MAYO CLINIC LABORATORIES

Test Definition: 3A5Q

Cytochrome P450 3A5 Genotype, Varies

Overview

Useful For

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

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 any cord blood specimen that is received, maternal cell contamination testing may 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

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

Patient Preparation: A previous hematopoietic stem cell transplant from an allogenic donor or liver transplant will interfere with testing. For more 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, 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:
-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)
-Kidney Transplant Test Request

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

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. The frequency of *CYP3A5* alleles varies by ancestral background. 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 is most common which has fully functional enzyme activity. In addition to the **3* allele, other alleles also are associated with reduced or no enzyme activity, including the **6, *7, *8,* and **9* alleles.

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 adverse effects and large interindividual variability in its pharmacokinetics, particularly in the dose required to reach target trough blood concentrations. Thus, routine therapeutic drug monitoring is used 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* or **1/*3*) require a higher dose of tacrolimus to reach the targeted whole blood concentration than those without a copy of a fully functional *CYP3A5* allele (ie, **3/*3*).(1-4) *CYP3A5* genotyping may predict dose requirements for tacrolimus but does not replace the need for therapeutic drug 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 decent. Individuals of European decent 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:

***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
**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

The interpretive report includes an overview of the findings as well as the associated clinical significance.

The genotype, with associated star alleles, is assigned using standard allelic nomenclature as published by Pharmacogene Variation (PharmVar) Consortium.(5)

For additional information regarding pharmacogenomic genes and their associated drugs, see the Pharmacogenomic Associations Tables. This resource also includes information regarding enzyme inhibitors and inducers.

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. 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
2. 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
3. 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
4. Clinical Pharmacogenetics Implementation Consortium (CPIC). Accessed May 15, 2025. https://cpicpgx.org/
5. PharmVar: Pharmacogene Variation Consortium. Updated April 29, 2025. Accessed May 15, 2025. Available at www.pharmvar.org/
6. Lee SJ, Usmani KA, Chanas B, et al. Genetic findings and functional studies of human CYP3A5 single nucleotide polymorphisms in different ethnic groups. Pharmacogenetics. 2003;13(8):461-472.

doi:10.1097/00008571-200308000-00004

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

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

81231-CYP3A5

LOINC® Information

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Test Definition: 3A5Q

Cytochrome P450 3A5 Genotype, Varies

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