Test Definition: CALJM

CALR Variant Analysis, Myeloproliferative Neoplasm, Reflex, Bone Marrow

Overview

Useful For

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

Evaluating for variants in *CALR* in an algorithmic process

Method Name

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

Polymerase Chain Reaction (PCR)/Fragment Analysis

NY State Available

No

Specimen

Specimen Type

Bone Marrow

Specimen Required

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

Container/Tube:
Preferred: Lavender top (EDTA)
Acceptable: None
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.
Note: Extracted DNA from bone marrow is **not** acceptable.

Specimen Minimum Volume

1 mL

Reject Due To

Gross hemolysis	Reject
Moderately to severely clotted	Reject
Extracted DNA from outside laboratory	Reject

Specimen Stability Information

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

Clinical & Interpretive

Clinical Information

The Janus kinase 2 gene (*JAK2*) codes for a tyrosine kinase (JAK2) that is 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 variant in *JAK2* characterized as c.G1849T; p.Val617Phe (V617F). *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 *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 variant (20%-30% of PMF and ET) and *MPL* exon 10 variant (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 MPNJM / Myeloproliferative Neoplasm (MPN), *JAK2* V617F with Reflex to *CALR* and *MPL*, Bone Marrow.

An interpretive report will be provided.

Interpretation

The interpretive report includes an overview of the findings.

Cautions

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

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

This test is a fragment analysis assay and only detects deletions and insertions and deletions (delins). It will not detect point alterations. However, all reported disease-causing variants in MPN described to date are delins.

This test may not differentiate between out-of-frame and in-frame delins in rare cases. However, in-frame delins are very rare (<0.5%) and have only been reported in few healthy individuals and in MPN patients with *JAK2*V617F variant or out-of-frame *CALR* variant. Most of the rare in-frame delins are considered germline variants and represent nonpathogenic alterations.

Infrequently, amplification failure can be encountered in a given sample, due to inadequate DNA, poor DNA quality, or a polymerase chain reaction inhibitor. In these circumstances, the assay will be reattempted and if persistently unsuccessful, the report will be issued with an "Invalid" result.

Supportive Data

This assay has an analytical sensitivity of approximately 6% (ie, 6 variant-containing cells in 100 total cells) in most variant types, except for the rare type of 1-base pair deletion, which has a sensitivity of approximately 20%.

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. doi:10.1056/NEJMoa1311347
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. Tefferi A, Barbui T. Polycythemia vera and essential thrombocythemia: 2021 update on diagnosis, risk-stratification and management. Am J Hematol. 2020;95(12):1599-1613
4. Luque Paz D, Kralovics R, Skoda RC. Genetic basis and molecular profiling in myeloproliferative neoplasms. Blood. 2023;141(16):1909-1921
5. Tefferi A, Vannucchi AM, Barbui T. Essential thrombocythemia: 2024 update on diagnosis, risk stratification, and management. Am J Hematol. 2024;99(4):697-718

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 Applied Biosystems Genetic Analyzer for fragment analysis to detect insertions and deletions.(Unpublished Mayo method)

PDF Report

No

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Day(s) Performed
Monday through Friday

Report Available
2 to 10 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
81219-*CALR* (calreticulin) (eg, myeloproliferative disorders), gene analysis, common variants in exon 9

LOINC® Information

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

Result ID	Test Result Name	Result LOINC® Value
614540	Final Diagnosis	22637-3