JAK2 Exon 12-15 Mutation Analysis

Background Information

Mutations involving the *JAK2* gene are identified in many patients with Philadelphia chromosome negative myeloproliferative neoplasms. Specifically, the *JAK2* V617F point mutation is found in >90% of cases of polycythemia vera and in approximately 50% of essential thrombocytosis and primary myelofibrosis cases.[1-6]

A subset of polycythemia vera patients, however, lack the typical V617F mutation and instead contain other mutations elsewhere in the *JAK2* pseudokinase domain. The majority of these alternative mutations occur in exon 12, but these may also be found in exons 13 through 15.[7-9]

The finding of an acquired mutation in *JAK2* exons 12-15 supports the diagnosis of a myeloproliferative neoplasm, especially polycythemia vera. Therefore, the Department of Molecular Pathology at Cleveland Clinic, has developed, validated and implemented a sequencing assay for the detection of mutations in *JAK2* exons 12-15.

Clinical Indications

JAK2 exon 12-15 mutation analysis is useful in the evaluation of suspected myeloproliferative disorders, especially polycythemia vera, that lack the common *JAK2* V617F point mutation. Note: For more sensitive detection of the *JAK2* V617F mutation, please order *JAK2* V617F mutation detection.

Interpretation

Normal results are reported as "*JAK2* exon 12-15 mutations are not detected." Positive results are reported using Human Genome Variation Society (HGVS) nomenclature, and an interpretation provided.

Methodology

RNA is extracted and cDNA prepared by reverse transcription. *JAK2* exon 12-15 is amplified by PCR, and the PCR product is subjected to bidirectional cycle sequencing using the BigDye Terminator Cycle Sequencing Kit (Applied Biosystems, Carlsbad, CA) on the ABI 3730 Genetic Analyzer. Sequences are aligned to wild type reference sequence and assessed for the presence of mutations.

Limitations of the Assay

The lower limit of reliable mutation detection is 15-20% mutant alleles. Formalin-fixed, paraffin embedded tissue is not accepted.

References

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7. Ma W, Kantarfian H, Zhang X, *et al*. Mutation profile of *JAK2* transcripts in patients with chronic myeloproliferative neoplasias. *J Mol Diagn*. 2009;11:49-53.
8. Gong JZ, Cook JR, Greiner TC, *et al*. Laboratory practice guidelines for detecting and reporting *JAK2* and *MPL* mutations in myeloproliferative neoplasms: A report of the Association for Molecular Pathology. *J Mol Diagn*. 2013;15:733-44.
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Test Overview

Test Name	*JAK2* Exon 12-15 Sequencing
Reference Range	Normal results are reported as "*JAK2* exon 12-15 mutations are not detected".
Specimen Requirement	Peripheral Blood; 8mL EDTA (Lavender).
Ordering Mnemonic	JAKNON
Billing Code	87775
CPT Code	81403 (x1)

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