may be treated with Irinotecan Therapy

Testing Methodology
Polymerase Chain Reaction (PCR) amplification of the promoter of UGT1A1 is performed with fluorescently-tagged analyte specific reagent primers as described (Shulman K, 2011). PCR Products are separated by capillary electrophoresis. (PCR is utilized pursuant to a license agreement with Roche Molecular Systems, Inc).

Interpretation of DNA analysis
The active form of Irinotecan, an antineoplastic agent, is deactivated by glucuronidation action of the UGT1A1 enzyme. Studies of patients treated with irinotecan have reported that major dose-limiting toxicities are associated with polymorphisms in the TATA box of the UGT1A1 gene. 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. Many studies report that patients who possess the UGT1A1*28 genotype have a greater risk for irinotecan-induced toxicities, including severe diarrhea or grades 4 neutropenia. Patients who have 2 alleles each with 6 TA repeats (6/6 homozygous) demonstrate full glucuronidation activity of SN-38, the active metabolite of irinotecan, with standard risk of toxicity. Patients with one 6 TA allele and one 7 TA allele (6/7 heterozygous) demonstrate reduced glucuronidation activity of SN-38, with about 12.5% risk of neutopenia toxicity. Patients with 2 alleles each with 7 TA repeat (7/7 homozygous) demonstrate severely reduced glucuronidation activity of SN-38, with about 50% risk of severe toxicity. The homozygous 7/7 copy patient is at significant risk for grade 4 neutropenia or severe diarrhea following irinotecan treatment.

Specimen Requirements
**Peripheral Blood**--1 lavender-top (EDTA) tube. Invert several times to mix blood. Do not freeze, forward promptly at ambient temperature to the following address:

Molecular Diagnostic Laboratory
Barnes-Jewish Hospital, Institute of Health
Mail Stop 90-28-344
425 South Euclid Avenue, Room 5970
St. Louis, MO 63110

Current Pricing
Contact Lab Customer Service for current pricing 314 362-1470.
CPT code: 81350