MAYO CLINIC LABORATORIES

Test Definition: 1A2Q

Cytochrome P450 1A2 Genotype, Varies

Overview

Useful For

Identifying individuals who are poor, intermediate, normal (extensive) or rapid metabolizers of drugs metabolized by cytochrome P450 1A2 to assist drug therapy decision making

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
CULFB	Fibroblast Culture for Genetic Test	Yes	No
CULAF	Amniotic Fluid Culture/Genetic Test	Yes	No
_STR1	Comp Analysis using STR (Bill only)	No, (Bill only)	No
_STR2	Add'l comp analysis w/STR (Bill Only)	No, (Bill only)	No
MATCC	Maternal Cell Contamination, B	Yes	No

Testing Algorithm

For cord blood specimens that have an accompanying maternal blood specimen, maternal cell contamination studies will be performed at an additional charge.

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

Testing is available as the single gene assay (this test) or as a part of a focused pharmacogenomics panel, which includes testing for the following genes: *CYP*s *1A2, 2C9, 2C19, 2D6, 3A4, 3A5, 4F2, SLCO1B1,* and *VKORC1*. If multiple pharmacogenomic genotype testing is desired, order PGXQP / Focused Pharmacogenomics Panel, Varies .

CYP1A2 is also available as part of a panel designed for psychotropic pharmacogenomics. If this testing is desired, order PSYQP / Psychotropic Pharmacogenomics Gene Panel, 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.

Patient Preparation: A previous hematopoietic stem cell transplant from an allogenic donor or a liver transplant 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: Lavender top (EDTA) or yellow top (ACD)
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 (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 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: Extracted DNA
Container/Tube:
Preferred: Screw Cap Micro Tube, 2 mL 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 1 of the following forms with the specimen:
-Neurology Specialty Testing Client Test Request (T732)
-Therapeutics Test Request (T831)

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

The cytochrome P450 (CYP) family is involved in the primary metabolism of many drugs. The CYPs are a group of oxidative/dealkylating enzymes localized in the microsomes of many tissues including the intestines and liver. One of these CYP enzymes, CYP1A2, is wholly or partially responsible for the hydroxylation or dealkylation of many commonly prescribed drugs.

Cytochrome P450 1A2-mediated drug metabolism is highly variable. A number of variants have been identified in the *CYP1A2* gene that results in increased, diminished, or abolished catalytic activity and substrate metabolism. The frequency of these variants varies by ancestry.

Dosing of drugs that are metabolized through CYP1A2 may require adjustment based on the *CYP1A2* genotype. Individuals who are poor metabolizers may require lower than usual doses to achieve optimal response, whereas individuals who are ultrarapid metabolizers may benefit from increased doses. The CYP1A2 phenotype is predicted based upon the number of functional, partially functional, nonfunctional, and inducible alleles present in a sample.

The following table outlines the relationship between the variations (star alleles) detected in this assay and the effect on the activity of the enzyme produced by that allele.

Table. Variations and Effect on Enzyme Metabolism

***CYP1A2* allele**	**Nucleotide change (legacy nomenclature)**	**cDNA nucleotide change (NM_000761.4)**	**Effect on enzyme metabolism(a)**
**1*	None (wild type)	None (wild type)	Normal (extensive) activity
**1F* (renamed *30 on 12/16/2024)	-163C>A	c.-9-154C>A	Increased inducibility
**1K*	-729C>T	c.-10+113C>T	Decreased activity and decreased inducibility
**6*	5090C>T	c.1291C>T	No activity
**7*	3533G>A	c.1253+1G>A	No activity

a. Effect of a specific allele on the activity of the CYP1A2 enzyme can only be estimated since the literature does not provide precise data.(1-5)

A complicating factor in correlating *CYP1A2* genotype to CYP1A2 phenotype is that some drugs or their metabolites are inhibitors of CYP1A2 catalytic activity. These drugs may reduce CYP1A2 catalytic activity. Consequently, an individual may require a dose decrease greater than predicted based upon genotype alone. Another complicating factor is that *CYP1A2* is inducible by several drugs and environmental agents (eg, cigarette smoke) and the degree of inducibility is under genetic control. It is important to interpret the results of testing in the context of other coadministered drugs and environmental factors.

Reference Values

An interpretive report will be provided.

Interpretation

An interpretive report will be provided.

The genotype, with associated star alleles, is assigned based on historical nomenclature as curated by the Karolinska Institutet Human Cytochrome P450 Nomenclature Database. *CYP1A2* was transitioned to the Pharmacogene Variation (PharmVar) Consortium on December 16, 2024, and variants upstream of position -920 bp (based on the ATG) are no longer included in star allele definitions.(6) The *1K allele designation was not transferred to PharmVar and is based on the Karolinska Institutet's historical allele nomenclature.

Cytochrome P450 (CYP) 1A2 activity is also dependent upon hepatic function status, as well as age. Renal function may be important for drugs that are excreted in urine. Patients may develop drug toxicity if hepatic or renal function is decreased. Drug metabolism is known to decrease with age. It is important to interpret the results of testing and dose adjustments in the context of hepatic and renal function and age.

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 variants may be present that could lead to false-negative or false-positive results. If results obtained do not match the clinical findings (phenotype), additional testing should be considered.

Samples may contain donor DNA if obtained from patients who received non-leukocyte reduced blood transfusions or allogeneic hematopoietic stem cell 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 hematopoietic stem cell transplantation, a pretransplant DNA specimen is recommended for testing.

CYP1A2 genetic test results in patients who have undergone liver transplantation may not accurately reflect the patient's CYP1A2 status.

This method may not detect all variants that result in altered CYP1A2 activity. Therefore, absence of a detectable variant does not rule out the possibility that a patient has altered CYP1A2 metabolism due to other *CYP1A2* variants that cannot be detected with this method. Furthermore, when 2 or more variants are identified, the cis-/trans- status (whether the variants are on the same or opposite chromosomes) is not always known. It should be noted that other laboratories may use different phenotype prediction methods as there is no consensus on this for *CYP1A2* at this time. However, the method used here represents the findings of the majority of literature available at this time.

The frequency of variants which cause altered CYP1A2 metabolism has not been fully characterized in all populations. CYP1A2 enzyme activity may be inhibited or induced by a variety of substances, medications, or their metabolites.

Clinical Reference

1. Ito M, Katono Y, Oda A, Hirasawa N, Hiratsuka M. Functional characterization of 20 allelic variants of CYP1A2. Drug Metab Pharmacokinet. 2015;30(3):247-252. doi:10.1016/j.dmpk.2015.03.001
2. Zhou H, Josephy PD, Kim D, Guengerich FP. Functional characterization of four allelic variants of human cytochrome P450 1A2. Arch Biochem Biophys. 2004;422(1):23-30. doi:10.1016/j.abb.2003.11.019
3. Murayama N, Soyama A, Saito Y, et al. Six novel nonsynonymous CYP1A2 gene polymorphisms: catalytic activities of the naturally occurring variant enzymes. J Pharmacol Exp Ther. 2004;308(3):1219
4. Murayama N, Soyama A, Saito Y, et al. J Pharmacol Exp Ther. 2004;308(1):300-306. doi:10.1124/jpet.103.055798

5. Saito Y, Hanioka N, Maekawa K, et al. Functional analysis of three CYP1A2 variants found in a Japanese population. Drug Metab Dispos. 2005;33(12):1905-1910. doi:10.1124/dmd.105.005819
6. PharmVar. Pharmacogene Variation Consortium. Updated December 16, 2024. Accessed May 15, 2025. Available at www.pharmvar.org/

Performance

Method Description
Genomic DNA is extracted from whole blood or saliva. Genotyping for the *CYP1A2* 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 DNA section 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
Varies

Report Available
3 to 8 days

Specimen Retention Time
Whole blood: 28 days (if available); Saliva: 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

Test Definition: 1A2Q

Cytochrome P450 1A2 Genotype, Varies

81479

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
1A2Q	CYP1A2 Genotype, V	80687-7

Result ID	Test Result Name	Result LOINC® Value
610075	CYP1A2 Genotype	72884-0
610076	CYP1A2 Phenotype	94254-0
610077	Interpretation	69047-9
610078	Additional Information	48767-8
610079	Method	85069-3
610080	Disclaimer	62364-5
610081	Reviewed by	18771-6