

JAK2 Exon 12 Mutation by PCR

FOR DIAGNOSIS OF MYELOPROLIFERATIVE DISORDERS

Test Highlights

- Rapid and sensitive allele-specific detection of mutation.
- Sequence verification of mutation.
- Simple sample type: peripheral blood.

Disease Overview

- The human myeloproliferative disorders (MPD) are relatively rare hematologic malignancies that include polycythemia vera (PV), essential thrombocythemia (ET), and primary myelofibrosis (PMF). This heterogeneous group of disorders is believed to result from the clonal proliferation of one or more myeloid stem cells following some undefined molecular pathogenetic event.
- The primary characteristics of PV and ET are the increased production of red blood cells and platelets leading to the clinical manifestation of thrombosis or hemorrhage. In the long term, some patients suffering from PV or ET can develop PMF. This condition, which can also arise de novo, is characterized by bone marrow fibrosis, cytopenia, and splenomegaly.
- MPD disorders may also develop into acute myeloid leukemia.

Genetics

- The *JAK2* gene is located on chromosome 9 and produces the tyrosine kinase JAK2, which is involved in the regulation of hematopoiesis.
- Mutations within the *JAK2* gene cause a deregulation of the hematopoietic process, which is expressed in a wide spectrum of disorders involving the expansion of erythrocytes, granulocytes, or leucocytes. The primary lesion associated with these disorders was discovered in exon 14. However, many MPD cases negative for the exon 14 mutation were found to carry a number of mutations in the 3' terminus of exon 12. These mutations vary within codons 537–544 and consist of single- and multiple-base substitutions and small deletions.
- Ten different mutations have been identified to date, comprised of base substitutions, small-base deletions, and sequence duplication through this region. These mutations have been primarily observed in patients with isolated erythrocytosis. In addition to the varied types of mutations observed in this region, the proportion of mutation within a sample may be small and therefore difficult to detect in a high background of normal sequence.

Indication for Ordering

Patient is suspected of having a myeloproliferative disorder (PV, ET, or PMF) but is negative for the *JAK2* (V617F) mutation.

Interpretation

- A positive result identifies a *JAK2* exon 12 mutation and is strongly supportive of a diagnosis of PV, ET, or IMF.
- A “not detected” result does not rule out the presence of a *JAK2* exon 12 mutation or a diagnosis of PV, ET, or PMF. The mutation has been correlated to disease state in 2–15 percent of patients negative for the *JAK2* (V617F) mutation (the higher frequency being correlated in patients with PV and the lower frequency correlated in patients with ET).

Limitations

Detection and sequence verification is limited to samples containing mutations within the 3' terminus of exon 12.

Methodology

Polymerase chain reaction (PCR) and sequencing.

References

1. Schnittger S, et al. Detection of *JAK2* exon 12 mutations in 15 patients with *JAK2*V617F negative polycythemia vera. *Haematol* 2009;94(3):414–8.
2. Scott LM, et al. *JAK2* exon 12 mutations in polycythemia vera and idiopathic erythrocytosis. *N Engl J Med* 2007;356(5):459–68.

Test Information

2002357

JAK2 Exon 12 Mutation Analysis by PCR

For specific collection, transport, and testing information, refer to the ARUP website at www.aruplab.com.

For information on test selection, ordering, and interpretation, refer to ARUP Consult® at www.arupconsult.com.

AUTHORS

N. Scott Reading, PhD

Daniel Anderson, MT(ASCP)

Josef Prchal, MD