Test Definition: MPLFM

MPL Exon 10 Mutation Detection, Bone Marrow

Overview

Useful For

Diagnosis or differential diagnosis of myeloproliferative disorders by *MPL* gene analysis using bone marrow specimens

Method Name

Sanger Sequencing

NY State Available

No

Specimen

Specimen Type

Bone Marrow

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 of collection
4. Specimen source

Specimen Required

Container/Tube: Lavender top (EDTA)

Specimen Volume: 3 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 Minimum Volume

1 mL

Reject Due To

Gross hemolysis	Reject

Moderately to severely clotted	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Bone Marrow	Ambient (preferred)	7 days	
	Refrigerated	7 days	

Clinical & Interpretive

Clinical Information

Mutations in the *JAK2*, *CALR* and *MPL* genes are considered driver events in the *BCR::ABL1* negative myeloproliferative neoplasms (MPN) including polycythemia vera (PV), primary myelofibrosis (PMF) and essential thrombocythemia (ET). The *JAK2* V617F mutation occurs in 95% to 98% of patients with PV, 50% to 60% of patients with PMF and 50% to 60% of patients with ET respectively at diagnosis. Other *JAK2* mutations in exons 12 to 15 occur in the remaining patients with PV. Mutations in the *CALR* gene occur in 20% to 30% of patients with PMF and 20% to 30% of patients with ET at diagnosis. A 52 base pairs deletion (53%) and a 5 bp deletion (32%) are the most common mutations in the *CALR* gene while other types of mutations may occur in the remaining cases. *MPL* exon 10 mutations occur in 5% to 10% of patients with PMF and 5% to 10% of patients with ET. Mutations in *JAK2*, *CALR* and *MPL* are mutually exclusive. The *JAK2* V617F mutation is detected by quantitative polymerase chain reaction (PCR). The *CALR* mutations are detected by PCR targeting exon 9. The *MPL* mutations in exon 10 are detected by Sanger sequencing. All mutations in *JAK2*, *CALR* and *MPL* can also be detected by next generation of sequencing (NGS). In addition to the mutations in *JAK2*, *CALR* and *MPL*, mutations in many other genes including *ASXL1*, *TET2*, *DNMT3A*, *SRSF2*, *SF3B1*, *U2AF1*, *ZRSR2*, *EZH2*, *IDH1*, *IDH2*, *CBL*, *KRAS*, *NRAS*, *STAG2*, and *TP53* can occur in MPN. These additional mutations are more frequent in PMF and advanced disease, as compared to PV and ET. It is known that mutations in the *ASXL1*, *SRSF2*, *U2AF1*, *EZH2*, *IDH1* and *IDH2* are correlated with a poor prognostic risk. While a single gene test on *JAK2*, *CALR* and *MPL* can be clinically useful, all above mentioned gene mutations can be detected by NGS.

Reference Values

An interpretive report will be provided.

Interpretation

The results will be reported as 1 of 2 states:
-Negative for myeloproliferative leukemia virus oncogene (*MPL*) exon 10 mutation
-Positive for *MPL* exon 10 mutation

If the result is positive, a description of the mutation at the nucleotide level and the altered protein sequence is reported.

Positive mutation status is highly suggestive of a myeloproliferative neoplasm but must be correlated with clinical and other laboratory features for a definitive diagnosis. Negative mutation status does not exclude the presence of a

myeloproliferative or other neoplasm.

Cautions

A positive result is not specific for a particular diagnosis, and clinicopathologic correlation is necessary in all cases.

A negative result does not exclude the presence of a myeloproliferative or other neoplasm.

Supportive Data

Analytical sensitivity is approximately 20% meaning there must be about 20% of the altered DNA in the specimen for reliable detection.

Clinical Reference

1. Klampfl T, Gisslinger H, Harutyunyan AS, et al. Somatic mutations of calreticulin in myeloproliferative neoplasms. N Engl J Med. 2013;369(25):2379-2390
2. Rumi E, Pietra D, Ferretti V, et al. JAK2 or CALR mutation status defines subtypes of essential thrombocythemia with substantially different clinical course and outcomes. Blood. 2014;123(10):1544-1551
3. Greenfield G, McMullin MF, Mills K. Molecular pathogenesis of the myeloproliferative neoplasms. J Hematol Oncol. 2021;14(1):103
4. Khoury JD, Solary E, Abla O, et al. The 5th edition of the World Health Organization classification of haematolymphoid tumors: myeloid and histiocytic/dendritic neoplasms. Leukemia 2022; 36:1703-1719.

Performance

Method Description

Genomic DNA is extracted from bone marrow, and the *MPL* exon 10 amplified using standard polymerase chain reaction. The entire exon 10 sequence is obtained using Sanger sequencing (BigDye terminator V3.1 cycle sequencing kid from Applied Bioscience) with analysis on an automated genetic analyzer.(Unpublished Mayo method)

PDF Report

No

Day(s) Performed

Monday through Friday

Report Available

1 to 8 days

Specimen Retention Time

Bone marrow: 2 weeks; Extracted DNA: 1 year

Performing Laboratory Location

Mayo Clinic Jacksonville Clinical Lab

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

81339

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
MPLFM	MPL Exon 10 Mutation, BM	75033-1

Result ID	Test Result Name	Result LOINC® Value
618662	Final Diagnosis	69047-9
618663	Method	85069-3
618664	Signing Pathologist	18771-6
618666	Additional Information	48767-8
618667	Disclaimer	62364-5