UDP Glucuronosyltransferase 1A1 (UGT1A1) Genotyping
ARUP test code 0051332

<table>
<thead>
<tr>
<th>UGT1A1 Genotyping Specimen</th>
<th>Whole Blood</th>
</tr>
</thead>
<tbody>
<tr>
<td>UGT1A1 Genotyping Allele 1</td>
<td>(TA)7 or *28 *</td>
</tr>
<tr>
<td>UGT1A1 Genotyping Allele 2</td>
<td>(TA)7 or *28 *</td>
</tr>
</tbody>
</table>

**UGT1A1 Genotyping Interpretation**

Section 79-1 of New York State Civil Rights Law requires informed consent be obtained from patients (or their legal guardians) prior to pursuing genetic testing. These forms must be kept on file by the ordering physician. Consent forms for genetic testing are available at www.aruplab.com. Incidental findings are not reported unless clinically significant but are available upon request.

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

**Homozygous UGT1A1 (TA)7:** Two copies of the UGT1A1 *28 (TA)7 variant were detected. This is associated with decreased UGT1A1 enzyme and increased risk for irinotecan toxicity, namely neutropenia and diarrhea. Dose reduction is recommended. This genotype has been reported to be associated with Gilbert's syndrome (benign familial hyperbilirubinemia).

This result has been reviewed and approved by

---

**Legend:**
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

ALLELIC 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.

ANALYTICAL SENSITIVITY: Greater than 99 percent.

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.

This test was developed and its performance characteristics determined by ARUP Laboratories. It has not been cleared or approved by the US Food and Drug Administration. This test was performed in a CLIA certified laboratory and is intended for clinical purposes.

Counseling and informed consent are recommended for genetic testing. Consent forms are available online.
### VERIFIED/REPORTED DATES

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Accession</th>
<th>Collected</th>
<th>Received</th>
<th>Verified/Reported</th>
</tr>
</thead>
<tbody>
<tr>
<td>UGT1A1 Genotyping Specimen</td>
<td>23-125-141196</td>
<td>00/00/0000 00:00</td>
<td>00/00/0000 00:00</td>
<td>00/00/0000 00:00</td>
</tr>
<tr>
<td>UGT1A1 Genotyping Allele 1</td>
<td>23-125-141196</td>
<td>00/00/0000 00:00</td>
<td>00/00/0000 00:00</td>
<td>00/00/0000 00:00</td>
</tr>
<tr>
<td>UGT1A1 Genotyping Allele 2</td>
<td>23-125-141196</td>
<td>00/00/0000 00:00</td>
<td>00/00/0000 00:00</td>
<td>00/00/0000 00:00</td>
</tr>
<tr>
<td>UGT1A1 Genotyping Interpretation</td>
<td>23-125-141196</td>
<td>00/00/0000 00:00</td>
<td>00/00/0000 00:00</td>
<td>00/00/0000 00:00</td>
</tr>
</tbody>
</table>

*H=High, L=Low, *=Abnormal, C=Critical*