

Dihydropyrimidine Dehydrogenase (DPYD) and UPD Glucuronosyltransferase 1A1 (UGT1A1) 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.¹ 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.²

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

Test Interpretation

Analytic Sensitivity/Specificity

DPYD: 99%

UGT1A1: 99%

Featured ARUP Testing

[Dihydropyrimidine Dehydrogenase \(DPYD\) and UPD Glucuronosyltransferase 1A1 \(UGT1A1\) Genotyping 3017866](#)

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](#).

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 UGT1A1 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.

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