Quantitative *JAK2* c.1849G>T (p.V617F) Mutation in Myeloproliferative Neoplasms

The UNC Molecular Genetics Laboratory performs a molecular test to detect and quantify the *JAK2* c.1849G>T (p.V617F) acquired mutation associated with myeloproliferative neoplasms (MPN), specifically polycythemia vera (PV), essential thrombocythemia (ET), and primary myelofibrosis (PMF).

Biology of the disease:

Somatic mutation c.1849G>T (p.V617F) in exon 14 of the Janus kinase 2 gene (*JAK2*) has been identified as an oncogenic event and a molecular marker of PV, ET, and PMF. The vast majority of PV cases (> 95%), and about half of ET and PMF cases harbor the *JAK2* V617F mutation. Homozygous or hemizygous mutation is often seen in PV and PMF, whereas heterozygous mutation is common in ET and is associated with a lower mutant allele burden. The mutation is 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.

Clinical Indications for *JAK2* mutation testing:

Testing is recommended in patients suspected of having myeloproliferative neoplasia. This includes uncertain etiology for elevated hemoglobin (no volume depletion or hypoxia, low or normal erythropoietin level), granulocytosis (no active infection), or thrombocytosis (no hyposplenism, iron deficiency, or inflammation). This is a quantitative assay that can be used to assist in diagnosis or monitor response to therapy. Results are reported to a limit of detection of 0.1% variant allele fraction.

Laboratory Testing for *JAK2* mutation:

The preferred sample is 3mL of EDTA anticoagulated blood or 1mL of bone marrow (lavender-top) which may be refrigerated up to 72 hours before analysis by droplet digital PCR. Results are reported as positive or negative with a limit of detection of 0.1% variant allele fraction. All positive samples will be reported with a quantitative value.

References:

1. Lee, E., Lee, K. J., Park, H., Chung, J. Y., Lee, M. N., Chang, M. H., … Eom, H. S. *Clinical Implications of Quantitative JAK2 V617F Analysis using Droplet Digital PCR in Myeloproliferative Neoplasms*. Annals of Laboratory Medicine, 38(2), 147–154, 2018.
2. Nystrand, C. F., Ghanima, W., Waage, A., & Jonassen, C. M.. *JAK2 V617F mutation can be reliably detected in serum using droplet digital PCR*. International Journal of Laboratory Hematology, 40(2), 181–186, 2018.
3. Waterhouse, M., Follo, M., Pfeifer, D., von Bubnoff, N., Duyster, J., Bertz, H., & Finke, J. *Sensitive and accurate quantification of JAK2 V617F mutation in chronic myeloproliferative neoplasms by droplet digital PCR.* Annals of Hematology, 95(5), 739–744, 2016.

Website: http://labs.unchealthcare.org/directory/molecular_pathology/index_html
Questions? Call the Molecular Genetics Lab at (984) 974-1825