TEST ID: MPNR
MYELOPROLIFERATIVE NEOPLASM (MPN), JAK2 V617F WITH REFLEX TO CALR AND MPL

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

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 mutation in JAK2 characterized as c.G1849T; p. Val617Phe (V617F). This mutation is identified overall in approximately two-thirds of all MPN\textsuperscript{1-3}, but the prevalence varies by MPN subtype. The JAK2 V617F is present in 95% to 98% of polycythemia vera, 50% to 60% of primary myelofibrosis (PMF) and 50% to 60% of essential thrombocythemia (ET). It has also been described infrequently in other myeloid neoplasms, including chronic myelomonocytic leukemia and myelodysplastic syndrome\textsuperscript{4}. This mutation is not seen in chronic myelogenous leukemia (CML) or in reactive conditions with elevated blood counts. Detection of the JAK2 V617F is useful to help establish the diagnosis of MPN. However, a negative JAK2 V617F result does not indicate absence of a MPN. Other important molecular markers in BCR-ABL1-negative MPN include CALR exon 9 mutation (20% to 30% of PMF and ET) and MPL exon 10 mutation (5% to 10% of PMF and 3% to 5% of ET)\textsuperscript{5-9}. Mutations in JAK2, CALR and MPL are essentially mutually exclusive.

INTERPRETATION
The results will be reported as 1 of the 2 states:
- Negative for JAK2 V617F mutation
- Positive for JAK2 V617F mutation

Positive mutation status is highly suggestive of a myeloid neoplasm, but must be correlated with clinical and other laboratory features for definitive diagnosis.

Negative mutation status does not exclude the presence of a myeloproliferative neoplasm or other neoplasm.

Results below the laboratory cutoff for positivity are of unclear clinical significance at this time.

MOBILE APPS FROM MAYO MEDICAL LABORATORIES
- Lab Catalog for iPad and Lab Reference for iPhone and iPod Touch
  Requires iOS 5.1+

REFERENCE VALUES
An interpretive report will be provided.

ANALYTIC TIME
7 days

REFLEX TESTS
Test ID: CALM
Reporting Name: CALR, Gene Mutation, Exon 9, R
Available Separately: Yes (order CALR)
Always Performed: No

Test ID: MPLR
Reporting Name: MPL Exon 10 Mutation Detection, R
Available Separately: Yes (order MPLB, MPLM or MPVLA)
Always Performed: No

CONTENT AND VALUES SUBJECT TO CHANGE. SEE THE MAYO MEDICAL LABORATORIES TEST CATALOG FOR CURRENT INFORMATION.
TESTING ALGORITHM

This reflex test sequentially evaluates for the common major gene mutations associated with non-BCR/ABL1-positive myeloproliferative neoplasms until a mutation is identified. The testing sequence is based on the reported frequency of gene mutations in this disease group. Initial testing evaluates for the presence of the JAK2 V617F mutation. If this result is negative, testing proceeds with assessment for CALR mutations. If the CALR result is also negative, then testing proceeds to evaluate for mutations in exon 10 of the MPL gene. If either JAK2 V617F or CALR mutations are detected first in the process, the testing algorithm ends; therefore, the complete reflex is followed only in the event of sequential negative mutation. An integrated report is issued with the summary of test results.

The following algorithms are available on our website:

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

CLINICAL REFERENCE