MPL Exon 10 Codon 515 Mutation Detection

Effective Date: January 9, 2017 **Performing Department:** Molecular Pathology

Clinical Significance:

Myeloproliferative neoplasms (MPNs) are clonal myeloid-cell derived disorders characterized by expansion of mature peripheral blood cell populations such as granulocytes, red blood cells and/or platelets. Typically patients also show bone marrow hypercellularity and have a predisposition to thrombosis, hemorrhage, and/or marrow fibrosis. Classic myeloproliferative neoplasms are negative for the *BCR/ABL* translocation and do not include chronic myelogenous leukemia (CML). These are: polycythemia vera (PV), primary myelofibrosis (PMF), and essential thrombocythemia (ET). A single point mutation, *JAK2* V617F, is present in the majority of PV cases, and is also detectable in approximately 50% and 40-50% of PMF and ET cases, respectively. The recent discovery of this mutation and rapid translation of testing into clinical practice has significantly streamlined the diagnosis of MPNs. Because of the high percentage of *JAK2* V617F positive classic MPN cases, testing for this mutation should always be performed first when evaluating a possible case of MPN. However, there are now additional mutations known to be associated with *JAK2* V617F-negative, classic MPN categories PMF and ET. One is a group of point mutations in *MPL*, codon 515. This test will identify these *MPL* W515 mutations which are found in about 1% of ET and 5% of PMF cases. Identification of *JAK2* V617F or a *MPL* mutation is particularly useful in establishing clonality and excluding reactive cytoses. Like *JAK2* V617F, *MPL* mutations are thought to result in constitutive activation of downstream *JAK2/STAT* signaling transduction and contribute to development of the MPN phenotype.

So-called triple-negative MPN patients with no mutation in *JAK2*, *MPL* or a third gene, calreticulin (*CALR*), carry a poor prognosis and demonstrate a high rate of leukemic transformation in some studies.

Use:

- Assist with diagnostic confirmation and classification of myeloproliferative neoplasia
- Clarify the distinction between a reactive cytosis and a myeloproliferative neoplasm
- Provide prognostic information regarding myeloproliferative neoplasia to assist with treatment planning

Method:

Polymerase Chain Reaction (PCR) amplification of mutation specific targets followed by capillary electrophoresis (fragment analysis).

Reference Values:

Negative: No mutation detected

Positive: Mutation detected

Interpretive Information:

This test is designed to detect mutations in exon 10, codon 515, of the MPL gene, including W515K and W515L. Mutations in other locations within the MPL gene or in other genes will not be detected.

Genomic DNA is isolated from either whole blood or bone marrow. PCR followed by capillary electrophoresis is performed to detect mutations. The limit of detection for this test is 5% mutant allele.

Results of this test must be interpreted with other clinical data and should not be used alone to diagnose a malignancy.

Specimen Requirement and Collection:

Collect: Lavender (EDTA) OR bone marrow (EDTA)

Specimen Preparation: Do not freeze. Transport 5mL whole blood (Min: 1mL) or Transport 3mL bone marrow (Min: 1mL)

Storage/Transport Temperature: Refrigerated

Unacceptable Condition: Serum; specimens collected in anticoagulants other than EDTA; clotted or grossly hemolyzed specimens; frozen specimens

Stability: Ambient: 24 hours; Refrigerated: 10 days; Frozen: Unacceptable

Day Run: Monday

Time Run: 9AM

Time Reported: Within 24 hours of run

TAT: 7-12 days

Test Type: GENETIC

Order: 36054

CPT Code: 81402

Related Tests:

Test Code	Test Name
36140	JAK2 (V617F) Mutation Analysis
36053	CALR (Calreticulin) Exon 9 Mutation Detection
36052	JAK2 (V617F) Mutation Analysis with Reflex to CALR(Calreticulin) Exon 9 Mutation Detection with Reflex to MPL codon 515 Mutation Detection

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