

# UPD Glucuronosyltransferase 1A1 (UGT1A1) and Dihydropyrimidine Dehydrogenase (DPYD) Genotyping

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Dihydropyrimidine dehydrogenase, an enzyme encoded by the *DPYD* gene, is responsible for metabolizing 5-fluorouracil (5-FU), a chemotherapeutic drug frequently used to treat many types of cancer, including colorectal adenocarcinomas. Germline variants in *DPYD* affect enzyme production, which may result in dose-related toxicity or in a reduction of treatment effectiveness.<sup>1</sup> Similarly, variants in *UGT1A1* can cause a deficiency in the enzymes involved in metabolizing the chemotherapeutic drug irinotecan and therefore increase the risk of drug toxicity.<sup>2</sup>

For more information on pharmacogenetic testing, refer to the ARUP Consult [Germline Pharmacogenetics - PGx](#) topic.

## Disease Overview

### Genetics

#### Genes/Variants Tested

##### *DPYD*

- c.1024G>A (rs183385770)
- c.1129-5923C>G (rs75017182)
- c.1774C>T (rs59086055)
- c.2279C>T (rs112766203)
- c.557A>G (rs115232898)
- c.868A>G (rs146356975)
- c.1679T>G (*DPYD*\*13, rs55886062)
- c.1905+1G>A (*DPYD*\*2A, rs3918290)
- c.2846A>T (rs67376798)

##### *UGT1A1*

- *UGT1A1*\*36, (TA)5
- *UGT1A1*\*28, (TA)7
- *UGT1A1*\*37, (TA)8
- *UGT1A1*\*1, (TA)6

#### Inheritance

*DPYD*: autosomal codominant

*UGT1A1*: varies

## Featured ARUP Testing

### [UPD Glucuronosyltransferase 1A1 \(UGT1A1\) and Dihydropyrimidine Dehydrogenase \(DPYD\) Genotyping 3019841](#)

**Method:** Polymerase Chain Reaction (PCR) / Fluorescence Monitoring / Fragment Analysis

Predicts risk of dose-related toxicity to 5-FU therapy. May be useful in dosage planning for individuals who will receive high-dose irinotecan, have personal or family history of sensitivity to irinotecan, or have experienced neutropenia while receiving irinotecan.

For more information about individual *DPYD* testing, refer to the [Dihydropyrimidine Dehydrogenase \(DPYD\) Test Fact Sheet](#).

For more information about individual *UGT1A1* testing, refer to the [UGT1A1 Gene Analysis Test Fact Sheet](#).

# Test Interpretation

## Analytic Sensitivity/Specificity

*DPYD*: 99%

*UGT1A1*: 99%

## Results

Gene	Result	Clinical Significance
<i>DPYD</i>	Positive: target variants of significance detected	Predicts decreased DPD enzymatic activity Associated with an increased risk for grade 3-4 5-FU toxicity
	Negative: *1/*1 detected	Predicts normal metabolizer phenotype and average risk for 5-FU toxicity
<i>UGT1A1</i>	Positive: target variants of significance detected	Associated with an increased risk of irinotecan toxicity
	Negative: *1, (TA)6 detected	Associated with normal <i>UGT1A1</i> enzyme levels and average risk of irinotecan toxicity

## Limitations

### Dihydropyrimidine Dehydrogenase (*DPYD*)

- Only targeted variants in the *DPYD* gene will be detected.
- Diagnostic errors may occur due to rare sequence variations.
- Genetic and/or nongenetic factors not detected by this test may affect 5-FU drug metabolism and efficacy and the risk for toxicity.
- Genotyping does not replace the need for therapeutic drug monitoring or clinical observation.
- A negative result for the targeted *DPYD* variants does not rule out risk for 5-FU toxicity or predict degree of responsiveness to 5-FU.

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

- Only targeted variations in the *UGT1A1* gene will be detected.
- Diagnostic errors can occur due to rare sequence variations.
- The clinical significance of the rare \*36, (TA)5 and \*37, (TA)8 alleles in predicting irinotecan toxicity is not well established.
- Genetic and nongenetic factors other than *UGT1A1* may contribute to irinotecan toxicity and efficacy, and risk for bilirubin-related discontinuation of atazanavir.

## References

1. Dean L, Kane M. [Fluorouracil therapy and \*DPYD\* genotype](#). In: Pratt VM, Scott SA, Pirmohamed M, et al, eds. *Medical Genetics Summaries*. Bethesda, Maryland. Updated Jan 2021; accessed Aug 2024.
2. Dean L. [Irinotecan therapy and \*UGT1A1\* genotype](#). In: Pratt VM, Scott SA, Pirmohamed M, et al, eds. *Medical Genetics Summaries*. Bethesda, Maryland. Updated Apr 2018; accessed Aug 2024.

