MAYO CLINIC LABORATORIES

Test Definition: JAKXB

JAK2 Exon 12 and Other Non-V617F Mutation Detection, Blood

Overview

Useful For

Second-order testing to aid in the distinction between a reactive cytosis and a myeloproliferative neoplasm, particularly when a diagnosis of polycythemia is being considered, using blood specimens

Testing Algorithm

This is a second-order test that should be used when the test for the JAK2B / *JAK2* V617F Mutation Detection, Blood test is negative. The sensitivity of this assay is much less than that of the JAK2B test. This is because the sequencing technique is required to evaluate for many potential mutations. The sensitive JAK2B test should always be performed first, as the *JAK2* mutation burden may be very low in some specimens. If the JAK2B test is negative, then this assay should be performed for detection of non-V617F *JAK2* mutations.

For more information see:
-Myeloproliferative Neoplasm: A Diagnostic Approach to Peripheral Blood Evaluation
-Erythrocytosis Evaluation Testing Algorithm

Special Instructions

- Myeloproliferative Neoplasm: A Diagnostic Approach to Peripheral Blood Evaluation
- Hematopathology Patient Information
- Erythrocytosis Evaluation Testing Algorithm

Method Name

Sanger Sequencing

NY State Available

Yes

Specimen

Specimen Type

Whole blood

Ordering Guidance

In all cases being evaluated for *JAK2* mutation status, the initial test that should be ordered is JAK2B / *JAK2* V617F Mutation Detection, Blood, a sensitive assay for detection of the mutation. However, if no *JAK2* V617F mutation is found, further evaluation of *JAK2* may be clinically indicated.

Shipping Instructions

Specimen must arrive within 5 days (120 hours) of collection. Collect and package specimen as close to shipping time as

possible.

Necessary Information
Date of collection is required.

Specimen Required
Container/Tube:
Preferred: Lavender top (EDTA)
Acceptable: Yellow top (ACD)
Specimen Volume: 10 mL
Collection Instructions:
1. Invert several times to mix blood.
2. Send whole blood specimen in original tube. **Do not aliquot.**

Forms
1. Hematopathology Patient Information (T676)
2. If not ordering electronically, complete, print, and send a Hematopathology/Cytogenetics Test Request (T726) with the specimen.

Specimen Minimum Volume
8 mL

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Whole blood	Refrigerated (preferred)	5 days	PURPLE OR PINK TOP/EDTA
	Ambient	5 days	PURPLE OR PINK TOP/EDTA

Clinical & Interpretive

Clinical Information
DNA sequence mutations in the Janus kinase 2 gene (*JAK2*) are found in the hematopoietic cells of several myeloproliferative neoplasms (MPN), most frequently polycythemia vera (close to 100%), essential thrombocythemia (approximately 50%), and primary myelofibrosis (approximately 50%). Mutations in *JAK2* have been reported at much lower frequency in other MPN, chronic myelomonocytic leukemia and mixed MPN/myelodysplastic syndromes, but essentially never in chronic myeloid leukemia (CML), reactive cytoses, or normal patients. Mutations are believed to cause constitutive activation of the JAK2 protein, which is an intracellular tyrosine kinase important for signal transduction in many hematopoietic cells. Since it is often difficult to distinguish reactive conditions from the non-CML MPN, identification of a *JAK2* mutation has diagnostic value. Potential prognostic significance of *JAK2* mutation detection in chronic myeloid disorders has yet to be clearly established.

The vast majority of *JAK2* mutations occur at base pair 1849 in the gene, resulting in a *JAK2* V617F protein change. In all cases being evaluated for *JAK2* mutation status, the initial test that should be ordered is JAK2B / *JAK2* V617F Mutation Detection, Blood, a sensitive assay for detection of the mutation. However, if no *JAK2* V617F mutation is found, further

evaluation of *JAK2* may be clinically indicated. Over 50 different mutations have now been reported within exons 12 through 15 of *JAK2* and essentially all of the non-V617F mutations have been identified in polycythemia vera. 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, research in this area is ongoing.

This assay for non-V617F/alternative *JAK2* mutations is designed to obtain the sequence for *JAK2* exons 12 through the first 90% of exon 15, which spans the region containing all mutations reported to date.

Reference Values

An interpretive report will be provided.

Interpretation

The results will be reported as 1 of 2 states:
1. Negative for *JAK2* mutation
2. Positive for *JAK2* mutation

If the result is positive, a description of the mutation at the nucleotide level and the altered protein sequence is reported.

Positive mutation status is highly suggestive of a myeloproliferative neoplasm but must be correlated with clinical and other laboratory features for a definitive diagnosis. Negative mutation status does not exclude the presence of a myeloproliferative or other neoplasm.

Cautions

A positive result is not specific for a particular diagnosis and clinicopathologic correlation is necessary in all cases. A negative result does not exclude the presence of a myeloproliferative or other neoplasm.

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.

Supportive Data

Analytical sensitivity is approximately 20% meaning there must be about 20% of the mutated DNA in the sample for reliable detection.

Clinical Reference

1. 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
2. Kilpivaara O, Levine RL: *JAK2* and *MPL* mutations in myeloproliferative neoplasms: discovery and science. Leukemia. 2008;22:1813-1817
3. Kravolics R: Genetic complexity of myeloproliferative neoplasms. Leukemia. 2008;22:1841-1848
4. 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
Total RNA is extracted from whole blood 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
5 to 8 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

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
JAKXB	JAK2 Exon 12 Mutation Detection, B	55300-8

Test Definition: JAKXB

JAK2 Exon 12 and Other Non-V617F Mutation Detection, Blood

Result ID	Test Result Name	Result LOINC® Value
20194	Final Diagnosis:	34574-4
39467	JAK2 Sequencing Result	55300-8