JAK2 (V617F) Mutation Reflex Testing

Myeloproliferative neoplasms (MPNs) are a group of blood cancers that cause excess blood cell production in the bone marrow and often in the peripheral blood, and are characterized by clonal genetic changes. Classic *BCR-ABL1* negative MPNs, such as polycythemia vera (PV), essential thrombocythemia (ET) and primary myelofibrosis (PMF), lack the *BCR-ABL1* fusion gene.[1] The majority of patients with PV, ET, and PMF have a mutation in the *JAK2*, *CALR*, or *MPL* gene, and genetic testing is an important tool for the classification and diagnosis of these disorders. A quantitative *JAK2* V617F assay can provide additional information such as whether the allele fraction is very low (as can sometimes be seen in healthy individuals). It can also suggest hemi/homozygosity, as seen more frequently with PV and PMF, and can be used in monitoring disease burden with ruxolitinib therapy.

For detailed information on the testing used in MPN, including genetic testing for variants in the *CALR* and *MPL* genes, see the ARUP Consult Myeloproliferative Neoplasms topic.

Testing Strategy

Standard practice for molecular evaluation of *BCR-ABL1*-negative MPNs:

- Assess for *JAK2* V617F variant.[1]
- If *JAK2* V617F variant is not detected, assess for *CALR* then *MPL* mutations in patients with suspected ET or PMF.[1]
- If *JAK2* V617F variant is not detected but PV is still suspected, assess for *JAK2* exon 12 variants.[1]
- If *JAK2*, *MPL*, and *CALR* are all negative in a patient with ET or PMF, consider testing for other mutations (Myeloid Malignancies Mutation Panel by Next Generation Sequencing).[1]

Genetics

Variants Detected

JAK2 (V617F) Mutation by ddPCR, Quantitative

- Point mutation c.1849G>T (V617F) of the *JAK2* gene (quantitative analysis)

JAK2 Gene, V617F Mutation, Qualitative with Reflex to *CALR* (Calreticulin) Exon 9 Mutation Analysis by PCR with Reflex to *MPL* Mutation Detection

- Point mutation c.1849G>T (V617F) of the *JAK2* gene (qualitative analysis)
- Exon 9 insertion/deletion mutations in the *CALR* gene
- W515K, W515L, W515A, and S505N mutations in exon 10 of the *MPL* gene

JAK2 Gene, V617F Mutation, Qualitative with Reflex to *JAK2* Exon 12 Mutation Analysis by PCR

- Point mutation c.1849G>T (V617F) of the *JAK2* gene (qualitative analysis)
- Exon 12 mutations in the *JAK2* gene, located between codons 537 and 544

Tests to Consider

JAK2 (V617F) Mutation by ddPCR, Quantitative 3003751

Method: Droplet Digital Polymerase Chain Reaction

- Aids in the assessment of suspected MPNs.
- Use to detect the *JAK2* V617F mutation in peripheral blood or bone marrow.

JAK2 (V617F) Mutation by ddPCR, Qualitative with Reflex to CALR (Calreticulin) Exon 9 Mutation Analysis by PCR with Reflex to MPL Mutation Detection 3003800

Method: Droplet Digital Polymerase Chain Reaction/Capillary Electrophoresis

- Aids in the assessment of MPN when diagnosis of essential thrombocythemia or primary myelofibrosis is suspected.
- If *JAK2* V617F is not detected, then *CALR* exon 9 mutation analysis by PCR will be added; if *CALR* is not detected, then *MPL* mutation detection will be added.

JAK2 (V617F) Mutation by ddPCR, Qualitative with Reflex to JAK2 Exon 12 Mutation Analysis by PCR 3003801

Method: Droplet Digital Polymerase Chain Reaction/Polymerase Chain Reaction

- Aids in the assessment of MPN when diagnosis of polycythemia vera is suspected.
- If *JAK2* V617F is not detected, then *JAK2* exon 12 mutation analysis will be added.

See Related Tests.

Test Interpretation

Analytical Specificity

JAK2 V617F by ddPCR: >99%

Limit of Detection

JAK2 V617F by ddPCR: >0.5%

Results

JAK2 V617F Mutation by ddPCR Analysis	
Result	**Interpretive Data**
Positive	Evidence of the *JAK2* V617F mutation Results are reported as a percent of mutated alleles versus wild type alleles
Low positive	*JAK2* V617F T-allele is detected but is below the quantifiable limits of the test
Negative[a]	No evidence of the *JAK2* V617F mutation Does not entirely exclude the possibility that a point mutation exists in the sample below the detection limit of the test, nor does it exclude mutations other than the V617F mutation

[a]Negative result will reflex to additional genetic testing if reflex testing is ordered.

Limitations

JAK2 V617F Mutation by ddPCR Analysis

- Variants in genes other than *JAK2* are not detected. Variant alleles of *JAK2* other than V617F (c.1849G>T) are not reported.
- Samples with *JAK2* V617F mutations below the limit of reporting may not be detected.
- Results of this test must always be interpreted in the context of morphologic and other relevant data and should not be used alone for a diagnosis of malignancy.
- This test is not intended to detect minimal residual disease.

References

1. National Comprehensive Cancer Network. NCCN clinical practice guidelines in oncology: myeloproliferative neoplasms, Version 1.2020. [Last update: May 2020; Accessed: Mar 2021]

Related Information

Myeloproliferative Neoplasms
BCR-ABL1 Qualitative and Quantitative Testing

Related Tests

JAK2 (V617F) Mutation by ddPCR, Qualitative 3004046

Method: Droplet Digital PCR (ddPCR)

JAK2 Exon 12 Mutation Analysis by PCR 2002357

Method: Polymerase Chain Reaction

CALR (Calreticulin) Exon 9 Mutation Analysis by PCR 2010673

Method: Capillary Electrophoresis

MPL Mutation Detection by Capillary Electrophoresis 2005545

Method: Capillary Electrophoresis

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