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

Determining a potential statin lipid lowering response, especially when using pravastatin

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.

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.

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) 9 days/Refrigerated 30 days

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: 1 swab
Collection Instructions: Collect and send specimen per kit instructions.
Specimen Stability Information: Ambient 30 days

Specimen Type: Extracted 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:
-Cardiovascular Test Request (T724)
-Therapeutics Test Request (T831)

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
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, renal 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 *5, *15, and *17, 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. While 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) there is less evidence demonstrating a clinical association between the *SLCO1B1* genotype and myopathy with statins other than simvastatin.(2)

Frequency of the *SLCO1B1* alleles varies across different racial and ethnic groups.

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-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. *SLCO1B1* genetic test results in patients who have undergone liver transplantation may not accurately reflect the patient's *SLCO1B1* status.

Simvastatin-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 simvastatin-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 [published correction appears in Nat Rev Drug Discov. 2008;7(2):185]. 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

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 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. A genotype is assigned based on the allele-specific fluorescent signals that are detected.(Unpublished Mayo method)

PDF Report

No

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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
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