

Overview

Useful For

Aiding in the distinction between a reactive cytosis and a chronic myeloproliferative disorder

Evaluating mutations in *CALR* in an algorithmic process for the MPNR / Myeloproliferative Neoplasm, *JAK2* V617F with Reflex to *CALR* and *MPL*, Varies

Method Name

Only orderable as a reflex. For more information see MPNR / Myeloproliferative Neoplasm, *JAK2* V617F with Reflex to *CALR* and *MPL*, Varies.

Polymerase Chain Reaction (PCR) and Fragment Analysis

NY State Available

Yes

Specimen

Specimen Type

Varies

Specimen Required

Only orderable as a reflex. For more information see MPNR / Myeloproliferative Neoplasm, *JAK2* V617F with Reflex to *CALR* and *MPL*, Varies.

Specimen Minimum Volume

Blood and Bone Marrow: 1 mL

Reject Due To

Gross hemolysis	Reject
Paraffin embedded bone marrow aspirate clot or biopsy blocks, slides, paraffin shavings	Reject

Moderately to severely clotted	
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Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Varies	Varies	7 days	

Clinical & Interpretive

Clinical Information

The *JAK2* (Janus kinase 2) gene codes for a tyrosine kinase (*JAK2*) associated with the cytoplasmic portion of a variety of transmembrane cytokine and growth factor receptors important for signal transduction in hematopoietic cells. Signaling via *JAK2* activation causes phosphorylation of downstream signal transducers and activators of transcription (*STAT*) proteins (eg, *STAT5*) ultimately leading to cell growth and differentiation. *BCR::ABL1*-negative myeloproliferative neoplasms (MPN) frequently harbor an acquired single nucleotide mutation in *JAK2* characterized as c.G1849T; p.Val617Phe (V617F). The *JAK2* V617F is present in 95% to 98% of polycythemia vera, and 50% to 60% of primary myelofibrosis (PMF) and essential thrombocythemia (ET). It has also been described infrequently in other myeloid neoplasms, including chronic myelomonocytic leukemia and myelodysplastic syndrome. Detection of the *JAK2* V617F is useful to help establish the diagnosis of 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 mutation (20%-30% of PMF and ET) and *MPL* exon 10 mutation (5%-10% of PMF and 3%-5% of ET). Mutations in *JAK2*, *CALR*, and *MPL* are essentially mutually exclusive. A *CALR* mutation 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 MPNR / Myeloproliferative Neoplasm, *JAK2* V617F with Reflex to *CALR* and *MPL*, Varies.

An interpretive report will be provided.

Interpretation

An interpretation will be provided under the MPNR / Myeloproliferative Neoplasm, *JAK2* V617F with Reflex to *CALR* and *MPL*, Varies.

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.

In rare cases, a mutation other than the V617F may be present in an area that interferes with primer or probe binding and cause a false-negative result.

Clinical Reference

1. Klampfl T, Gisslinger H, Harutyunyan AS, et al. Somatic mutation 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 mutation in myeloproliferative neoplasms with nonmutated JAK2. N Engl J Med. 2013;369(25):2391-2405
3. 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
4. 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
5. 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

Performance

Method Description

Polymerase chain reaction (PCR) amplification of *CALR* exon 9 is performed on DNA isolated from the patient sample. The PCR product is then run on an ABI Genetic Analyzer for fragment analysis to detect insertions and deletions. An unmutated *CALR* will show an amplicon at 266 base pairs (bp), a mutated *CALR* with insertion will show an amplicon greater than 266 bp, and a mutated *CALR* with deletion will show an amplicon smaller than 266 bp. This assay has an analytical sensitivity of approximately 6% (ie, 6 mutation-containing cells in 100 total cells) in most mutation types, except for the rare type of 1-bp deletion, which has a sensitivity of approximately 20%. (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

81219-CALR (calreticulin) (eg, myeloproliferative disorders), gene analysis, common variants in exon 9

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
CALX	CALR, Gene Mutation, Exon 9, Reflex	77174-1

Result ID	Test Result Name	Result LOINC® Value
36998	Final Diagnosis	22637-3