MAYO CLINIC LABORATORIES

Test Definition: SLC1Q

Solute Carrier Organic Anion Transporter Family Member 1B1 (SLCO1B1) Genotype, Statin, Varies

Overview

Useful For

Predicting risk for statin-associated myopathy in patients beginning statin therapy, especially simvastatin therapy

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

Genetics Test Information

This is a pharmacogenomic test for genotype for the rs4149056 (c.521T>C) variant found in the *5 allele. Presence of the *5 allele is associated with an increased risk for simvastatin-associated myopathy.

Testing Algorithm

Cord blood:

For cord blood specimens that have an accompanying maternal blood specimen, maternal cell contamination studies will 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

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: *CYP*s *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 for a list of tests that can be ordered together.

Patient Preparation: A previous hematopoietic stem cell transplant or liver transplant from an allogenic donor will interfere with testing. Call 800-533-1710 for instructions for testing patients who have received a hematopoietic stem cell or liver transplant.

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**.
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, 2 mL 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:
-Cardiovascular Test Request (T724)
-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

The most common adverse drug reaction associated with statins is skeletal muscle toxicity, which can include myalgia (with and without elevated creatine kinase levels), muscle weakness, muscle cramps, myositis, and rhabdomyolysis.(1) Rhabdomyolysis, while rare, is of clinical concern because of the risk for death as a result of cardiac arrhythmia, kidney failure, and disseminated intravascular coagulation. While the underlying causes of statin-associated myopathy are not known, several hypotheses have been formulated, including those related to the biochemical pathway of cholesterol synthesis inhibition and statin metabolism.

SLCO1B1 encodes the organic anion-transporting polypeptide 1B1 (OATP1B1) influx transporter located on the basolateral membrane of hepatocytes. OATP1B1 facilitates the hepatic uptake of statins as well as other endogenous compounds (eg, bilirubin). Changes in the activity of this transporter (eg, through genetic variations or drug-drug interactions) can increase the severity of statin-associated myopathy (ie, statin intolerance).(2)

SLCO1B1 rs4149056 (c.521T>C, p.V174A), which is found in the *5 and *15 alleles, interferes with localization of the transporter to the plasma membrane and can lead to increased systemic statin concentrations.(3,4) All statins are substrates of OATP1B1, but the association of *SLCO1B1* c.521T>C with statin intolerance varies depending on statin and dose and is most pronounced with higher doses of simvastatin therapy. A case-control study of simvastatin-induced myopathy observed an odds ratio (OR) for myopathy of 4.5 for *5 heterozygotes and 16.9 for *5 homozygotes (compared to individuals who did not carry *5) among patients receiving high-dose (80 mg/day) simvastatin therapy.(4) A dose relationship was also demonstrated in a replication cohort of patients taking 40 mg/day simvastatin with a relative risk of 2.6 per copy of the *5 allele. The *SLCO1B1* c.521T>C genotype has also been shown to affect systemic exposure of other statins (eg, atorvastatin, pravastatin, rosuvastatin) in addition to simvastatin.(3) Additional genes (eg, *ABCG2* and *CYP2C9*) also play a role.

Frequency of the *SLCO1B1* alleles varies across ancestral populations.

Reference Values

An interpretive report will be provided.

Interpretation

An interpretive report will be provided. The complementary DNA positions are based on NM_006446.4.

For additional information regarding pharmacogenomic genes and their associated drugs, see Pharmacogenomic Associations Tables. 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.

Specimens may contain donor DNA if obtained from patients who received non-leukocyte reduced 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 non-leukocyte reduced 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. *SLCO1B1* genetic test results in patients who have undergone liver transplantation may not accurately reflect the patient's *SLCO1B1* status.

Statin-related myopathy can occur in the absence of *SLCO1B1* c.521T>C.

The presence of *SLCO1B1* c.521T>C does not confer absolute risk for statin-associated myopathy.

Absence of a variant allele does not rule out the possibility that a patient harbors another variant that can impact medication efficacy and side effects.

Clinical Reference

1. Wilke RA, Lin DW, Roden DM, et al. Identifying genetic risk factors for serious adverse drug reactions: current progress and challenges. Nat Rev Drug Discov. 2007;6(11):904-916. doi:10.1038/nrd2423
2. Ramsey LB, Johnson SG, Caudle KE, et al. The Clinical Pharmacogenetics Implementation Consortium guideline for SLCO1B1 and simvastatin-induced myopathy: 2014 update. Clin Pharmacol Ther. 2014;96(4):423-428. doi:10.1038/clpt.2014.125
3. Niemi M. Transporter pharmacogenetics and statin toxicity. Clin Pharmacol Ther. 2010;87(1):130-133. doi:10.1038/clpt.2009.197
4. SEARCH Collaborative Group, Link E, Parish S, et al. SLCO1B1 variants and statin-induced myopathy--a genomewide study. N Engl J Med. 2008;359(8):789-799. doi:10.1056/NEJMoa0801936
5. Cooper-DeHoff RM, Niemi M, Ramsey LB, et al. The Clinical Pharmacogenetics Implementation Consortium guideline for SLCO1B1, ABCG2, and CYP2C9 genotypes and statin-associated musculoskeletal symptoms. Clin Pharmacol Ther. 2022;111(5):1007-1021. doi:10.1002/cpt.2557

Performance

Method Description

Genomic DNA is extracted from whole blood or saliva. Genotyping for *SLCO1B1* 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 DNA section 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. A genotype is assigned based on the allele-specific fluorescent signals that are detected.(Unpublished Mayo method)

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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
81328

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
SLC1Q	SLCO1B1 Genotype, V	93412-5

Result ID	Test Result Name	Result LOINC® Value
610152	SLCO1B1 Genotype	93412-5
610153	SLCO1B1 Phenotype	79722-5
610154	Interpretation	69047-9
610155	Additional Information	48767-8
610156	Method	85069-3
610157	Disclaimer	62364-5

610158	Reviewed by	18771-6