Test Definition: MPNML

MPL Exon 10 Sequencing, Reflex

Overview

Useful For

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

Evaluates 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: Blood

Container/Tube: Lavender top (EDTA) or yellow top (ACD solution B)

Specimen Volume: 4 mL

Collection Instructions:

1. Invert several times to mix blood.

2. Send specimen in original tube.

3. Label specimen as blood.

Specimen Stability Information: Ambient (preferred) 7 days/Refrigerate 7 days

Specimen Type: Bone marrow

Container/Tube: Lavender top (EDTA) or yellow top (ACD solution B)

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 Information: Ambient (preferred) 7 days/Refrigerate 7 days

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 and provide indication of volume and concentration of the DNA.

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

Specimen Minimum Volume

Blood/bone marrow: 0.5 mL

Reject Due To

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

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Varies	Varies		

Clinical and Interpretive

Clinical Information

JAK2 V617F variant is present in 95% to 98% of polycythemia vera (PV), and 50% to 60% of primary myelofibrosis (PMF) and essential thrombocythemia (ET). Detection of the *JAK2* V617F is useful to help 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 PMF patients. 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 mutation of calreticulin in myeloproliferative neoplasms. N Engl J Med 2013;369:2379-2390

2. Nangalia J, Massie CE, Baxter EJ, et al: Somatic CALR mutation in myeloproliferative neoplasms with nonmutated JAK2. N Engl J Med 2013;369:2391-2405

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;123:1552-1555

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 advance online publication 21 January 2014

5. Pikman Y, Lee BH, Mercher T, et al: MPLW515L is a novel somatic activating mutation in myelofibrosis with myeloid metaplasia. FLoS Med 2006;3:e270

6. Pardanani A, Levine R, Lasho T, et al: *MPL*515 mutations in myeloproliferative and other myeloid disorders: a study of 1182 patients. Blood 2006;15:3472

Performance

Method Description

Genomic DNA was extracted and Sanger sequencing used to evaluate for alterations in *MPL*, exon 10. The

sensitivity of this assay is approximately 20%, such that samples containing lower percentages of mutated 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

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 US Food and Drug Administration.

CPT Code Information

81339-MPL (myeloproliferative leukemia virus oncogene, thrombopoietin receptor, TPOR) (eg, myeloproliferative disorder), exon 10 sequence