MAYO CLINIC LABORATORIES

Test Definition: HL58R

HLA-B*5801 Genotype, Allopurinol Hypersensitivity, Varies

Overview

Useful For

Identifying individuals with an increased risk of severe cutaneous adverse reactions to allopurinol based on the presence of the human leukocyte antigen *HLA-B*58:01* allele

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

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

Qualitative Allele-Specific Real-Time Polymerase Chain Reaction (PCR)

NY State Available

Yes

Specimen

Specimen Type

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 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: 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 (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 a Therapeutics Test Request (T831) with the specimen.

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 human leukocyte antigen (HLA) genes help the immune system recognize and respond to foreign substances (such as viruses and bacteria). The *HLA-B* gene encodes a class I HLA molecule in the major histocompatibility complex, which acts by presenting peptides to immune cells. There are many different *HLA-B* alleles identified, one of which is the *HLA-B*58:01* allele. The frequency of the *HLA-B*58:01* allele varies among ancestral groups, with a frequency of 10% to 17% in Han Chinese, 6% in Korean, 6% to 8% in Thai, and 3% to 6% in African American populations. This allele is present at a lower frequency (approximately 1%-2%) among White and Hispanic populations.(1)

Allopurinol is a drug widely used for hyperuricemia-related diseases such as gout, Lesch-Nyhan syndrome, and recurrent urate kidney stones. Allopurinol has been associated with severe cutaneous adverse reactions (SCAR), including drug reaction with eosinophilia and systemic symptoms, toxic epidermal necrolysis, Stevens-Johnson syndrome, and allopurinol hypersensitivity syndrome (AHS). These reactions have a reported mortality rate of 20% to 25%. The *HLA-B*58:01* allele is associated with a markedly elevated risk for SCAR/AHS.

Guidelines from the Clinical Pharmacogenomics Implementation Consortium recommend *HLA-B*58:01* genotyping be performed when considering prescribing allopurinol, and that allopurinol should not be prescribed to patients who test positive for the allele due to the increased risk of SCAR.(2) In addition, the 2020 American College of Rheumatology Guideline for the Management of Gout recommends testing for the *HLA-B*58:01* allele prior to initiation of allopurinol in patients of Southeast Asian descent (eg, Han Chinese, Korean, Thai) and for African American patients.(3)

Reference Values

An interpretive report will be provided.

Interpretation

Positivity for *HLA-B*58:01* confers increased risk for hypersensitivity to allopurinol.

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, as well as potential alternate drug choices.

Cautions

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 non-leukoreduced blood transfusions, the genotype usually reverts to that of the recipient within 6 weeks. The impact of hematopoietic stem cell or liver transplantation on risk of severe cutaneous adverse reactions with allopurinol is not defined in the literature. Risk is unknown for stem cell or liver transplant recipients with mismatch of the *HLA-B*58:01* allele.

Rare or novel variants may be present that could lead to false-negative or false-positive results. This assay also detects closely related rare alleles including *HLA-B*57:05*, **58:04, *58:05, *58:09, *58:10, *58:11, *58:12, *58:13, *58:15, *58:17, *58:19, *58:21, *58:22, *58:23, *58:24, and *58:28*. There is currently no data indicating whether these or any

other alleles or subtypes are associated with allopurinol-induced severe cutaneous adverse reactions.

Clinical Reference

1. Gonzalez-Galarza FF, McCabe A, Santos EJMD, et al. Allele Frequency Net Database (AFND) 2020 update: gold-standard data classification, open access genotype data, and new query tools. Nucleic Acids Res. 2020;48(D1):D783-D788
2. Saito Y, Stamp LK, Caudle KE, et al. Clinical Pharmacogenetics Implementation Consortium (CPIC) guidelines for human leukocyte antigen B (HLA-B) genotype and allopurinol dosing: 2015 update. Clin Pharmacol Ther. 2016;99(1):36-37. doi:10.1002/cpt.161
3. FitzGerald JD, Dalbeth N, Mikuls T, et al. 2020 American College of Rheumatology Guideline for the management of gout. Arthritis Rheumatol. 2020;72(6):879-895
4. Hershfield MS, Callaghan JT, Tassaneeyakul W, et al. Clinical Pharmacogenetics Implementation Consortium guidelines for human leukocyte antigen-B genotype and allopurinol dosing. Clin Pharmacol Ther. 2013;93(2):153-158
5. Chung WH, Hung SI, Chen YT. Human leukocyte antigens and drug hypersensitivity. Curr Opin Allergy Clin Immunol. 2007;7(4):317-323

Performance

Method Description

Genomic DNA is extracted from whole blood or saliva. Amplification for the *HLA-B*58:01* allele and an internal control gene is performed by real-time polymerase chain reaction in the presence of SYBR green, which fluoresces when bound to double-stranded DNA. A genotype is assigned based on the allele-specific SYBR green fluorescent signals that are detected.(Unpublished Mayo method)

PDF Report

No

Day(s) Performed

Varies

Report Available

3 to 5 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

81381

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
HL58R	HLA-B 5801 Genotype, V	79711-8

Result ID	Test Result Name	Result LOINC® Value
610665	HLA-B *58:01 Genotype	79711-8
610666	HLA-B *58:01 Phenotype	93308-5
610667	Interpretation	69047-9
610668	Additional Information	48767-8
610669	Method	85069-3
610670	Disclaimer	62364-5
610671	Reviewed by	18771-6