

## Overview

### Useful For

Evaluation of hematologic neoplasms, specifically of myeloid origin (eg, acute myeloid leukemia, myelodysplastic syndrome, myeloproliferative neoplasm, myelodysplastic/myeloproliferative neoplasm) at the time of diagnosis or possibly disease relapse, to help determine diagnostic classification and provide prognostic or therapeutic information for clinical management

Determine the presence of new clinically important gene mutation changes at relapse

### Genetics Test Information

This test includes next-generation sequencing to evaluate for the following 42 genes and select intronic regions: *ANKRD26, ASXL1, BCOR, CALR, CBL, CEBPA, CSF3R, DDX41, DNMT3A, ELANE, ETNK1, ETV6, EZH2, FLT3, GATA1, GATA2, IDH1, IDH2, JAK2, KDM6A, KIT, KRAS, MPL, NPM1, NRAS, PHF6, PTPN11, RAD21, RUNX1, SETBP1, SH2B3, SF3B1, SRP72, SMC3, SRSF2, STAG2, TERT, TET2, TP53, U2AF1, WT1, and ZRSR2.*

### Highlights

Next-generation sequencing detection of somatic gene mutations, including type, pattern and distribution, has diagnostic, prognostic, and potential therapeutic implications for patients with hematologic cancers of myeloid origin.

### Testing Algorithm

The following are available in Special Instructions:

-[Acute Leukemias of Ambiguous Lineage Testing Algorithm](#)

-[Acute Myeloid Leukemia: Testing Algorithm](#)

-[Acute Myeloid Leukemia: Relapsed with Previous Remission Testing Algorithm](#)

-[Myelodysplastic Syndrome: Guideline to Diagnosis and Follow-up](#)

-[Myeloproliferative Neoplasm: A Diagnostic Approach to Bone Marrow Evaluation](#)

-[Targeted Genes Interrogated by OncoHeme Next-Generation Sequencing](#); this is a list of the genes and exons targeted by this test.

### Special Instructions

- [Myeloproliferative Neoplasm: A Diagnostic Approach to Bone Marrow Evaluation](#)
- [Hematopathology Patient Information](#)
- [Myelodysplastic Syndrome: Guideline to Diagnosis and Follow-up](#)
- [Targeted Genes Interrogated by OncoHeme Next-Generation Sequencing](#)
- [Acute Leukemias of Ambiguous Lineage Testing Algorithm](#)
- [Acute Myeloid Leukemia: Testing Algorithm](#)
- [Acute Myeloid Leukemia: Relapsed with Previous Remission Testing Algorithm](#)

### Method Name

Somatic Mutation Detection by Next-Generation Sequencing (NGS)

### NY State Available

Yes

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## Specimen

### Specimen Type

Varies

### Shipping Instructions

Peripheral blood and bone marrow specimens must arrive within 14 days of collection.

### Necessary Information

The following information is required:

1. Clinical diagnosis
2. Pertinent clinical history, including disease phase (diagnostic, remission, relapse/refractory) and therapy status (especially if patient has received a hematopoietic stem cell transplant).
3. Clinical or morphologic suspicion
4. Date of collection
5. Specimen source

### Specimen Required

Submit only 1 of the following specimens:

**Specimen Type:** Bone marrow aspirate (preferred)

**Container/Tube:**

**Preferred:** EDTA (lavender top) or ACD (yellow top)

**Acceptable:** Heparin (green top), but not preferred

**Specimen Volume:** 2 mL

**Collection Instructions:**

1. Invert several times to mix bone marrow.
2. Send specimen in original tube.
3. Label specimen as bone marrow.

**Specimen Stability:** Ambient (preferred)/Refrigerate

**Specimen Type:** Peripheral blood

**Container/Tube:**

**Preferred:** EDTA (lavender top) or ACD (yellow top)

**Acceptable:** Heparin (green top), but not preferred

**Specimen Volume:** 3 mL

**Collection Instructions:**

1. Invert several times to mix blood.
2. Send specimen in original tube.
3. Label specimen as blood.

**Specimen Stability:** Ambient (preferred)/Refrigerate

**Specimen Type:** Extracted DNA from blood or bone marrow

**Container/Tube:** 1.5- to 2-mL tube with indication of volume and concentration of the DNA

**Specimen Volume:** Entire specimen

**Collection Instructions:** Label specimen as extracted DNA and source of specimen

**Specimen Stability:** Frozen (preferred)/Refrigerate/Ambient

**Forms**

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

**Specimen Minimum Volume**

Blood, Bone Marrow: 1 mL  
Extracted DNA: 100 mcL at 20 ng/mcL concentration

**Reject Due To**

Gross hemolysis	Reject
Gross lipemia	OK
Bone marrow biopsies Slides Paraffin shavings or frozen tissues and paraffin-embedded tissues Paraffin-embedded bone marrow aspirates Moderately to severely clotted	Reject

**Specimen Stability Information**

Specimen Type	Temperature	Time	Special Container
Varies	Varies	14 days	

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## Clinical and Interpretive

### Clinical Information

Next-generation sequencing (NGS) is a comprehensive molecular diagnostic methodology that can interrogate multiple regions of genomic tumor DNA in a single assay. Many hematologic neoplasms are characterized by morphologic or phenotypic similarities, but can have characteristic somatic mutations in many genes. In addition, many myeloid neoplasms lack a clonal cytogenetic finding at diagnosis (normal karyotype) but can be diagnosed and classified according to the gene mutation profile. The presence and pattern of gene mutations can provide critical diagnostic, prognostic, and sometimes therapeutic information for the managing physicians.

### Reference Values

An interpretive report will be provided.

### Interpretation

Mutations (gene alterations) identified, if present, using human reference genome build GRCh37 (hg19). An interpretive report will be provided.

If this test is ordered in the setting of erythrocytosis and suspicion of polycythemia vera, interpretation requires correlation with a concurrent or recent prior bone marrow evaluation.

### Cautions

This test is a targeted next-generation sequencing (NGS) (panel) assay that encompasses 42 genes with variable full exon, partial region (including select intronic or non-coding regions), or hot spot coverage (depending on specific 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, but it does not detect gene rearrangements (ie, translocations), gene fusions, copy number alterations, or large scale (segmental chromosome region) deletions and complex changes.

This assay does not distinguish between somatic and germline alterations in analyzed gene regions, particularly with variant allele frequencies (VAF) near 50% or 100%. If nucleotide alterations in genes associated with germline mutation syndromes are present and there is also a strong clinical suspicion or family history of malignant disease predisposition, additional genetic testing and appropriate counseling may be indicated. Mutation cells detected between 5% and 10% VAF may indicate low-level (ie, subclonal) tumor populations, although the clinical significance of these findings may not be clear. A low incidence of gene mutations associated with myeloid neoplasms can be detected in nonmalignant hematopoietic cells in individuals with advancing age (clonal hematopoiesis of indeterminate potential, CHIP) and these may not be clearly distinguishable from tumor-associated mutations. Some apparent mutations classified as variants of undetermined significance (VUS) may represent rare or low frequency polymorphisms.

Prior treatment for hematologic malignancy could affect the results obtained in this assay. In particular, prior allogeneic hematopoietic stem cell transplant (HSCT) may cause difficulties in 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.

Correlation with clinical, histopathologic and additional laboratory findings is required for final interpretation of these results. The final interpretation of results for clinical management of the patient is the responsibility of the managing physician.

### Clinical Reference

1. Patel JP, Levine RL: How do novel molecular genetic markers influence treatment decisions in acute myeloid

leukemia? Hematology Am Soc Hematol Educ Program 2012;2012:28-34

2. Lindsley RC, Ebert BL: The biology and clinical impact of genetic lesions in myeloid malignancies. Blood 2013;23:3741-3748

3. Patel JP, Gonen M, Figueroa ME, et al: Prognostic relevance of integrated genetic profiling in acute myeloid leukemia. N Engl J Med 2012;366:1079-1089

4. Haferlach T, Nagata Y, Grossman V, et al: Landscape of genetic lesions in 944 patients with myelodysplastic syndromes. Leukemia 2014;28:241-247

5. Vainchenker W, Delhommeau F, Constantinescu SN, Bernard OA: New mutations and pathogenesis of myeloproliferative neoplasms. Blood 2011;118:1723-1735

## Performance

### Method Description

Next-generation sequencing is performed for the presence of a mutation in targeted regions of the following 42 genes: ANKRD26, ASXL1, BCOR, CALR, CBL, CEBPA, CSF3R, DDX41, DNMT3A, ELANE, ETNK1, ETV6, EZH2, FLT3, GATA1, GATA2, IDH1, IDH2, JAK2, KDM6A, KIT, KRAS, MPL, NPM1, NRAS, PHF6, PTPN11, RAD21, RUNX1, SETBP1, SH2B3, SF3B1, SRP72, SMC3, SRSF2, STAG2, TERT, TET2, TP53, U2AF1, WT1, and ZRSR2. See [Targeted Gene Regions Interrogated by OncoHeme Next-Generation Sequencing](#) in Special Instructions for details regarding the targeted gene regions identified in this test. This is a laboratory-developed test using Research Use Only reagents. Extracted DNA from the clinical specimen is fragmented, adapter ligated, and a sequence library of fragments is prepared using a custom capture hybridization method. Individual patient samples are indexed ("bar-coded") for identification and the library is sequenced on an Illumina platform. Sequence data are processed through the Mayo Clinic Clinical Genome Sequencing Lab bioinformatics pipeline and a variant call file is generated for final analysis and reporting. (Unpublished Mayo method)

### PDF Report

No

### Day(s) and Time(s) Test Performed

Monday, Wednesday, Friday

### Analytic Time

14 days

### Maximum Laboratory Time

21 days

### Specimen Retention Time

DNA 3 months

### Performing Laboratory Location

Rochester

## Fees and 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 Regional Manager. 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. This test has not been cleared or approved by the U.S. Food and Drug Administration.

### CPT Code Information

81450

### LOINC® Information

Test ID	Test Order Name	Order LOINC Value
NGSHM	NGS for Myeloid Neoplasms (NGSHM)	In Process

Result ID	Test Result Name	Result LOINC Value
MP024	Specimen Type	31208-2
NGSD	Indication for Test	42349-1
601696	NGSHM Result	No LOINC Needed
37276	Pathogenic Mutations Detected	41103-3
37283	Interpretation	69047-9
37282	Clinical Trials	82786-5
37277	Variants of Unknown Significance	93367-1
37278	Additional Notes	48767-8
37279	Method Summary	49549-9
37420	Disclaimer	62364-5
37280	OncoHeme Panel Gene list	36908-2
37287	Reviewed By:	19139-5