Test Definition: DPYDQ

Dihydropyrimidine Dehydrogenase Genotype, Varies

Overview

Useful For

Identifying individuals with genetic variants in *DPYD* who are at increased risk of toxicity when prescribed 5-fluorouracil (5-FU) or capecitabine chemotherapy treatment

Genetics Test Information

This is a pharmacogenomic test associated with 5-fluorouracil and capecitabine drug sensitivity. Biallelic variation in the *DPYD* gene is also associated with dihydropyrimidine dehydrogenase deficiency.(1) Individuals who have variants identified in the *DPYD* gene may benefit from genetic consultation.

Special Instructions

- Informed Consent for Genetic Testing
- Pharmacogenomic Association Tables
- Multiple Genotype Test List
- Informed Consent for Genetic Testing (Spanish)

Method Name

Real-Time Polymerase Chain Reaction (PCR) with Allelic Discrimination Analysis

NY State Available

Yes

Specimen

Specimen Type

Varies

Ordering Guidance

This test does not detect or report variants other than the *2A, *7, *8, *10, *13, rs67376798, rs75017182, and rs115232898 alleles. Sequencing of the full gene is available for detection of additional variants as well as the alleles listed: order DPYDZ / Dihydropyrimidine Dehydrogenase, *DPYD* Full Gene Sequencing, Varies.

Multiple genotype tests can be performed on a single specimen after a single extraction. See Multiple Genotype Test List for a list of tests that can be ordered together.

Specimen Required

Patient Preparation: A previous hematopoietic stem cell transplant from an allogenic donor will interfere with testing. For instructions for testing patients who have a hematopoietic stem cell transplant, call 800-533-1710.

Submit only 1 of the following specimens:

Specimen Type: Whole blood
Container/Tube: Lavender top (EDTA)
Specimen Volume: 3 mL
Collection Instructions:
1. Invert several times to mix blood.
2. Send whole blood specimen in original tube. **Do not aliquot**.
Specimen Stability Information: Ambient (preferred) 4 days/Refrigerated 4 days/Frozen 4 days
Additional Information:
1. Specimens are preferred to be received within 4 days of collection. Extraction will be attempted for specimens received after 4 days, and DNA yield will be evaluated to determine if testing may proceed.
2. To ensure minimum volume and concentration of DNA is met, the requested volume must be submitted. Testing may be canceled if DNA requirements are inadequate.

Specimen Type: Cord blood
Container/Tube: Lavender top (EDTA)
Specimen Volume: 3 mL
Collection Instructions:
1. Invert several times to mix blood.
2. Send cord blood specimen in original tube. **Do not aliquot.**
Specimen Stability Information: Ambient (preferred) 4 days/Refrigerated 4 days/Frozen 4 days
Additional Information:
1. Specimens are preferred to be received within 4 days of collection. Extraction will be attempted for specimens received after 4 days, and DNA yield will be evaluated to determine if testing may proceed.
2. To ensure minimum volume and concentration of DNA is met, the requested volume must be submitted. Testing may be canceled if DNA requirements are inadequate.
3. While a properly collected cord blood sample may not be at risk for maternal cell contamination, unanticipated complications may occur during collection. Therefore, maternal cell contamination studies are recommended to ensure the test results reflect that of the patient tested and are available at an additional charge. Order MATCC / Maternal Cell Contamination, Molecular Analysis, Varies on the maternal specimen.

Specimen Type: Saliva
Patient Preparation: Patient should not eat, drink, smoke, or chew gum 30 minutes prior to collection.
Supplies: Saliva Collection Kit (T786)
Specimen Volume: 1 Swab
Collection Instructions: Collect and send specimen per kit instructions.
Specimen Stability Information: Ambient (preferred) 30 days/Refrigerated 30 days
Additional information: Saliva specimens are acceptable but not recommended. Due to lower quantity/quality of DNA yielded from saliva, some aspects of the test may not perform as well as DNA extracted from a whole blood sample. When applicable, specific gene regions that were unable to be interrogated will be noted in the report. Alternatively, additional specimen may be required to complete testing.

Specimen Type: Extracted DNA

Container/Tube:
Preferred: Screw Cap Micro Tube, 2mL with skirted conical base
Acceptable: Matrix tube, 1 mL
Collection Instructions:
1. The preferred volume is at least 100 mcL at a concentration of 75 ng/mcL.
2. Include concentration and volume on tube.
Specimen Stability Information: Frozen (preferred) 1 year/Ambient/Refrigerated
Additional Information: DNA must be extracted in a CLIA-certified laboratory or equivalent and must be extracted from a specimen type listed as acceptable for this test (including applicable anticoagulants). Our laboratory has experience with Chemagic, Puregene, Autopure, MagnaPure, and EZ1 extraction platforms and cannot guarantee that all extraction methods are compatible with this test. If testing fails, one repeat will be attempted, and if unsuccessful, the test will be reported as failed and a charge will be applied. If applicable, specific gene regions that were unable to be interrogated due to DNA quality will be noted in the report.

Forms

1. **New York Clients-Informed consent is required.** Document on the request form or electronic order that a copy is on file. The following documents are available:
-Informed Consent for Genetic Testing (T576)
-Informed Consent for Genetic Testing (Spanish) (T826)
2. If not ordering electronically, complete, print, and send a Therapeutics Test Request (T831) with the specimen.

Specimen Minimum Volume

See Specimen Required

Reject Due To

All specimens will be evaluated at Mayo Clinic Laboratories for test suitability.

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Varies	Varies		

Clinical & Interpretive

Clinical Information

5-Fluorouracil (5-FU) and its orally administered prodrug, capecitabine, are fluoropyrimidine-based chemotherapeutic agents that are widely used for the treatment of colorectal cancer and other solid tumors.

The dihydropyrimidine dehydrogenase (*DPYD*) gene encodes the rate-limiting enzyme for fluoropyrimidine catabolism and eliminates over 80% of administered 5-FU. Dihydropyrimidine dehydrogenase (DPD) activity is subject to wide variability, mainly due to genetic variation. This results in a broad range of enzymatic deficiency from partial (3%-5% of population) to complete loss (0.2% of population) of enzyme activity.(2-5) Patients who are deficient in DPD are at an increased risk for side effects and toxicity when undergoing 5-FU treatment.(6) In addition, pathogenic homozygous or compound heterozygous variants within *DPYD* are associated with DPD deficiency. DPD deficiency shows large

phenotypic variability, ranging from no symptoms to a convulsive disorder with motor and intellectual disabilities.

The following table displays the *DPYD* variants detected by this assay, the corresponding star allele, and the effect on DPD enzyme activity. Other or novel variants, besides those listed here, may also impact fluoropyrimidine-related adverse effects and tumor response.

Table. Enzyme Activity of Individual Star Alleles

***DPYD* allele**	**cDNA nucleotide change**	**Effect on enzyme activity**
**1*	None (wild type)	Normal activity
**2A*	c.1905+1G>A	No activity
**7*	c.299_302del	No activity
**8*	c.703C>T	No activity
**10*	c.2983G>T	No activity
**13*	c.1679T>G	No activity
rs67376798	c.2846A>T	Decreased activity
rs75017182	c.1129-5923C>G	Decreased activity
rs115232898	c.557A>G	Decreased activity

Reference Values

DPYD Phenotype: Normal metabolizer
DPYD Activity Score: 2.00
DPYD Genotype: No variants were detected in the *DPYD* gene.

An interpretive report will be provided.

Interpretation

The interpretive report includes an overview of the findings as well as the associated clinical significance.

For additional information regarding pharmacogenomic genes and their associated drugs, see Pharmacogenomic Associations Tables. This resource also includes information regarding enzyme inhibitors and inducers, as well as potential alternate drug choices.

Cautions

Rare genetic variants may be present that could lead to false-negative or false-positive results. Other variants in the primer binding regions can affect the testing, and ultimately, the genotype assessment made.

Dihydropyrimidine dehydrogenase genotype (DPYDQ) is a genotyping test that evaluates 8 of the more common functionally significant variants in the *DPYD* gene only. It is important to note that patients with a negative test result may have a rare variant resulting in increased risk of fluoropyrimidine toxicity that is not detected by this test. A sequencing test is available that can detect rare variants located in the exons of *DPYD*; however, this test will not detect copy number variation. For the sequencing test, order DPYDZ / Dihydropyrimidine Dehydrogenase, *DPYD* Full Gene Sequencing, Varies.

Specimens may contain donor DNA if obtained from patients who have received non-leukocyte-reduced blood

transfusions or allogeneic hematopoietic stem cell transplantation. Results from specimens obtained under these circumstances may not accurately reflect the recipient's genotype. For individuals who have received non-leukocyte-reduced blood transfusions, the genotype usually reverts to that of the recipient within 6 weeks. For individuals who have received allogeneic hematopoietic stem cell transplantation, a pretransplant DNA specimen is recommended for testing.

Dihydropyrimidine dehydrogenase (*DPYD*) genetic test results in patients who have undergone liver transplantation may not accurately reflect the patient's *DPYD* status.

Test results should be interpreted in the context of clinical findings, family history, and other laboratory data. Large deletions or rearrangements are not detected by this assay, and these may affect DPD protein expression and the impact on fluoropyrimidine-related side effects and tumor response.

This test is not designed to provide specific dosing or drug selection recommendations and is to be used as an aid to clinical decision making only. Drug-label guidance should be used when dosing patients with medications regardless of the predicted phenotype.

Clinical Reference

1. OMIM: Dihydropyrimidine dehydrogenase; DPYD. 2009. Updated December 13, 2023. Accessed April 1,2025. Available at www.omim.org/entry/612779
2. Clinical Pharmacogenetics Implementation Consortium (CPIC): Guideline for Fluoropyrimidines and DPYD. Updated March 2024. Accessed December 23, 2024. Available at https://cpicpgx.org/guidelines/guideline-for-fluoropyrimidines-and-dpyd/
3. Amstutz U, Henricks LM, Offer SM, et al. Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for dihydropyrimidine dehydrogenase genotype and fluoropyrimidine dosing: 2017 Update. Clin Pharmacol Ther. 2018;103(2):210-216. doi:10.1002/cpt.911
4. Lunenburg CATC, van der Wouden CH, Nijenhuis M, et al. Dutch Pharmacogenetics Working Group (DPWG) guideline for the gene-drug interaction of DPYD and fluoropyrimidines. Eur J Hum Genet. 2020;28(4):508-517. doi:10.1038/s41431-019-0540-0
5. Morel A, Boisdron-Celle M, Fey L, et al. Clinical relevance of different dihydropyrimidine dehydrogenase gene single nucleotide polymorphisms on 5-fluorouracil tolerance. Mol Cancer Ther. 2006;5(11):2895-2904. doi:10.1158/1535-7163.MCT-06-0327
6. Offer SM, Fossum CC, Wegner NJ, Stuflesser AJ, Butterfield GL, Diasio RB. Comparative functional analysis of DPYD variants of potential clinical relevance to dihydropyrimidine dehydrogenase activity. Cancer Res. 2014;74(9):2545-2554. doi:10.1158/0008-5472.CAN-13-24826
7. U.S. Food and Drug Administration: Table of Pharmacogenomic Biomarkers in Drug Labeling. FDA; Updated September 23, 2024. Accessed April 1, 2025. Available at www.fda.gov/drugs/scienceresearch/researchareas/pharmacogenetics/ucm083378.htm

Performance

Method Description

Genomic DNA is extracted from whole blood, cord blood, or saliva. Genotyping for *DPYD* alleles is performed using a polymerase chain reaction (PCR)-based 5'-nuclease assay. Fluorescently labeled detection probes anneal to the target DNA. PCR is used to amplify the section of DNA that contains the variant. If the detection probe is an exact match to the target DNA, the 5'-nuclease polymerase degrades the probe, the reporter dye is released from the effects of the quencher dye, and a fluorescent signal is detected. Genotypes are assigned based on the allele-specific fluorescent signals that are detected.(Unpublished Mayo method)

PDF Report
No

Day(s) Performed
Monday through Friday

Report Available
3 to 10 days

Specimen Retention Time
Whole blood: 28 days (if available); Salvia: 30 days (if available); Extracted DNA: 3 months

Performing Laboratory Location
Mayo Clinic Laboratories - Rochester Main Campus

Fees & Codes

Fees
- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact Customer Service.

Test Classification
This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. It has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information
81232

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
DPYDQ	DPYD Genotype, V	93199-8

Result ID	Test Result Name	Result LOINC® Value
610138	DPYD Phenotype	79719-1

610139	DPYD Activity Score	104665-5
613999	DPYD Genotype	45284-7
610140	Interpretation	69047-9
610141	Additional Information	48767-8
610142	Method	85069-3
610143	Disclaimer	62364-5
610144	Reviewed by	18771-6