MAYO CLINIC LABORATORIES

Test Definition: DPYDQ

DPYD Genotype, V

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

Special Instructions

- Informed Consent for Genetic Testing
- Pharmacogenomic Associations 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 DPYDG / Dihydropyrimidine Dehydrogenase, *DPYD* Full Gene Sequencing, Varies.

Specimen Required

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.

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) 9 days/Refrigerated 30 days

Specimen Type: Saliva

Patient Preparation: Patient should not eat, drink, smoke, or chew gum 30 minutes prior to collection.

Supplies: Saliva Swab Collection Kit (T786)

Specimen Volume: 1 Swab

Collection Instructions: Collect and send specimen per kit instructions.

Specimen Stability Information: Ambient 30 days

Specimen Type: Extracted DNA

Container/Tube: 2-mL screw top tube

Specimen Volume: 100 mcL (microliters)

Collection Instructions:

1. The preferred volume is 100 mcL at a concentration of 50 ng/mcL.

2. Provide concentration of DNA and volume on tube.

Specimen Stability Information: Frozen (preferred)/Ambient/Refrigerated

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.

Reject Due To

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

Specimen Minimum Volume

Blood: 0.4 mL

Saliva extracted DNA: see Specimen Required

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Varies	Varies (preferred)		

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 (DPYD) 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 DPYD 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 dihydropyrimidine dehydrogenase (DPD) deficiency. DPD deficiency shows large phenotypic variability, ranging from no symptoms to a convulsive disorder with motor and mental retardation.

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

side 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*	1905+1G>A	No activity
**7*	299_302delTCAT	No activity
**8*	703C>T	No activity
**10*	2983G>T	No activity
**13*	1679T>G	No activity
rs67376798	2846A>T	Decreased activity
rs75017182	1129-5923C>G	Decreased activity
rs115232898	557A>G	Decreased activity

Reference Values

An interpretive report will be provided.

Interpretation

An interpretive report will be provided.

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.

Samples may contain donor DNA if obtained from patients who received heterologous blood transfusions or allogeneic blood or marrow transplantation. Results from samples obtained under these circumstances may not accurately reflect the recipient's genotype. For individuals who have received blood transfusions, the genotype usually reverts to that of the recipient within 6 weeks. For individuals who have received allogeneic blood or marrow 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 DPYD protein expression and their 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 22, 2017. Accessed October 14, 2020. Available at www.omim.org/entry/612779

2. 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 Feb;103(2):210-216. doi:10.1002/cpt.911

3. 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 Apr;28(4):508-517. doi: 10.1038/s41431-019-0540-0

4. 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 Nov;5(11):2895-2904. doi: 10.1158/1535-7163.MCT-06-0327

5. 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 May 1;74(9):2545-2554. doi: 10.1158/0008-5472.CAN-13-24826

6. U.S. Food and Drug Administration: Table of Pharmacogenomic Biomarkers in Drug Labeling. FDA; Updated August 18, 2020. Accessed October 14, 2020. Available at www.fda.gov/drugs/scienceresearch/researchareas/pharmacogenetics/ucm083378.htm

Performance

Method Description

Genomic DNA is extracted from whole 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.(Instruction manual: TaqMan SNP Genotyping Assay User Guide. Applied Biosystems; Revision A.0, 01/2014)

PDF Report

No

Specimen Retention Time

Whole blood/Saliva: 2 weeks; Extracted DNA: 2 months

Performing Laboratory Location

Rochester

Fees & Codes

Test Classification

This test was developed, and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. This test 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	Reporting Name	LOINC®
610138	DPYD Phenotype	79719-1
610139	DPYD Activity Score	In Process
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