MAYO CLINIC LABORATORIES

Test Definition: MPNML

MPL Exon 10 Sequencing, Reflex, Varies

Overview

Useful For

Aiding in the distinction between a reactive cytosis and a myeloproliferative neoplasm when *JAK2* V617F testing result is negative

Evaluating for variants in *MPL* in an algorithmic process for MPNCM / Myeloproliferative Neoplasm, *CALR* with Reflex to *MPL*, Varies

Method Name

Only orderable as a reflex. For more information see MPNCM / Myeloproliferative Neoplasm, *CALR* with Reflex to *MPL*, Varies.

Sanger Sequencing

NY State Available

Yes

Specimen

Specimen Type

Varies

Specimen Required

Only orderable as a reflex. For more information see MPNCM / Myeloproliferative Neoplasm, *CALR* with Reflex to *MPL*, Varies.

Submit only 1 of the following specimens:

Specimen Type: Whole Blood
Container/Tube: Lavender top (EDTA) or yellow top (ACD-B)
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 whole blood.
Specimen Stability Information: Ambient (preferred)/Refrigerate

Specimen Type: Bone marrow
Container/Tube: Lavender top (EDTA) or yellow top (ACD-B)
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:
1. DNA must be extracted from blood or bone marrow within 7 days of collection.
2. Label specimen as extracted DNA and source of specimen.
3. Provide volume and concentration of the DNA.
Specimen Stability Information: Frozen (preferred) 1 year/Refrigerate/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.

Reject Due To

Gross hemolysis	Reject
Paraffin-embedded bone marrow aspirate clot or biopsy blocks	Reject
Slides	Reject
Paraffin shavings	Reject
Moderately to severely clotted	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Varies	Varies		

Clinical & Interpretive

Clinical Information

The *JAK2* V617F variant is present in 95% to 98% of patients with polycythemia vera, 50% to 60% of patients with

primary myelofibrosis (PMF), and 50% to 60% of patients with essential thrombocythemia (ET). Detection of the *JAK2* V617F variant helps establish the diagnosis of a myeloproliferative neoplasm (MPN). However, a negative *JAK2* V617F result does not indicate the absence of MPN. Other important molecular markers in *BCR::ABL1*-negative MPN include *CALR* exon 9 alterations (20%-30% of PMF and ET) and MPL exon 10 alterations (5%-10% of PMF and 3%-5% of ET). Variants in *JAK2*, *CALR*, and *MPL* are essentially mutually exclusive. A *CALR* variant is associated with decreased risk of thrombosis in both ET and PMF and confers a favorable clinical outcome in patients with PMF. A triple negative (*JAK2* V617F, *CALR*, and *MPL*-negative) genotype is considered a high-risk molecular signature in PMF.

Reference Values

Only orderable as a reflex. For more information see MPNCM / Myeloproliferative Neoplasm, *CALR* with Reflex to *MPL*, Varies.

An interpretive report will be provided.

Interpretation

The results will be reported as 1 of the 3 following states:
-Positive for *CALR* variant
-Positive for *MPL* variant
-Negative for *CALR* and *MPL* variants

Positive variant status is highly suggestive of a myeloid neoplasm and clinicopathologic correlation is necessary in all cases.

Negative variant status does not exclude the presence of a myeloproliferative neoplasm or other neoplasms.

Cautions

A positive result is not specific for a particular subtype of myeloproliferative neoplasm and clinicopathologic correlation is necessary in all cases.

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

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. Nangalia J, Massie CE, Baxter EJ, et al. Somatic CALR mutations in myeloproliferative neoplasms with nonmutated JAK2. N Engl J Med. 2013;369(25):2391-2405
3. Rotunno G, Mannarelli C, Guglielmelli P, et al. Impact of calreticulin mutations on clinical and hematological phenotype and outcome in essential thrombocythemia. Blood. 2014;123(10):1552-1555
4. Tefferi A, Lasho TL, Finke CM, et al. CALR vs JAK2 vs MPL-mutated or triple-negative myelofibrosis: clinical, cytogenetic and molecular comparisons. Leukemia. 2014;28(7):1472-1477
5. Pikman Y, Lee BH, Mercher T, et al. MPLW515L is a novel somatic activating mutation in myelofibrosis with myeloid metaplasia. PLoS Med. 2006;3(7):e270
6. Pardanani AD, Levine RL, Lasho T, et al. *MPL*515 mutations in myeloproliferative and other myeloid disorders: a study of 1182 patients. Blood. 2006;108(10):3472-3476
7. Greenfield G, McMullin MF, Mills K. Molecular pathogenesis of the myeloproliferative neoplasms. J Hematol Oncol. 2021;14(1):103

Performance

Method Description
Genomic DNA is extracted, and Sanger sequencing is used to evaluate for alterations in *MPL*, exon 10. The sensitivity of this assay is approximately 20%, such that samples containing lower percentages of altered DNA will appear negative.(Unpublished Mayo method)

PDF Report
No

Day(s) Performed
Monday through Friday

Report Available
7 to 10 days

Specimen Retention Time
Whole blood/Bone marrow: 2 weeks; 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
81339-MPL (myeloproliferative leukemia virus oncogene, thrombopoietin receptor, TPOR) (eg, myeloproliferative disorder), exon 10 sequence