

## 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 Association 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](#) for a list of tests that can be ordered together.

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**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)/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:** 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) 1 year/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 1 of the following forms with the specimen:

-[Neurology Specialty Testing Client Test Request](#) (T732)

-[Therapeutics Test Request](#) (T831)

-[Renal Diagnostics Test Request](#) (T830)

## Specimen Minimum Volume

Blood: 0.4 mL

Saliva: 1 swab

## Reject Due To

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

## Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
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Varies	Varies		
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## Clinical & Interpretive

### Clinical Information

*CYP3A5* is a member of the *CYP3A* family of genes located on chromosome 7. The cytochrome P450 (CYP) 3A subfamily of enzymes responsible for the metabolism of more than 50% of medications that undergo hepatic metabolism and first-pass metabolism in intestinal epithelial cells. The *CYP3A5* expression level and enzymatic activity can be modulated by genetic variation. *CYP3A5* allelic frequency depends upon ethnicity. For example, in individuals of European descent the most common allele is the *CYP3A5*\*3 allele (c.219-237A>G), which results in a splicing defect and absence of enzyme activity. In individuals of African descent, the \*1 allele (functional enzyme) is most common. The distribution of *CYP3A5*\*3 allele frequencies ranges from 0.14 among sub-Saharan Africans to 0.95 in European populations.

*CYP3A5* testing is commonly ordered for patients receiving tacrolimus. Tacrolimus is an immunosuppressive calcineurin inhibitor used in transplant recipients. Tacrolimus has a low therapeutic index with a wide range of side effects and large interindividual variability in its pharmacokinetics, particularly in the dose required to reach target trough blood concentrations, thus necessitating routine therapeutic drug monitoring in clinical practice.

Tacrolimus dose requirements are most closely associated with *CYP3A5* genotype even though the drug is metabolized by both *CYP3A4* and *CYP3A5*. According to existing literature and Clinical Pharmacogenetics Implementation Consortium (CPIC) guidelines, individuals with at least one copy of fully functional *CYP3A5* (ie, \*1/\*1 and \*1/\*3) require a higher dose of tacrolimus to reach the targeted whole blood concentrations than those without a copy of a fully functional *CYP3A5* allele (ie, \*3/\*3) (2-5). *CYP3A5* genotyping may predict dose requirements for tacrolimus but does not replace the need for therapeutic monitoring to guide tacrolimus dose adjustments. For a patient with the *CYP3A5*\*3/\*3 genotype, initiating tacrolimus therapy with a standard (normal) dose is recommended. One of the complications in interpreting *CYP3A5* genotyping results and the effect of genotype on drug dosing is the fact that most individuals involved in drug trials have been of European descent. Individuals of European descent are more likely to have the *CYP3A5*\*3/\*3 genotype, which predicts a poor metabolizer phenotype. Dosing requirements were derived from these clinical trials so individuals with 1 or 2 copies of *CYP3A5*\*1, will functionally behave as though they have increased activity and may require higher doses of *CYP3A5* metabolized drugs.

The following table displays the *CYP3A5* variants detected by this assay, the corresponding star allele, and the effect on *CYP3A5* enzyme activity:

<b><i>CYP3A5</i> allele</b>	<b>cDNA nucleotide change (NM_000777.4)</b>	<b>Effect on enzyme activity</b>
*1	None (wild type)	Normal activity
*3	c.219-237A>G	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

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**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.

Specimens may contain donor DNA if obtained from patients who received non-leukoreduced blood transfusions or allogeneic hematopoietic stem cell transplantation. Results from specimens 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 September 26, 2023. Accessed October 25, 2023. Available at [www.pharmvar.org/](http://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, Lorient 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 25, 2023. <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. ([Unpublished Mayo method](#))

### PDF Report

No

### Day(s) Performed

Monday through Friday

### Report Available

3 to 8 days

### Specimen Retention Time

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

### Performing Laboratory Location

Rochester

## 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

81231-CYP3A5

### LOINC® Information

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