Myeloproliferative Neoplasia Cascade: JAK2 (V617F) Mutation Analysis with Reflex to CALR Exon 9 and MPL Codon 515

- **TMF No:**
  36052

- **Performance Lab Name:**
  TMF Flow Cytometry / Molecular Pathology

- **Test Mnemonic:**
  JAK2 RFLX

- **CPT Code:**
  81270: if reflexed add 81219; if reflexed again add 81402

- **Test Includes:**

Component Test Code	Component test name
36140	JAK2 (V617F) Mutation Analysis
36053	CALR (Calreticulin) Exon 9 Mutation Detection
36054	MPL Exon 10 Codon 515 Mutation Detection

  Reflexive Testing:
  This reflex test sequentially evaluates for the common major gene mutations associated with non-*BCR/ABL 1*-positive myeloproliferative neoplasms. Initial testing evaluates for the presence of the *JAK2* V617F. If JAK2 (V617F) is negative, then CALR (Calreticulin) Exon 9 Mutation Detection will be added. If CALR Exon 9 is negative, then MPL Exon 10 Codon 515 Mutation Detection will be added. Additional charges apply.
  36053 CALR (Calreticulin) Exon 9 Mutation Detection
  36054 MPL Exon 10 Codon 515 Mutation Detection

- **Also Known As:**

  Janus kinase 2 gene, Tyrosine Kinase Mutations, CARL (Calreticulin), Essential Thrombocythemia, JAK20negative Myeloproliferative Neoplasma, Myelofibrosis, Myeloproliferative Disorder, Myeloproliferative Neoplasm (MPN), Primary Myelofibrosis, MPL S505, MPL W515, Myeloproliferative leukemia virus oncogene

- **Patient Prep:**
  Third-party payers (e.g. insurance, Medicare, Medicaid) may require pre-authorization or pre-certification for genetic testing. The ordering physician or patient should contact the payer and obtain any required pre-authorization or pre-certification before the specimen is collected.

- **Spec Collect:**
  Lavender top (EDTA) tube; whole blood or bone marrow. Mix by inverting tube 8 times.

- **Spec Process:**
  Transport 5 mL whole blood (Min: 1 mL) **OR** 3 mL bone marrow (Min: 1 mL)

- **Spec Store Transport:**
  Refrigerated.

- **Spec Stability:**
  Room temperature: 24 hours
  Refrigerated: 10 days
  Frozen: Unacceptable

- **Spec Reject:**
  Serum or plasma. Specimens collected in anticoagulants other than EDTA. Frozen specimens. Clotted or grossly hemolyzed specimens.

- **Methodology:**
  Real-Time Polymerase Chain Reaction (PCR) (JAK2)

- Polymerase Chain Reaction (PCR) amplification of mutation specific targets followed by capillary electrophoresis (fragment analysis) (CALR and MPL)

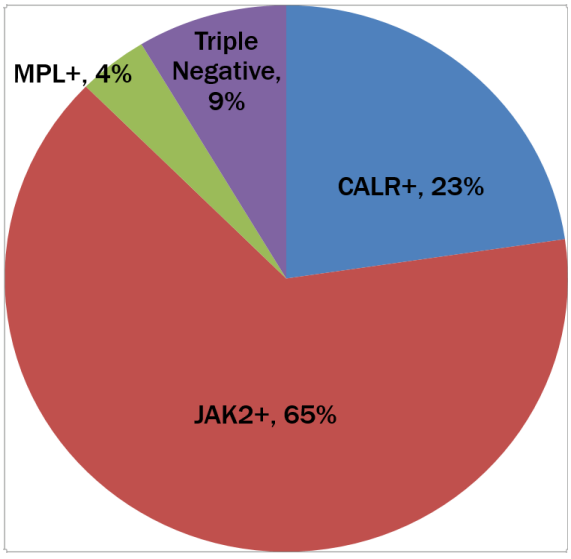
- **Use:**

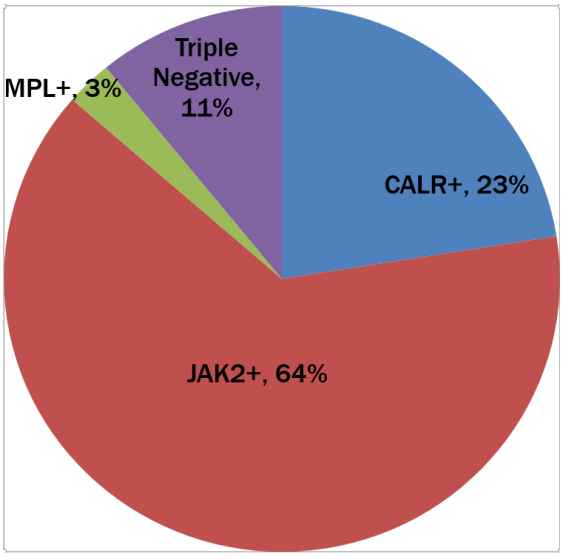
  When diagnosis of essential thrombocytemia (ET) or primary myelofibrosis (PMF) is suspected.

- **Clinical Significance:**

BCR-ABL1 negative myeloproliferative neoplasms (MPN) frequently harbor an acquired single nucleotide mutation in JAK2 characterized as c.G1849T; p. Val617Phe (V617F). The JAK2 V617F is present in 95–98% of polycythemia vera (PV), and 50–60% of primary myelofibrosis (PMF) and essential thrombocythemia (ET). It has also been described infrequently in other myeloid neoplasms, including chronic myelomonocytic leukemia and myelodysplastic syndrome. 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 and MPL exon 10 mutation. Mutations in JAK2, CALR and MPL are essentially mutually exclusive. A CALR mutation is associated with decreased risk of thrombosis in both ET and PMF, and confers a favorable clinical outcome in PMF patients. A triple negative (JAK2 V617F, CALR and MPL-negative) genotype is considered a high risk molecular signature in PMF.

MOLECULAR LANDSCAPE OF BCR-ABL1-NEGATIVE MYELOPROLIFERATIVE NEOPLASMS (MPN)





- **Interpretive Data:**

  Refer to report

- **Day Run:**
  Thu

- **Time Run:**
  8:00 am

- **Time Reported:**
  JAK2: 1-2 days (after set-up)

  CALR Exon 9: 2-7 days (after JAK2 completed)

  MPL Codon 515: 7-12 days (after JAK2 completed)

- **Test Type:**
  GENETIC

- **Clinical Reference**

1. Clinical effect of driver mutations of *JAK2*, *CALR*, or *MPL* in primary myelofibrosis. Blood. 2014 Aug 14; 124(7): 1062–1069
2. CALR vs JAK2 vs MPL-mutated or triple-negative myelofibrosis: clinical, cytogenetic and molecular comparison. Leukemia. 2014 Jul;28(7):1472-7
3. Frequencies, clinical characteristics, and outcome of somatic CALR mutations in JAK2-unmutated essential thrombocythemia. Ann Hematol. 2014 Dec;93(12):2029-36

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