MAYO CLINIC LABORATORIES

Test Definition: 3A5Q

CYP3A5 Genotype, V

Overview

Useful For

Aids in optimizing treatment with tacrolimus and other drugs metabolized by cytochrome P450 3A5

Special Instructions

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

Method Name

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) and as a part of a psychotropic or focused pharmacogenomics panel.
If multiple pharmacogenomic genotype testing is desired, order PGXQP / Focused Pharmacogenomics Panel, Varies.
If genotype testing for psychotropic medications is desired, order PSYQP / Psychotropic Pharmacogenomics Gene Panel, Varies.

Additional Testing Requirements

In general, most drugs metabolized by CYP3A5 are also metabolized by CYP3A4 and usually to a greater degree than CYP3A5. For this reason, substrates of these 2 enzymes are sometimes listed together in publications and genotyping of both genes might be needed to fully understand the metabolism of these drugs and predict phenotype. If *CYP3A4* genotyping is needed, order 3A4Q / Cytochrome P450 *3A4* Genotype, Varies.

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 specimenin original tube.
Specimen Stability Information: Ambient (preferred)/Refrigerated
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: One swab
Collection Instructions: Collect and send specimen per kit instructions.
Specimen Stability Information: Ambient
Specimen Type: DNA
Container/Tube: 2 mL screw top tube
Specimen Volume: 100mcL (microliters)
Collection Instructions:
1. The preferred volume is 100 mcL at a concentration of 50 ng/mcL.
2. Include concentration and volume on tube.

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

CYP3A5 allele	cDNA nucleotide change (NM_000777.4)	Effect on enzyme activity
*1	None (wild type)	Normal activity
*3	c.219-237A>G	No activity

*5	c.432+2T>C	No activity
*6	c.624G>A	No activity
*7	c.1035dup	No activity
*8	c.82C>T	Reduced activity
*9	c.1009G>A	Reduced 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 Pharmacogene Variation (PharmVar) Consortium.(1)

For additional information regarding pharmacogenomic genes and their associated drugs, see the 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 could 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.

CYP3A5 genetic test results in patients who have undergone liver transplantation may not accurately reflect the patient's CYP3A5 status.

This method may not detect all variants that result in altered CYP3A5 activity. Therefore, absence of a detectable variant does not rule out the possibility that a patient has altered CYP3A5 activity due to other *CYP3A5* 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.

Drug-drug interactions and drug-metabolite inhibition must be considered.

Drug-metabolite inhibition can occur, resulting in inhibition of CYP3A5 catalytic activity.

Clinical Reference

1. PharmVar: Pharmacogene Variation Consortium. Updated March 3, 2021. Accessed March 22, 2021. Available at www.pharmvar.org/

2. Birdwell KA, Decker B, Barbarino JM, et al. Clinical Pharmacogenetics Implementation Consortium (CPIC) Guidelines for CYP3A5 Genotype and Tacrolimus Dosing. Clin Pharmacol Ther. 2015;98(1):19-24. doi: 10.1002/cpt.113

3. Thervet E, Loriot MA, Barbier S, et al. Optimization of initial tacrolimus dose using pharmacogenetic testing. Clin Pharmacol Ther. 2010;87(6):721-726. doi: 10.1038/clpt.2010.17

4. Lamba J, Hebert JM, Schuetz EG, Klein TE, Altman RB. PharmGKB summary: very important pharmacogene information for CYP3A5. Pharmacogenet Genomics. 2012;22(7):555-558. doi: 10.1097/FPC.0b013e328351d47f

5. Clinical Pharmacogenetics Implementation Consortium (CPIC). Accessed October 14, 2020. https://cpicpgx.org/

Performance

Method Description

Genomic DNA is extracted from whole blood or saliva. Genotyping for *CYP3A5* 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 swab: 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

81231-CYP3A5

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
3A5Q	CYP3A5 Genotype, V	81140-6

Result ID	Test Result Name	Result LOINC Value
610117	CYP3A5 Genotype	81140-6
610118	CYP3A5 Phenotype	79717-5
610119	Interpretation	69047-9
610120	Additional Information	48767-8
610121	Method	85069-3
610122	Disclaimer	62364-5
610123	Reviewed by	18771-6