MAYO CLINIC LABORATORIES

Test Definition: 3A4Q

Cytochrome P450 3A4 Genotype, Varies

Overview

Useful For

Aids in determining therapeutic strategies for drugs that are metabolized by cytochrome P450 3A4, including quetiapine

This test is **not useful for** managing patients receiving fluvastatin, rosuvastatin, or pravastatin since these drugs are **not** metabolized appreciably by CYP3A4.

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

Most drugs metabolized by CYP3A4 are also metabolized by CYP3A5, but usually to a lesser extent, so testing of CYP3A5 may also be relevant and should be determined on a case by case basis. If CYP3A5 genotyping is needed, order 3A5Q / Cytochrome P450 *3A5* 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.

Patient Preparation: A previous hematopoietic stem cell transplant from an allogenic donor or a 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 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:
-Pharmacogenomics Test Request (T797)
-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

CYP3A4 is a member of the *CYP3A* family of genes located on chromosome 7. The cytochrome P450 (CYP) 3A subfamily of enzymes is responsible for the metabolism of more than 50% of medications that undergo hepatic metabolism and first-pass metabolism in intestinal epithelial cells, including some lipid-lowering drugs. The CYP3A4 enzyme activity is highly variable. Interindividual differences in enzyme expression may be due to several factors including: variable homeostatic control mechanisms, disease states that alter homeostasis, up- or down-regulation by environmental stimuli, and genetic variation.(1)

One variant, *CYP3A4*22* (NM_017460.6: c.522-191C>T, rs35599367), has been studied extensively. This variant affects hepatic expression of CYP3A4 and is associated with reduced CYP3A4 activity. Studies show that in livers with the reference (wild-type) genotype (homozygous C or CC) the *CYP3A4* mRNA level and enzyme activity were 1.7- and 2.5-fold greater than in *CYP3A4*22* heterozygotes (CT) and homozygotes (TT), respectively. The Dutch Pharmacogenetics Working Group published a guideline related to pharmacogenomic interactions with antipsychotic medications. This guideline recommends avoiding quetiapine in favor of an alternate medication to treat depression, or a dose reduction for other indications; however, the guideline indicates that the evidence is limited. Of note, there is currently no standardized method for translation of *CYP3A4* genotype to CYP3A4 phenotype, and the method used in this guideline differs slightly from that used in this genotyping test. The reported allele frequency of *CYP3A4*22* is 5% to 8% in the white population and 4.3% in African American and Chinese populations.

Other alleles have not been as extensively studied in clinical trials but are expected to have similar impacts on statin metabolism and the metabolism of other drugs primarily metabolized by CYP3A4.

The following table displays the *CYP3A4* variants detected by this assay, the corresponding star allele, and the effect on CYP3A4 enzyme activity. Individuals without a detectable *CYP3A4* variant are designated as *CYP3A4*1/*1*.

***CYP3A4* allele**	**cDNA nucleotide change (NM_017460.5)**	**Effect on enzyme activity**
**1*	None (wild type)	Normal activity
**8*	c.389G>A	No activity
**11*	c.1088C>T	Reduced activity
**12*	c.1117C>T	Reduced activity
**13*	c.1247C>T	No activity
**16*	c.554C>G	Minimal activity
**17*	c.566T>C	No activity
**18*	c.878T>C	Reduced activity
**22*	c.522-191C>T	Reduced activity
**26*	c.802C>T	No activity

Genotype to phenotype predictions are based on a review of the *CYP3A4* literature.

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 the Pharmacogene Variation (PharmVar) Consortium.(3)

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

CYP3A4 genetic test results in patients who have undergone liver transplantation may not accurately reflect the patient's CYP3A4 status.

This test does not detect all variants that result in altered CYP3A4 activity. Therefore, absence of a detectable variant does not rule out the possibility that a patient has altered CYP3A4 metabolism due to other *CYP3A4* 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 CYP3A4 catalytic activity.

Clinical Reference

1. Evans WE, Relling MV. Pharmacogenomics: translating functional genomics into rational therapeutics. Science. 1999;286(5439):487-491. doi: 10.1126/science.286.5439.487
2. Wang D, Guo Y, Wrighton SA, Cooke GE, Sadee W. Intronic polymorphism in CYP3A4 affects hepatic expression and response to statin drugs. Pharmacogenomics J. 2011;11(4):274-286. doi:10.1038/tpj.2010.28
3. PharmVar: Pharmacogene Variation Consortium. Updated April 29, 2025. Accessed May 15, 2025. Available at www.pharmvar.org/

4. Lamba JK, Lin YS, Schuetz EG, Thummel KE. Genetic contribution to variable human CYP3A-mediated metabolism. Adv Drug Deliv Rev. 2002;54(10):1271-1294. doi: 10.1016/s0169-409x(02)00066-2
5. Elens L, Becker ML, Haufroid V, et al. Novel CYP3A4 intron 6 single nucleotide polymorphism is associated with simvastatin-mediated cholesterol reduction in the Rotterdam Study. Pharmacogenet Genomics. 2011;21(12):861-866. doi: 10.1097/FPC.0b013e32834c6edb
6. Elens L, van Schaik RH, Panin N, et al. Effect of a new functional CYP3A4 polymorphism on calcineurin inhibitors' dose requirements and trough blood levels in stable renal transplant patients. Pharmacogenomics. 2011;12(10):1383-1396. doi: 10.2217/pgs.11.90
7. Clinical Pharmacogenetics Implementation Consortium (CPIC). Accessed May 15. 2025. https://cpicpgx.org/
8. Beunk L, Marga N, Bianca S, et al. Dutch Pharmacogenetics Working Group (DPWG) guideline for the gene-drug interaction between CYP2D6, CYP3A4, and CYP1A2 and antipsychotics. Eur J Hum Genet. 2024;32(3):278-285. doi:10.1038/s41431-023-01347-3

Performance

Method Description
Genomic DNA is extracted from whole blood or saliva. Genotyping for the *CYP3A4* 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: 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

81230-CYP3A4

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
3A4Q	CYP3A4 Genotype, V	74007-6

Result ID	Test Result Name	Result LOINC® Value
610110	CYP3A4 Genotype	81139-8
610111	CYP3A4 Phenotype	81145-5
610112	Interpretation	69047-9
610113	Additional Information	48767-8
610114	Method	85069-3
610115	Disclaimer	62364-5
610116	Reviewed by	18771-6