MAYO CLINIC LABORATORIES

Test Definition: PVJAK

PV (JAK2 V617F, Exon 12-15) Reflex

Overview

Useful For

Aiding in the distinction between the myeloproliferative neoplasm polycythemia vera (PV) and other secondary erythrocytosis

Testing Algorithm

Both DNA and RNA are extracted. The algorithm starts with a highly sensitive DNA-based *JAK2* V617F test by allele specific polymerase chain reaction. If the *JAK2* V617F result is negative or very low positive (0.06%-0.6%), *JAK2* exon 12-15 Sanger sequencing test will be performed on the stored RNA sample. If a *JAK2* V617F mutation (>0.6%) is detected, the algorithm stops and no further testing will be performed.

The Sanger sequencing covers *JAK2* exons 12 through the first 90% of exon 15, which spans the region containing essentially all mutations reported in myeloproliferative neoplasms. The following algorithms are available in Special Instructions.

-Erythrocytosis Evaluation Testing Algorithm

-Myeloproliferative Neoplasm: A Diagnostic Approach to Bone Marrow Evaluation

-Myeloproliferative Neoplasm: A Diagnostic Approach to Peripheral Blood Evaluation

Special Instructions

- Myeloproliferative Neoplasm: A Diagnostic Approach to Peripheral Blood Evaluation
- Myeloproliferative Neoplasm: A Diagnostic Approach to Bone Marrow Evaluation
- Erythrocytosis Evaluation Testing Algorithm

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
JAKXR	JAK2 Exon 12-15 Sequencing, Reflex	Yes	No

Method Name

Allele-Specific Polymerase Chain Reaction (AS-PCR) and Sanger Sequencing

NY State Available

Yes

Specimen

Specimen Type

Varies

Shipping Instructions

Specimen must arrive within 5 days (120 hours) 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

Submit only 1 of the following specimens:
Specimen Type: Blood
Container/Tube: Lavender top (EDTA) or yellow top (ACD-B)
Specimen Volume: 10 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 blood.
Specimen Type: Bone marrow aspirate
Container/Tube: Lavender top (EDTA) or yellow top (ACD-B)
Specimen Volume: 4 mL
Collection Instructions:
1. Invert several times to mix blood.
2. Send bone marrow specimen in original tube. **Do not aliquot.**
3. Label specimen as bone marrow.

Forms

If not ordering electronically, complete, print, and send a Hematopathology/Cytogenetics Test Request (T726) with the specimen.

Reject Due To

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

Specimen Minimum Volume

Blood: 4 mL
Bone Marrow: 2 mL

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Varies	Refrigerated (preferred)	5 days	
	Ambient	5 days	

Clinical & Interpretive

Clinical Information

The Janus kinase 2 (*JAK2*) gene 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. The *JAK2* V617F mutation is located in exon 14 and present in 50% to 60% of primary myelofibrosis and essential thrombocythemia and in 95% to 98% of polycythemia vera (PV). In the rest of the PV cases, over 50 different mutations have been reported within exons 12 through 15 of *JAK2*, and essentially all of the non-V617F *JAK2* mutations have been identified in PV. These mutations include point mutations and small insertions or deletions. Several of the exon 12 mutations have been shown to have biologic effects similar to those caused by the V617F mutation such that it is currently assumed other nonpolymorphic mutations have similar clinical effects. However, some mutations may not be well characterized and requires further clinical and research evaluation.

Reference Values

An interpretive report will be provided.

Interpretation

The results will be reported as 1 of the 3 following states:
-Positive for *JAK2* V617F mutation
-Positive for *JAK2* mutation (other than V617F)
-Negative for *JAK2* mutations
If the result is positive, a description of the mutation at the nucleotide level and the altered protein sequence are reported.
A positive mutation status is highly suggestive of a myeloid neoplasm and may support a diagnosis of polycythemia vera in the appropriate clinical setting. Correlation with clinicopathologic findings and other laboratory results is necessary in all cases.
A negative mutation status makes a diagnosis of polycythemia vera highly unlikely, although it does not completely exclude this possibility, other myeloproliferative neoplasms or other neoplasms.

Cautions

A positive result is not specific for a particular diagnosis. Correlation with clinicopathologic findings and other laboratory results is necessary in all cases.
If this test is ordered in the setting of erythrocytosis and suspicion of polycythemia vera, interpretation requires correlation with a concurrent or recent prior bone marrow evaluation.

Clinical Reference

1. Baxter EJ, Scott LM, Campbell PJ, et al: Acquired mutation of the tyrosine kinase JAK2 in human myeloproliferative disorders. Lancet. 2005 Mar;365(9464):1054-1061. doi: 10.1016/S0140-6736(05)71142-9
2. James C, Ugo V, Le Couedic JP, et al: A unique clonal *JAK2* mutation leading to constitutive signaling causes polycythaemia vera. Nature. 2005 Apr;434(7037):1144-1148. doi: 10.1038/nature03546
3. Kralovics R, Passamonti F, Buser AS, et al: A gain-of-function mutation of *JAK2* in myeloproliferative disorders. N Engl J Med. 2005 Apr;352(17):1779-1790. doi: 10.1056/NEJMoa051113
4. Steensma DP, Dewald GW, Lasho TL, et al: The *JAK2* V617F activating tyrosine kinase mutation is an infrequent event in both "atypical" myeloproliferative disorders and the myelodysplastic syndrome. Blood. 2005 Aug;106(4):1207-1209. doi: 10.1182/blood-2005-03-1183
5. Ma W, Kantarjian H, Zhang X, et al: Mutation profile of *JAK2* transcripts in patients with chronic myeloid neoplasias. J Mol Diagn 2009;11:49-53
6. Kilpivaara O, Levine RL: *JAK2* and *MPL* mutations in myeloproliferative neoplasms: discovery and science. Leukemia. 2008 Oct;22(10):1813-1817. doi: 10.1038/leu.2008.229

7. Kravolics R: Genetic complexity of myeloproliferative neoplasms. Leukemia. 2008 Oct;22(10):1841-1848. doi: 10.1038/leu.2008.233

Performance

Method Description

Normalized ratio =
mutated/wild-type (sample)

PDF Report

No

Specimen Retention Time

DNA and RNA: 3 months; Peripheral blood, bone marrow: 2 weeks

Performing Laboratory Location

Rochester

Fees & Codes

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

81270-JAK2 V617

0027U (if appropriate)