Test Definition: JAKXR

JAK2 Exon 12-15 Sequencing, Polycythemia Vera Reflex, Varies

Overview

Useful For

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

Evaluating for mutations within exons 12 to 15 of *JAK2* in an algorithmic process as part of PVJAK / Polycythemia Vera, *JAK2* V617F with Reflex to *JAK2* Exon 12-15, Sequencing for Erythrocytosis, Varies

Method Name

Only orderable as a reflex. For more information, see PVJAK / Polycythemia Vera, *JAK2* V617F with Reflex to *JAK2* Exon 12-15, Sequencing for Erythrocytosis, Varies.

Sanger Sequencing

NY State Available

Yes

Specimen

Specimen Type

Varies

Specimen Required

Only orderable as a reflex. For more information, see PVJAK / Polycythemia Vera, *JAK2* V617F with Reflex to *JAK2* Exon 12-15, Sequencing for Erythrocytosis, Varies.

Specimen Minimum Volume

Blood: 8 mL
Bone marrow: 2 mL

Reject Due To

Gross hemolysis	Reject
Paraffin-embedded bone marrow aspirate clot or biopsy blocks	Reject

Slides Paraffin shavings Moderately to severely clotted	

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 is located in exon 14 and present in 50% to 60% of primary myelofibrosis and essential thrombocythemia, and 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 alterations 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 require further clinical and research evaluation.

Reference Values

Only orderable as a reflex. For more information, see PVJAK / Polycythemia Vera, *JAK2* V617F with Reflex to *JAK2* Exon 12-15, Sequencing for Erythrocytosis, Varies.

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 March 16;365(9464):1054-1061
2. James C, Ugo V, Le Couedic JP, et al: A unique clonal *JAK2* mutation leading to constitutive signaling causes polycythaemia vera. Nature. 2005 April 28;434(7037):1144-1148
3. Kralovics R, Passamonti F, Buser AS, et al: A gain-of-function mutation of *JAK2* in myeloproliferative disorders. N Engl J Med. 2005;352:1779-1790
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;106:1207-1209
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;22:1813-1817
7. Kravolics R: Genetic complexity of myeloproliferative neoplasms. Leukemia. 2008;22:1841-1848
8. Defour JP, Chachoua I, Pecquet C, Constantinescu SN: Oncogenic activation of MPL/thrombopoietin receptor by 17 mutations at W515: implications for myeloproliferative neoplasms. Leukemia. 2016; 30:1214-1216. doi: 10.1038/leu.2015.271
9. Tefferi A: The classic myeloproliferative neoplasms: Chronic myelogenous leukemia, polycythemia vera, essential thrombocythemia, and primary myelofibrosis. In: Valle DL, Antonarakis S, Ballabio A, Beaudet AL, Mitchell GA, eds. The Online Metabolic and Molecular Bases of Inherited Disease. McGraw-Hill; 2019, Accessed March 16, 2022. Available at https://ommbid.mhmedical.com/content.aspx?sectionid=225078035&bookid=2709

Performance

Method Description

For the Sanger sequencing, total RNA is extracted from whole blood/bone marrow and complementary DNA synthesized from *JAK2* messenger RNA. A fragment spanning exons 12 through 15 is then amplified using standard polymerase chain reaction and the sequence is obtained using Sanger sequencing with analysis on an automated genetic

analyzer.(Unpublished Mayo method)

PDF Report
No

Day(s) Performed
Monday through Saturday

Report Available
7 to 10 days

Specimen Retention Time
Blood/Bone marrow: 2 weeks; Extracted RNA: 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
0027U-*JAK2* (Janus kinase 2) (eg, myeloproliferative disorder), exon 12 sequence and exon 13 sequence, if performed