MAYO CLINIC LABORATORIES

Test Definition: 1A2Q

CYP1A2 Genotype, V

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

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

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: *CYPs 1A2, 2C9, 2C19, 2D6, 3A4, 3A5, 4F2, SLCO1B1,* and *VKORC1*.
Order PGXQP / Focused Pharmacogenomics Panel, Varies if multiple pharmacogenomic genotype testing is desired.

Specimen Required

Multiple genotype tests can be performed on a single specimen after a single extraction. See Multiple Genotype Test List in Special Instructions 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 specimen in original tube.

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. Include concentration 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 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)

Reject Due To

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

Specimen Minimum Volume

Blood: 0.4 mL
Saliva: 1 swab

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Varies	Varies (preferred)		

Clinical & Interpretive

Clinical Information

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	-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

Reference Values

An interpretive report will be provided.

Interpretation

An interpretive report will be provided.

The genotype, with associated star alleles, is assigned using standard allelic nomenclature as published by the Pharmacogene Variation (PharmVar) Consortium.(6)

CYP1A2 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 in Special Instructions. 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-leukoreduced 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 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 ethnic groups.

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 Jun;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 Feb;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 Mar;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 March 3, 2021. Accessed March 22, 2021. 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 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

Blood: Refrigerate; Saliva: Ambient; Extracted DNA: Frozen

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

0031U

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