

Overview

Useful For

Aiding in establishing diagnosis, refining prognosis, and potentially identifying targeted therapies for the optimal management of patients with histiocytic neoplasms

Genetics Test Information

This test includes next-generation sequencing to evaluate the following 8 genes and select intronic regions: *ARAF*, *BRAF*, *CSF1R*, *KRAS*, *MAP2K1*, *NRAS*, *PIK3CA*, and *PTEN*. For a list of genes and exons targeted by this test, see [Targeted Genes Interrogated by MayoComplete Histiocytic Neoplasms Next-Generation Sequencing](#).

Special Instructions

- [Hematopathology Patient Information](#)
- [Targeted Genes Interrogated by MayoComplete Histiocytic Neoplasms Next-Generation Sequencing](#)

Highlights

This test utilizes next-generation sequencing for the detection of somatic mutations with diagnostic, prognostic, or therapeutic value in a set of genes associated with histiocytic neoplasms.

Method Name

Next-Generation Sequencing (NGS)

NY State Available

Yes

Specimen

Specimen Type

Varies

Shipping Instructions

Whole blood, bone marrow aspirate, and body fluid specimens must arrive within 14 days of collection.

Specimen Required

Submit only 1 of the following specimens:

Specimen Type: Bone marrow aspirate

Container/Tube:

Preferred: Lavender or pink top (EDTA) or yellow top (ACD)

Acceptable: Green top (sodium heparin)

Specimen Volume: 2 mL

Collection Instructions:

1. Invert several times to mix bone marrow.
2. Send bone marrow specimen in original tube. **Do not aliquot.**
3. Label specimen as bone marrow.

Specimen Stability Information: Ambient (preferred) 14 days/Refrigerate 14 days

Additional Information: To ensure minimum volume and concentration of DNA is met, the requested volume must be submitted. Testing may be canceled if DNA requirements are inadequate.

Specimen Type: Whole blood

Container/Tube:

Preferred: Lavender or pink top (EDTA) or yellow top (ACD)

Acceptable: Green top (sodium heparin)

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. Label specimen as blood.

Specimen Stability Information: Ambient (preferred) 14 days/Refrigerate 14 days

Additional Information: To ensure minimum volume and concentration of DNA is met, the requested volume must be submitted. Testing may be canceled if DNA requirements are inadequate.

Specimen Type: Paraffin-embedded tissue

Container/Tube: Paraffin block

Collection Instructions:

1. If available, send 1 representative hematoxylin and eosin-stained slide.
2. Minimum amount of tumor nuclei is 20%.
3. Required amount of tissue area is at least 25 mm².
4. Tissue should be fixed in 10% neutral-buffered formalin. Other fixatives are not acceptable.
5. Decalcified specimens (eg, bone marrow core biopsies) are not acceptable.

Specimen Stability Information: Ambient

Additional Information: If the quality of the biopsy specimen is poor or the target tumor cell population is below 20%, testing should not be ordered. Testing may be canceled if DNA requirements are inadequate.

Specimen Type: Tissue slide

Slides: 10 unstained slides

Container/Tube: Transport in plastic slide holders.

Collection Instructions:

1. Send 10 unstained, nonbaked slides with 5-micron thick sections of tissue.
2. If available, also send 1 representative hematoxylin and eosin-stained slide.
2. Minimum amount of tumor nuclei is 20%.
3. Required amount of tissue area is at least 25mm².
4. Tissue should be fixed in 10% neutral-buffered formalin. Other fixatives are not acceptable.
5. Decalcified specimens (eg, bone marrow core biopsies) are not acceptable.

Specimen Stability Information: Ambient

Additional Information: Testing may be canceled if resultant extracted DNA does not meet concentration requirements.

Specimen Type: Frozen tissue

Container/Tube: Plastic container

Specimen Volume: 100 mg

Collection Instructions: Freeze tissue within 1 hour of collection

Specimen Stability Information: Frozen

Additional Information: Testing may be canceled if resultant extracted DNA does not meet concentration requirements.

Specimen Type: Body fluid

Container/Tube: Sterile container

Specimen Volume: 5 mL

Collection Instructions: Specify the type of fluid being submitted.

Specimen Stability Information: Refrigerated 14 days/Frozen 14 days

Additional Information: Testing may be canceled if resultant extracted DNA does not meet concentration requirements.

Specimen Type: Extracted DNA

Container/Tube: 1.5- to 2-mL tube

Specimen Volume: Entire specimen

Collection Instructions:

1. Label specimen as extracted DNA and source of specimen
2. Indicate volume and concentration of DNA on label

Specimen Stability Information: Frozen (preferred)/Refrigerated/Ambient

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). We 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.

Forms

1. [Hematopathology Patient Information](#) (T676)
2. If not ordering electronically, complete, print, and send a [Hematopathology/Cytogenetics Test Request](#) (T726) with the specimen.

Specimen Minimum Volume

Whole blood, bone marrow aspirate, body fluid: 1 mL; Frozen tissue: 50 mg; Extracted DNA: 100 microliters (mCL) at 20 ng/mCL

Reject Due To

Gross hemolysis	Reject
Gross lipemia	OK
Specimens that have been	Reject

decalcified (all methods) Bone marrow core biopsies Paraffin shavings Fixatives other than 10% neutral-buffered formalin for paraffin-embedded tissue Moderately to severely clotted bone marrow aspirate	
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Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Varies	Varies	14 days	

Clinical & Interpretive

Clinical Information

Histiocytic neoplasms are a diverse group of disorders characterized by the infiltration of neoplastic histiocytes within various tissues. Traditionally classification has been based on histopathology and limited immunohistochemical markers, as well as specific clinical presentations. Distinction between entities can be diagnostically difficult. Recently, genomic profiling by next-generation sequencing has revealed recurrent mutations in several genes that can be used to better subclassify entities in this challenging group of neoplasms. Furthermore, mutations involving the mitogen-activated protein kinase (MAPK) pathway (eg, *BRAF*, *MAP2K1*) have potential therapeutic implications for the use of targeted *BRAF* and *MEK* inhibitors.

Reference Values

An interpretive report will be provided.

Interpretation

Genomic variants detected by this test will be documented in a detailed laboratory-issued report. This report will contain information regarding the detected alterations and their associations with prognosis or possible therapeutic implications in histiocytic neoplasms. The information in the clinical report may be used by the patient's healthcare professional to help guide decisions concerning management. Final interpretation of next-generation sequencing results requires correlation with all relevant clinical, pathologic, and laboratory findings and is the responsibility of the

managing healthcare professional.

Cautions

This test is a targeted next-generation sequencing (NGS) panel assay that encompasses 8 genes with variable full exon, partial region (including select intronic or noncoding regions), or hot spot coverage (depending on specific genetic locus). Therefore, this test will not detect other genetic abnormalities in genes or regions outside the specified target areas. The test detects single-base substitutions (ie, point mutations), as well as small insertion or deletion type events. This test is not configured to detect structural genomic rearrangements (ie, translocations), gene fusions, copy number alterations, or large-scale (segmental chromosome region) deletions and other complex genomic changes.

This assay does not distinguish between somatic mutations and germline alterations in analyzed gene regions, particularly with variant allele frequencies near approximately 50% or 100%. If nucleotide alterations in genes associated with germline variant syndromes are present and there is a strong clinical suspicion or family history of malignant disease predisposition, additional genetic testing and appropriate counseling may be indicated. Some apparent mutations classified as variants of undetermined significance may represent rare or low population frequency polymorphisms.

Prior treatment for hematologic malignancy could affect the results obtained in this assay. Particularly, a prior allogeneic hematopoietic stem cell transplant may cause difficulties in either resolving somatic or polymorphic alterations or in assigning variant calls correctly to donor and recipient fractions if pertinent clinical or laboratory information (eg, chimerism engraftment status) is not provided.

Inadequate specimens (eg, insufficient DNA quantity or quality) will preclude further testing and will be noted in the interpretive report. For formalin-fixed paraffin embedded specimens, NGS testing should not be pursued if the quality of the biopsy specimen is poor (eg, limited sample size, presence of extensive necrosis or fibrosis) or the target tumor cell population is low (<20%).

Clinical Reference

1. Swerdlow S, Campo E, Harris NL, et al, eds. WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues. 4th ed. IARC Press; 2017. WHO Classification of Tumours, Vol 2
2. Badalian-Very G, Vergilio JA, Degar BA, et al. Recurrent BRAF mutations in Langerhans cell histiocytosis. *Blood*. 2010;116(11):1919-1923. doi:10.1182/blood-2010-04-279083
3. Haroche J, Charlotte F, Arnaud L, et al. High prevalence of BRAF V600E mutations in Erdheim-Chester disease but not in other non-Langerhans cell histiocytoses. *Blood*. 2012;120(13):2700-2703. doi:10.1182/blood-2012-05-430140
4. Diamond EL, Durham BH, Haroche J, et al. Diverse and targetable kinase alterations drive histiocytic neoplasms. *Cancer Discov*. 2016;6(2):154-165. doi:10.1158/2159-8290.CD-15-0913
5. Durham BH, Lopez Rodrigo E, Picarsic J, et al. Activating mutations in CSF1R and additional receptor tyrosine kinases in histiocytic neoplasms. *Nat Med*. 2019;25(12):1839-1842. doi:10.1038/s41591-019-0653-6

Performance**Method Description**

This is a target-enriched next-generation sequencing (NGS) panel. DNA is extracted from validated specimen sources including, but not limited to, peripheral blood, bone marrow aspirate, and formalin-fixed paraffin embedded tissues. Library preparation for NGS is performed, followed by probe hybridization and capture. Sequencing of the final sample library is performed on a NGS instrument. Following bioinformatic processing of the sequencing data, the sequencing results are interpreted to provide a final clinical report. Genomic alterations are called according to human genome reference build GRCh37 (hg19).(Unpublished Mayo method)

PDF Report

No

Day(s) Performed

Monday through Friday

Report Available

16 to 21 days

Specimen Retention Time

Bone marrow aspirate/Whole blood: 2 weeks; Tissue: 1 month; Extracted DNA: 3 months; FFPE tissue: Unused portions of blocks will be returned to the client; Unstained slides/body fluid: Not retained

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

81450

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
NGHIS	Histiocytic Neoplasms, NGS, V	104240-7

Result ID	Test Result Name	Result LOINC® Value

Test Definition: NGHIS

MayoComplete Histiocytic Neoplasms,
Next-Generation Sequencing, Varies

MP077	Specimen Type	31208-2
MP078	Indication for Test	42349-1
618525	NGHIS Result	No LOINC Needed
618526	Pathogenic Mutations Detected	82939-0
618527	Interpretation	69047-9
618529	Variants of Unknown Significance	93367-1
618530	Additional Information	48767-8
618528	Clinical Trials	82786-5
618531	Method Summary	85069-3
618532	Disclaimer	62364-5
618533	Panel Gene List	36908-2
618534	Reviewed By	18771-6