Test Definition: DPYDZ

Dihydropyrimidine Dehydrogenase, DPYD Full Gene Sequencing, Varies

Overview

Useful For

Identifying individuals at increased risk of toxicity when considering 5-fluorouracil and capecitabine chemotherapy treatment

Identifying common and rare variants associated with decreased or absent dihydropyrimidine dehydrogenase (DPD) enzyme activity, including in individuals with suspected DPD deficiency

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
CULFB	Fibroblast Culture for Genetic Test	Yes	No

Genetics Test Information

This test utilizes next-generation sequencing to detect single nucleotide variants, small deletions and insertions, and copy number variants in the *DPYD* gene associated with sensitivity to fluoropyrimidine medications and dihydropyrimidine dehydrogenase deficiency. See Method Description for additional details.

This is a pharmacogenomic test that detects both common and rare variants associated with 5-fluorouracil and capecitabine drug sensitivity. In addition, identification of a disease-causing variant(s) may assist with diagnosis, prognosis, clinical management, recurrence risk assessment, familial screening, and genetic counseling for dihydropyrimidine dehydrogenase deficiency.

Testing Algorithm

For skin biopsy or cultured fibroblast specimens, fibroblast culture will be performed at an additional charge.

Special Instructions

- Informed Consent for Genetic Testing
- Pharmacogenomic Association Tables
- Blood Spot Collection Card-Spanish Instructions
- Blood Spot Collection Card-Chinese Instructions
- Informed Consent for Genetic Testing (Spanish)
- Blood Spot Collection Instructions

Method Name

Sequence Capture and Targeted Next-Generation Sequencing (NGS) followed by Polymerase Chain Reaction (PCR) and Sanger Sequencing

NY State Available

Yes

Specimen

Specimen Type
Varies

Ordering Guidance
This test and DPYDQ / Dihydropyrimidine Dehydrogenase Genotype, Varies both test for genetic variants in the *DPYD* gene. DPYDQ test is a targeted genotyping with a faster turnaround time and detects the common variants associated with fluoropyrimidine toxicity. DPYDZ test detects rare variants in addition to the common variants and has a higher detection rate than DPYDQ test, particularly for individuals of non-European ancestry. DPYDZ test is the most appropriate test for diagnosis of dihydropyrimidine dehydrogenase deficiency. DPYDZ test may detect and report variants of uncertain significance.

Because germline DNA results are not expected to change over time, it is generally not recommended to repeat this test. If full gene sequencing of the *DPYD* gene has been previously performed, this test may assist with identification of copy number variants in the *DPYD* gene associated with sensitivity to fluoropyrimidine medications and dihydropyrimidine dehydrogenase deficiency.

To obtain more information about these testing options, call 800-533-1710.

Specimen Required
Patient Preparation: A previous hematopoietic stem cell transplant or a liver transplant from an allogenic donor will interfere with testing. For information about testing patients who have received a hematopoietic stem cell or liver transplant, call 800-533-1710.

Submit only 1 of the following specimens:

Specimen Type: Whole blood
Container/Tube:
Preferred: Lavender top (EDTA) or yellow top (ACD)
Acceptable: Gray top (sodium fluoride/potassium oxalate)
Specimen Volume: 3 mL
Collection Instructions:
1. Invert several times to mix blood.
2. Send whole blood specimen in original tube. **Do not aliquot**.
3. Whole blood collected postnatal from an umbilical cord is also acceptable. See Additional Information
Specimen Stability Information: Ambient 4 days (preferred)/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 are met, the requested volume must be submitted. Testing may be canceled if DNA requirements are inadequate.
3. For postnatal umbilical cord whole blood specimens, maternal cell contamination studies are recommended to ensure

test results reflect that of the patient tested. A maternal blood specimen is required to complete maternal cell contamination studies. Order MATCC / Maternal Cell Contamination, Molecular Analysis, Varies on both the cord blood and maternal blood specimens under separate order numbers.

Specimen Type: Saliva
Patient Preparation: Patient should not eat, drink, smoke, or chew gum 30 minutes prior to collection.
Supplies:
DNA Saliva Kit High Yield (T1007)
Saliva Swab Collection Kit (T786)
Container/Tube:
Preferred: High-yield DNA saliva kit
Acceptable: Saliva swab
Specimen Volume: 1 Tube if using T1007 or 2 swabs if using T786
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: Skin biopsy
Supplies: Fibroblast Biopsy Transport Media (T115)
Container/Tube: Sterile container with any standard cell culture media (eg, minimal essential media, RPMI 1640). The solution should be supplemented with 1% penicillin and streptomycin.
Specimen Volume: 4-mm Punch
Specimen Stability Information: Ambient (preferred) <24 hours/Refrigerated <24 hours
Additional Information:
1. Specimens are preferred to be received within 24 hours of collection. Culture and extraction will be attempted for specimens received after 24 hours and will be evaluated to determine if testing may proceed.
2. A separate culture charge will be assessed under CULFB / Fibroblast Culture for Biochemical or Molecular Testing. An additional 3 to 4 weeks are required to culture fibroblasts before genetic testing can occur.

Specimen Type: Cultured fibroblasts
Source: Skin or tissue
Container/Tube: T-25 flask
Specimen Volume: 2 Flasks
Collection Instructions: Submit confluent cultured fibroblast cells from a skin biopsy. Cultured cells from a prenatal specimen will not be accepted.
Specimen Stability Information: Ambient (preferred) <24 hours/Refrigerated <24 hours
Additional Information:
1. Specimens are preferred to be received within 24 hours of collection. Culture and extraction will be attempted for specimens received after 24 hours and will be evaluated to determine if testing may proceed.
2. A separate culture charge will be assessed under CULFB / Fibroblast Culture for Biochemical or Molecular Testing. An additional 3 to 4 weeks are required to culture fibroblasts before genetic testing can occur.

Specimen Type: Tissue biopsy
Supplies: Hank's Solution (T132)
Container/Tube: Sterile container with sterile Hank's balanced salt solution, Ringer's solution, or normal saline
Specimen Volume: 0.5 to 3 cm(3) or larger
Specimen Stability Information: Ambient (preferred) <24 hours/Refrigerated <24 hours
Additional Information:
1. Specimens are preferred to be received within 24 hours of collection. Culture and extraction will be attempted for specimens received after 24 hours and will be evaluated to determine if testing may proceed.
2. A separate culture charge will be assessed under CULFB / Fibroblast Culture for Biochemical or Molecular Testing. An additional 3 to 4 weeks are required to culture fibroblasts before genetic testing can occur.

Specimen Type: Blood spot
Supplies: Card-Blood Spot Collection (Filter Paper) (T493)
Container/Tube:
Preferred: Collection card (Whatman Protein Saver 903 Paper)
Acceptable: PerkinElmer 226 filter paper or blood spot collection card
Specimen Volume: 2 to 5 Blood spots
Collection Instructions:
1. An alternative blood collection option for a patient older than 1 year is a fingerstick. For detailed instructions, see How to Collect a Dried Blood Spot Samples.
2. Let blood dry on the filter paper at ambient temperature in a horizontal position for a minimum of 3 hours.
3. Do not expose specimen to heat or direct sunlight.
4. Do not stack wet specimens.
5. Keep specimen dry.
Specimen Stability Information: Ambient (preferred)/Refrigerated
Additional Information:
1. Blood spot specimens are acceptable but not recommended. Due to lower quantity/quality of DNA yielded from blood spots, 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.
2. Due to lower concentration of DNA yielded from blood spot, it is possible that additional specimen may be required to complete testing.
3. For collection instructions, see Blood Spot Collection Instructions
4. For collection instructions in Spanish, see Blood Spot Collection Card-Spanish Instructions (T777)
5. For collection instructions in Chinese, see Blood Spot Collection Card-Chinese Instructions (T800)

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 in Special Instructions:
-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

Note: Where applicable, verbiage refers to sex assigned at birth.

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 *DPYD* gene encodes dihydropyrimidine dehydrogenase (DPD), the rate-limiting enzyme for fluoropyrimidine catabolism, which eliminates over 80% of administered 5-FU. DPD is highly expressed in the liver. Genetic variation in *DPYD* is the main cause for variability in DPD activity and can lead to partial or complete enzymatic deficiency (3-5% or 0.2% of the population, respectively).(1,2) Patients who are deficient in DPD are at an increased risk for adverse effects and toxicity when undergoing 5-FU treatment.(3) In addition, disease-causing homozygous or compound heterozygous variants within *DPYD* are associated with DPD deficiency. DPD deficiency shows a wide range of severity, from asymptomatic (albeit at risk for drug toxicity) to neurological problems, including seizures and intellectual disability, delayed motor development, and microcephaly.

DPYD variants impacting the metabolic pathway of fluoropyrimidines have been shown to contribute to the differences in clinical outcomes, including toxicity and tumor response. Common *DPYD* (NM_000110.4) variants that result in no activity include c.1905+1G>A (*2A), c.299_302del (*7), c.703C>T (*8), c.2983G>T (*10), and c.1679T>G (*13). Common *DPYD* variants resulting in reduced activity include c.2846A>T (rs67376798), c.1129-5923C>G (rs75017182, also part of the HapB3 haplotype), and c.557A>G (rs115232898). This test can detect all of the Association for Molecular Pathology (AMP) tier 1 and tier 2 alleles.(4) In addition to these more common variants, this sequencing test also detects rare variants, including deletions, that impact DPD activity. Although it may be possible to perform genetic testing on tumor tissue to detect *DPYD* genetic variants, testing a germline source of DNA (e.g., blood or saliva) is recommended because the majority of fluoropyrimidine metabolism occurs in hepatic tissue. *DPYD* testing on tumor tissue may identify somatic variants that are not present in the patient's liver or fail to detect a germline variant, and thus not reflect hepatic DPD activity.

The predicted DPD enzyme activity can be described as an activity score. For each allele, an activity score of 1.0 corresponds to normal activity (equivalent to reference or 'wild-type') while a score of 0 represents a no function allele and 0.5 corresponds to partial function. Most individuals have 2 copies of the *DPYD* gene, and therefore, an activity score of 2.0 corresponds to a normal metabolizer. This test reports the patient's *DPYD* genotype, predicted phenotype (metabolizer status), and activity score.

Reference Values

An interpretive report will be provided.

Interpretation

All detected variants are evaluated using the American College of Medical Genetics and Genomics (ACMG) recommendations as guidance, together with expertise in pharmacogenomics.(5) Variants are classified based on known, predicted, or possible pathogenicity and reported with interpretive comments detailing their potential or known significance. Additionally, variant functional status and activity score are assigned using the most recent published Clinical Pharmacogenetics Implementation Consortium (CPIC) recommendations as guidance.(1) Variants classified as benign or likely benign and expected to result in normal activity are not reported.

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

Cautions

Clinical Correlations:
Test results should be interpreted in the context of clinical findings, family history, and other laboratory data. Misinterpretation of results may occur if the information provided is inaccurate or incomplete.

DPYD genetic test results in patients who have undergone liver transplantation may not accurately reflect the patient's dihydropyrimidine dehydrogenase (DPD) status. Similarly, samples may contain donor DNA if obtained from patients who received an allogeneic hematopoietic stem cell transplantation or non-leukocyte reduced blood transfusions. Results from samples 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.

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 and activity score.

If testing was performed because of a clinically significant family history, it is often useful to first test an affected family member. Detection of a reportable variant in an affected family member would allow for more informative testing of at-risk individuals.

To discuss the availability of additional testing options or for assistance in the interpretation of these results, contact Mayo Clinic Laboratories genetic counselors at 800-533-1710.

Technical Limitations:
Next-generation sequencing may not detect all types of genomic variants. In rare cases, false-negative or false-positive results may occur. The depth of coverage may be variable for some target regions; assay performance below the minimum acceptable criteria or for failed regions will be noted. Given these limitations, negative results do not rule out the diagnosis of a genetic disorder. If a specific clinical disorder is suspected, evaluation by alternative methods can be considered.

There may be regions of the gene that cannot be effectively evaluated by sequencing or deletion and duplication analysis because of technical limitations of the assay, including regions of homology, high guanine-cytosine (GC) content, and repetitive sequences. Confirmation of select reportable variants will be performed by alternate methodologies based on internal laboratory criteria.

This test is validated to detect 95% of deletions up to 75 base pairs (bp) and insertions up to 47 bp. Deletions-insertions (delins) of 40 or more bp, including mobile element insertions, may be less reliably detected than smaller delins.

This analysis targets single and multi-exon deletions/duplications; however, in some instances single exon resolution cannot be achieved due to isolated reduction in sequence coverage or inherent genomic complexity. Balanced structural rearrangements (such as translocations and inversions) may not be detected.

Deletion/duplication events that extend past the genes included on the panel may occur. In these instances, genes included in the ordered test are provided on the report and interpreted, and genomic breakpoints are reported if they are confirmed. However, copy number variants for genes not listed in the Method Description are typically not reported or interpreted for haploinsufficiency/triplosensitivity. CMACB / Chromosomal Microarray, Congenital, Blood; WESPR / Panel to Whole Exome Sequencing Reflex Test, Varies; or WGSDX / Whole Genome Sequencing for Hereditary Disorders, Varies is recommended for a full interpretation of deletions/duplications predicted to extend past the genes included on the panel.

This test is not designed to detect low levels of mosaicism or to differentiate between somatic and germline variants. If there is a possibility that any detected variant is somatic, additional testing may be necessary to clarify the significance of results.

For detailed information regarding gene specific performance and technical limitations, see Method Description or

contact a laboratory genetic counselor.

Reclassification of Variants**:**
Currently, it is not standard practice for the laboratory to systematically review previously classified variants on a regular basis. The laboratory encourages health care professionals to contact the laboratory at any time to learn how the classification of a particular variant may have changed over time. Due to broadening genetic knowledge, it is possible that the laboratory may discover new information of relevance to the patient. Should that occur, the laboratory may issue an amended report.

Rarely, incidental or secondary findings may implicate another predisposition or presence of active disease. Incidental findings may include, but are not limited to, results related to the sex chromosomes. These findings will be carefully reviewed to determine whether they will be reported.

Clinical Reference

1. 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
2. Diasio RB and Offer SM. Testing for dihydropyrimidine dehydrogenase deficiency to individualize 5-Flurouracil therapy. Cancers. 2022;14(13):3207
3. U.S. Food and Drug Administration (FDA). Table of Pharmacogenomic Biomarkers in Drug Labeling. FDA; Updated September 23, 2024. Accessed September 10, 2025. Available at: www.fda.gov/drugs/scienceresearch/researchareas/pharmacogenetics/ucm083378.htm
4. Pratt VM, Cavallari LH, Fulmer ML, et al. DPYD genotyping recommendations: A joint consensus recommendation of the association for molecular pathology, American College of Medical Genetics and Genomics, Clinical Pharmacogenetics Implementation Consortium, College of American Pathologists, Dutch Pharmacogenetics Working Group of the Royal Dutch Pharmacists Association, European Society for Pharmacogenomics and Personalized Therapy, Pharmacogenomics Knowledgebase, and Pharmacogene Variation Consortium. J Mol Diagn. 2024;26(10):851-863. doi:10.1016/j.jmoldx.2024.05.015.
5. Richards S, Aziz N, Bale S, et al. Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. Genet Med. 2015;17(5):405-424
6. Offer SM, Fossum CC, Wegner NJ, et al. Comparative functional analysis of DPYD variants of potential clinical relevance to dihydropyrimidine dehydrogenase activity. Cancer Res. 2014;74(9):2545-2554
7. OMIM. 274270 Dihydropyrimidine dehydrogenase deficiency. Johns Hopkins University; 1986. Updated October 27, 2023. Accessed September 10, 2025. Available from www.omim.org/entry/274270

Performance

Method Description

Next-generation sequencing (NGS) and/or Sanger sequencing is performed to test for the presence of variants in coding regions and intron/exon boundaries of the *DPYD* gene, as well as the region surrounding c.1129-5923C>G. The human genome reference GRCh37/hg19 build was used for sequence read alignment. At least 99% of the bases are covered at a

read depth over 20X. Sensitivity is estimated at above 99% for single nucleotide variants, above 94% for deletions/insertions (delins) less than 40 base pairs (bp), above 95% for deletions up to 75 bp and insertions up to 47 bp. NGS and/or a polymerase chain reaction (PCR)-based quantitative method is performed to test for the presence of deletions and duplications in the *DPYD* gene.

There may be regions of genes that cannot be effectively evaluated by sequencing or deletion and duplication analysis because of technical limitations of the assay, including regions of homology, high guanine-cytosine (GC) content, and repetitive sequences.(Unpublished Mayo method)

The reference transcript for the *DPYD* gene is NM_000110.4. Reference transcript numbers may be updated due to transcript re-versioning. Always refer to the final patient report for gene transcript information referenced at the time of testing. Confirmation of select reportable variants may be performed by alternate methodologies based on internal laboratory criteria.

The following additional noncoding variant is being analyzed by this test: c.1129-5923C>G (HapB3, rs75017182).

PDF Report
No

Day(s) Performed
Varies

Report Available
6 to 10 days

Specimen Retention Time
Whole blood: 28 days (if available); Saliva: 30 days (if available); Extracted DNA: 3 months ; Blood Spots: 1 year (if available)

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.

Test Definition: DPYDZ

Dihydropyrimidine Dehydrogenase, DPYD Full Gene Sequencing, Varies

CPT Code Information

81232

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
DPYDZ	DPYD Full Gene Sequencing, V	94198-9

Result ID	Test Result Name	Result LOINC® Value
618600	DPYD Total Activity Score	104665-5
618601	DPYD Phenotype	79719-1
618602	Result Details	82939-0
618603	Interpretation	69047-9
618604	Method	85069-3
618605	Disclaimer	62364-5
618606	Additional Information	48767-8
618607	Reviewed by	18771-6