MPL Exon 10 Mutation Analysis

Somatic mutations of codons 515 and 505 in exon 10 of the "myeloproliferative leukemia virus oncogene" (MPL) represent clonal markers in essential thrombocythemia (ET) and primary myelofibrosis (PMF), and serve as WHO major criteria for the diagnosis of these diseases. MPL codon 515 (W515) mutations are found in an estimated 3-4% of patients with ET and 7% of patients with PMF, including approximately 8.5% and 13% of JAK2 V617Fnegative ET and PMF patients. In addition, MPL W515 mutations have been detected in patients who fall within the provisional WHO category of refractory anemia with ring sideroblasts associated with marked thrombocytosis (RARS-T).

A germline mutation in MPL codon 505 (S505N) was first identified in hereditary thrombocythemia but has also been reported to be somatic in both ET and PMF.

MPL is located at chromosome 1p34 and encodes for the thrombopoietin receptor. MPL exon 10 mutations appear to result in ligand independent activation of the thrombopoietin receptor and its downstream cell signaling pathways.

MPL Exon 10 Mutation Analysis can be ordered separately or as part of our myeloproliferative neoplasm suite of tests. When ordered as part of a reflex panel, if ET or PMF are suspected, patients in whom JAK2 V617F mutations are not detected will automatically undergo CALR. If CALR mutations are not detected, they will automatically undergo MPL exon 10. MPL exon 10 analysis will detect the MPL W515L/K/A/R mutations, as well as variants present in these and other exon 10 codons.

Indications for testing:

- Diagnosis of essential thrombocythemia and primary myelofibrosis.

Test method:

MPL exon 10 mutations are detected and characterized by PCR amplification and direct sequencing of the coding and junctional regions of MPL exon 10 in the absence and presence of a probe that suppresses amplification of wild-type MPL codon 515.

Assay sensitivity and limitations:

The lower limit of detection of the assay is approximately 2% (allele burden) for MPL codon 515 and approximately 20% for all other MPL exon 10 codons and splice junctions.

Reporting of results:

Mutations are reported as mutation detected or mutation not detected using standard nomenclature from Human Genome Variation Society (HGVS) nomenclature (https://www.hgvs.org/). Mutation detected results are classified and reported in accordance with standards and guidelines for the interpretation and reporting of sequence variants in cancer, a joint consensus recommendation of the Association for Molecular Pathology (AMP), American Society of Clinical Oncology (ASCO), and College of American Pathologists (CAP) published in J Mol Diagn. 2017 (PMID: 27993330). Variants interpreted to be tier I (strong clinical significance) or tier II (potential clinical significance) or tier III (unknown clinical significance) are reported. Variants classified as tier IV (likely benign or polymorphism) may be reported upon request.

Specimen requirements:

3-5 ml EDTA (lavender top) whole blood or 2-5 ml EDTA bone marrow aspirate or DNA, high quality, ≥500ng at 25 ng/ul.

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SHIP

Shipping requirements:

Place the room temperature specimen and requisition in plastic bags, seal and insert in a Styrofoam container. Seal the Styrofoam container, place in a sturdy cardboard box and tape securely. Ship the package in compliance with your overnight carrier guidelines

Send to:

Versiti Client Services/ Molecular Oncology Laboratory
638 N.18th St.
Milwaukee, WI 53233
800-245-3117, ext. 6250

ORDER

Required forms:

Please complete all pages of the requisition form.

CPT Codes/Billing/Turnaround time:

Turnaround Time: 5-10 days

CPT Codes: For recommended CPT codes, visit the versiti.org/test-catalog

Reflex Ordering:

MPN (Myeloproliferative Neoplasms) Reflex - ET/PMF (Order# 4644)

JAK2 V617F Mutation Analysis
Turnaround Time: 5-7 days

CALR Mutation Analysis (if indicated)
Turnaround Time: additional 5-7 days

MPL Exon 10 Mutation Analysis (if indicated)
Turnaround Time: additional 14 days

References:

1. Beer PA, Campbell PH, Scott LM, et al. MPL mutations in myeloproliferative disorders: analysis of the PT-1 cohort. Blood 2008;112:141-149.
2. Ding J, Komatsu H, Wakita A, et al. Familial essential thrombocythemia associated with a dominant-positive activating mutation of the c-MPL gene, which encodes for the receptor for thrombopoietin. Blood 2004;103:4198-4200.
3. Pardanani AD, Levine RL Lasho T, et al. MPL 515 mutations in myeloproliferative and other myeloid disorders: a study of 1182 patients. Blood 2006;108:3472-3476.
4. Schnittger S, Bacher U, Haferlach C, et al. Characterization of 35 new cases with four diff erent MPLW515 mutations and essential thrombocytosis or primary myelofi brosis. Haematologica 2009;94:141-144.
5. Teofili L, Foa R, Giona F, Larocca L. Childhood polycythemia vera and essential thrombocythemia: does their pathogenesis overlap with that of adult patients? Haematologica 2008;93:169-172.
6. Thiele J, Kvasnicka HM, Tefferi A, et al. Primary myelofi brosis. In: Swerdlow SH, Campo E, Harris NL, et al. WHO Classifi cation of Tumours of Haematopoietic and Lymphoid Tissues. 4th ed. Lyon, France: WHO Press, 2008:44-47.
7. Thiele J, Kvasnicka HM, Orazi A, et al. Essential thrombocythaemia. In: Swerdlow SH, Campo E, Harris NL, et al. WHO Classifi cation of Tumours of Haematopoietic and Lymphoid Tissues. 4th ed. Lyon, France: WHO Press, 2008:48-50.
8. Vannucchi AM, Antonioli E, Guglielmelli P, et al. Characteristics and clinical correlates of MPL 515W>L/K mutation in essential thrombocythemia. Blood 2008;112:844-847.
9. Vardiman JW, Bennett JM, Bain BJ, et al. Myelodysplastic/ myeloproliferative neoplasm, unclassifi able. In: Swerdlow SH, Campo E, Harris NL, et al. WHO Classifi cation of Tumours of Haematopoietic and Lymphoid Tissues. 4th ed. Lyon, France: WHO Press, 2008:85-86.

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