MAYO CLINIC LABORATORIES

Test Definition: KITE

KIT Mutation Exons 8-11 and 17, Hematologic Neoplasms, Sequencing, Varies

Overview

Useful For

Prognostic assessment of acute myeloid leukemias with core-binding factor translocations (inv16 or t[16;16] *CBFB-MYH11* or t[8;21] *RUNX1-RUNX1T1*)

This test is **not intended for** *KIT* evaluation in solid tumors (eg, melanoma, gastrointestinal stromal tumor).

Genetics Test Information

This test is intended to detect *KIT* gene mutations in exons 8 through 11 and 17 that occur in hematologic malignant neoplasms, including specifically acute myeloid leukemia and mastocytosis. This test identifies somatic (acquired) mutations in these tumors.

Testing Algorithm

The following algorithms are available:
-Acute Myeloid Leukemia: Testing Algorithm
-Mast Cell Disorder: Diagnostic Algorithm, Bone Marrow

Special Instructions

- Hematopathology Patient Information
- Acute Myeloid Leukemia: Testing Algorithm
- Mast Cell Disorder: Diagnostic Algorithm, Bone Marrow

Highlights

KIT mutations have been associated with adverse prognosis in "core-binding factor" (CBF) acute myeloid leukemias (AML) characterized by inv16 or t(16;16) *CBFB-MYH11* or t(8;21) *RUNX1-RUNX1T1* genetic abnormalities.

KIT mutations are involved in the pathogenesis of mastocytosis and detection of the common *KIT* mutation p.Asp816Val (D816V) is an important minor diagnostic criterion for systemic mastocytosis; however, other *KIT* mutations can be seen in a small number of cases negative for the D816V.

This test is intended primarily for detection of *KIT* mutations in CBF AML and may be useful in some cases of mastocytosis. However, if systemic mastocytosis is suspected, the more sensitive allele-specific polymerase chain reaction method to specifically identify the *KIT* D816V abnormality is strongly recommended prior to *KIT* sequencing given that mast cell abundance in bone marrow samples is often very limited (see Ordering Guidance and Cautions).

Method Name

Sanger Sequencing

NY State Available

Yes

Specimen

Specimen Type
Varies

Ordering Guidance
This test is intended for detection of *KIT* mutations in "core-binding factor" (CBF) acute myeloid leukemias (AML). For systemic mastocytosis, order KITVS / *KIT* Asp816Val Mutation Analysis, Varies.

This test is **not intended for** *KIT* evaluation in solid tumors (eg, melanoma, gastrointestinal stromal tumor); for these indications, refer to one of the following:
-Gastrointestinal Stromal Tumor (GIST) Targeted Gene Panel, Next-Generation Sequencing, Tumor
-Melanoma Targeted Gene Panel, Next-Generation Sequencing, Tumor
-Solid Tumor-Targeted Cancer Gene Panel, Next-Generation Sequencing, Varies

Shipping Instructions
Specimen must arrive within 7 days of collection.

Necessary Information
The following information is required:
1. Pertinent clinical history
2. Clinical or morphologic suspicion
3. Date and time of collection
4. Specimen source

Specimen Required
Submit only 1 of the following specimens:

Specimen Type: Blood
Container/Tube: Lavender top (EDTA) or yellow top (ACD)
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)/Refrigerate

Specimen Type: Bone marrow
Container/Tube: Lavender top (EDTA) or yellow top (ACD)
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)/Refrigerate

Specimen Type: Extracted DNA from blood or bone marrow
Container/Tube: 1.5- to 2-mL tube
Specimen Volume: Entire specimen
Collection Instructions: Label specimen as extracted DNA from blood or bone marrow with an indication of volume and concentration of the DNA.
Specimen Stability Information: Frozen (preferred)/Refrigerate/Ambient

Specimen Type: Paraffin-embedded tissue
Container/Tube: Paraffin block
Specimen Volume: Entire block
Additional Information: Tissue must demonstrate involvement by a hematologic neoplasm (eg, acute myeloid leukemia: AML), not solid tumors.
Specimen Stability Information: Ambient

Specimen Type: Paraffin-embedded bone marrow aspirate clot
Container/Tube: Paraffin block
Specimen Volume: Entire block
Specimen Stability Information: Ambient

Specimen Type: Tissue
Slides: Unstained slides
Specimen Volume: 10 Slides
Additional Information: Tissue must demonstrate involvement by a hematologic neoplasm (eg, AML), not solid tumors.
Specimen Stability Information: 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 from blood or bone marrow: 50 microliters (mcL) at 20 ng/mcL

Reject Due To

Gross hemolysis	Reject
Bone marrow core biopsies Paraffin shavings	Reject

Frozen tissues Moderately to severely clotted	

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Varies	Varies	7 days	

Clinical & Interpretive

Clinical Information

Acquired mutations in the *KIT* gene are identified in a subset of acute myeloid leukemias (AML) characterized by inv16 or t(16;16) *CBFB-MYH11* or t(8;21) *RUNX1-RUNX1T1* genetic abnormalities (approximately 10%-20% of cases) and in this setting, the additional presence of a *KIT* gene mutation has been described as an adverse prognostic factor in some studies. *KIT* mutations in AML tend to involve exons 8 through 11 and 17, although the p.Asp816Val (D816V) variant, which is highly prevalent in systemic mastocytosis (SM), is less common in AML.

Mastocytosis is a hematologic disorder characterized by abnormal mast cell expansion in the bone marrow and extramedullary organ sites (eg, skin, gastrointestinal tract). Disease can be localized to skin (ie, cutaneous mastocytosis: CM) or present systemically, with variable features of disease aggressiveness and symptomatology. Variants in the *KIT* gene are identified in a large majority of patients with both CM and SM. The D816V abnormality is identified in most patients with SM, and this finding represents an important minor diagnostic criterion in the 2008 WHO classification. The D816V is less commonly seen in CM, although single nucleotide variants are present in other *KIT* exons. Rare cases of familial mastocytosis are also described with *KIT* mutations involving exons 8 and 9. Although *KIT* gene mutation represents an important diagnostic marker for SM, the number of bone marrow mast cells is often limited in aspirate samples. Therefore, if SM is clinically and pathologically suspected, *KIT* testing should first proceed with a sensitive and specific screen for the D816V (KITVS / *KIT* Asp816Val Mutation Analysis, Varies) prior to consideration of *KIT* gene sequencing, based on the greatly enhanced sensitivity of the polymerase chain reaction test for this particular variant. In AML, *KIT* sequencing is preferred, given the wider spectrum of mutations in other *KIT* exons.

Reference Values

An interpretive report will be provided

Interpretation

Mutations detected or not detected. An interpretive report will be provided.

Cautions

This test is intended to evaluate for the presence of somatically acquired *KIT* mutations in hematologic malignant neoplasms, specifically core-binding factor (CBF) acute myeloid leukemia with t(8;21)/*RUNX1-RUNX1T1* or inv(16) or t(16;16)/*CBFB-MYH11*, although it may be useful in some cases of mastocytosis. This test does not detect mutations in the entire *KIT* gene, but is limited to alterations in exons 8, 9, 10, 11, and 17. The analytic sensitivity of this assay is

approximately 20%. It is important to note that in many instances of systemic mastocytosis (SM), mast cell abundance in bone marrow aspirates is very limited and this test may result a false-negative for *KIT* mutation. Therefore, if SM is suspected clinically or pathologically, testing for the specific p.Asp816Val (D816V) by allele-specific PCR method should be strongly considered as the initial test (KITVS / *KIT* Asp816Val Mutation Analysis, Varies), prior to pursuing *KIT* sequencing.

Clinical Reference

1. Orfao A, Garcia-Montero AC, Sanchez L, Escribano L; REMA: Recent advances in the understanding of mastocytosis: the role of KIT mutations. Br J Haematol. 2007 Jul;138(1):12-30. doi: 10.1111/j.1365-2141.2007.06619.x
2. Arock M, Sotlar K, Broesby-Olsen S, et al: KIT mutation analysis in mast cell neoplasms: recommendations of the European Competence Network on Mastocytosis. Leukemia. 2015 Jun;29(6):1223-1232. doi: 10.1038/leu.2015.24
3. Paschka P, Du J, Schlenk RF, et al: Secondary genetic lesions in acute myeloid leukemia with inv(16) or t(16;16): a study of the German-Austrian AML Study Group (AMLSG). Blood. 2013 Jan;121(1):170-177. doi: 10.1182/blood-2012-05-431486
4. Pardanani A: Systemic mastocytosis in adults: 2012 Update on diagnosis, risk stratification, and management. Am J Hematol. 2012 Apr;87(4):402-411. doi: 10.1002/ajh.23134
5. Paschka P, Marcucci G, Rupprt AS, et al: Adverse prognostic significance of *KIT* mutations in adult acute myeloid leukemia with inv(16) and t(8;21): a Cancer and Leukemia Group B Study. J Clin Oncol. 2006 Aug;24(24):3905-3911. doi: 10.1200/JCO.2006.06.9500

Performance

Method Description

Total DNA is extracted from the sample and exons 8, 9, 10, 11, and 17 of the *KIT* gene are amplified by polymerase chain reaction followed by Sanger sequencing with evaluation by capillary electrophoresis. Review of the sequence data is performed using a combination of automated calls and manual inspection.(Unpublished Mayo method)

PDF Report

No

Day(s) Performed

Monday through Friday

Report Available

5 to 8 days

Specimen Retention Time

DNA: 3 months; Peripheral blood, bone marrow: 2 weeks

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. This test has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information

81272-KIT (v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog) (eg, gastrointestinal stromal tumor [GIST], acute myeloid leukemia, melanoma), gene analysis, targeted sequence analysis (eg, exons 8, 11, 13, 17, 18)

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
KITE	KIT Mutation, Hematologic Neoplasm	55201-8

Result ID	Test Result Name	Result LOINC® Value
39426	KIT Sequencing Result	No LOINC Needed
MP027	Specimen Type	31208-2
37921	Final Diagnosis	50398-7