

JAK2 (V617F) Mutation by PCR

*FOR DIAGNOSIS OF MYELOPROLIFERATIVE DISORDERS:
POLYCYTHEMIA VERA, ESSENTIAL THROMBOCYTHEMIA, AND
IDIOPATHIC MYELOFIBROSIS.*

Test Highlights

- Rapid and sensitive allele-specific detection of mutation.
- Sample type: peripheral blood.

Clinical Background

The human myeloproliferative disorders (MPD) are relatively rare hematologic malignancies which include polycythemia vera (PV), essential thrombocythemia (ET), and idiopathic myelofibrosis (IMF). This clinically 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 IMF, which is characterized by bone marrow fibrosis, cytopenia, and splenomegaly. Additionally, these diseases may also transform to acute myeloid leukemia. In 2005, four independent research groups identified a single acquired mutation in the Janus Kinase 2 (JAK2) gene on chromosome 9 that had a high incidence of occurrence in patients with PV, ET, or IMF¹⁻⁴. The point mutation in exon 14 of JAK2 alters codon 617 from a valine to a phenylalanine. This amino acid alteration in the JH2 domain of JAK2 causes a constitutive activation of the tyrosine kinase, which is believed to confer erythropoietin hypersensitivity and erythropoietin-independent survival to the myeloid stem cell. Greater than 80 percent of PV and 40 percent of ET and IMF cases used in the recent studies harbored the JAK2 point mutation. The detection of the JAK2 (V617F) mutation provides a qualitative diagnostic parameter for the identification of the non-chronic myelogenous leukemia subgroup of myeloproliferative disorders. Rapid and accurate diagnosis is essential for prognostication.

Indications for Use

Patient is suspected of having a myeloproliferative disorder (PV, ET, or IMF).

Interpretation

- A positive result identifies a JAK2 (V617F) mutation and is strongly supportive of a diagnosis of PV, ET, or IMF.
- A negative result does not rule out the presence of a JAK2 (V617F) mutation nor the possibility of diagnosis of PV, ET, or IMF. The mutation has been correlated to disease state in 80 percent, 40 percent, and 40 percent of patients, respectively, with these myeloproliferative disorders.

Limitations

Sequence verification is limited to samples with a mutation presence greater than 10 percent in each peripheral blood sample.

Methodology

Polymerase chain reaction (PCR)

References

1. Baxter EJ, Scott LM, Campbell PJ, et al. "Acquired mutation of the tyrosine kinase JAK2 in human myeloproliferative disorders." *Lancet* 2005;365:1054-1061.
2. James C, Ugo V, Le Couedic JP, et al. "A unique clonal JAK2 mutation leading to constitutive signalling causes polycythaemia vera." *Nature* 2005;434:1144-1148.
3. Levine RL, Wadleigh M, Cools J, et al. "Activating mutation in the tyrosine kinase JAK2 in polycythemia vera, essential thrombocythemia, and myeloid metaplasia with myelofibrosis." *Cancer Cell* 2005;7:387-397.
4. Zhao R, Xing S, Li Z, et al. "Identification of an acquired JAK2 mutation in polycythemia vera." *J Biol Chem* 2005;280:22788-22792.

Test Information

0051245

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