

JAK2 1849G>T [V617F] Mutation in Myeloproliferative Neoplasms

The UNC Molecular Genetics Laboratory performs a molecular test to detect *JAK2* 1849G>T [V617F], an acquired mutation that is associated with myeloproliferative neoplasms (MPN) including polycythemia vera, essential thrombocythemia, and primary myelofibrosis.

Biology of the disease: A somatic mutation 1849G>T in exon 12 of the Janus kinase 2 gene (*JAK2*) has been identified as an oncogenic event and as a molecular marker in the following MPNs: polycythemia vera (PV), essential thrombocythemia (ET), and primary myelofibrosis (PMF). The majority of PV cases (90%), and about half of ET and PMF cases harbor the *JAK2* 1849G>T mutation. The mutated ET cases may represent an early presentation of PV or a variant of PV. The mutation is quite specific for these (and a very low proportion of other) myeloproliferative or myelodysplastic diseases, meaning that a positive result is indicative of a clonal myeloid neoplasm while a negative result does not exclude any of these diseases. Correlation with blood and bone marrow examination is essential to proper classification of myeloproliferative diseases.

Clinical Indications for *JAK2* mutation testing:

Testing is recommended in patients with an uncertain etiology for elevated hemoglobin (e.g. no volume depletion or hypoxia, EPO low or normal) or thrombocytosis (e.g. no hyposplenism or inflammation), and in patients having an atypical myeloproliferation (or erythroid-only dysplasia) that is cytogenetically normal.

Laboratory Testing for *JAK2* mutation: The preferred sample is 2mL of EDTA anticoagulated blood (lavender-top), which may be refrigerated up to 48 hours before analysis by real-time PCR and probe hybridization followed by melt curve analysis on a LightCycler. Results are reported as positive, or as negative to a sensitivity of 5% of DNA in the sample.

References:

1. Smith CA, Fan G: *The saga of JAK2 mutations and translocations in hematologic disorders: pathogenesis, diagnostic and therapeutic prospects, and revised World Health Organization diagnostic criteria for myeloproliferative neoplasms.* Hum Pathol 39:795-810, 2008
2. Murugesan G, et al: *Identification of the JAK2 V617F Mutation in Chronic Myeloproliferative Disorders Using FRET Probes and Melting Curve Analysis.* Am J Clin Pathol, 125:625-633, 2006.
3. Vannucchi AM, et al, *Clinical correlates of JAK2 V617F presence or allele burden in myeloproliferative neoplasms: a critical reappraisal.* Leukemia 22:1299-307, 2008.

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