Myeloproliferative Neoplasm (MPN) Hotspot Panel

The UNC Molecular Genetics Laboratory performs a hotspot panel targeting selected regions of JAK2, CALR, and MPL using next-generation sequencing to facilitate diagnosis of MPNs.

Rationale for testing:
Testing for the presence of somatic gene mutations may assist in diagnosis or exclusion of BCR-ABL1 negative myeloproliferative neoplasms (MPNs).

Clinical Indications for Myeloproliferative Neoplasm Hotspot Panel testing:
The three most common BCR-ABL1 negative myeloproliferative neoplasms are polycythemia vera (PV), essential thrombocythemia (ET), and primary myelofibrosis (PMF). PV and ET are characterized by non-physiologic elevation of hemoglobin or platelet count, respectively. Primary myelofibrosis is characterized by a constellation of bone marrow findings, ultimately leading to bone marrow fibrosis. Mutational features of these neoplasms are shown below

1) PV: JAK2 p.V617F (exon 14) is present >95% of cases of PV and nearly all remaining cases having a mutation in exon 12.
2) ET and PMF: JAK2, CALR, or MPL mutations are present in approximately 90% of cases of ET and PMF. For patients with low to moderate clinical suspicion for a MPN, a negative result greatly diminishes the likelihood of a neoplastic process. When there is a high suspicion for a myeloproliferative neoplasm, the broader Myeloid Mutation Panel (MDS and MPN) may be warranted to help identify rare JAK2/CALR/MPL triple negative cases of ET or PMF.

Specimen Requirements for the Myeloid Mutation Panel:
Bone marrow aspirate (1 mL, EDTA) or peripheral blood (3mL, EDTA) having at least 30% myeloid cells, and refrigerated for up to 72 hours. Unacceptable sample types include: fresh, frozen, or paraffin embedded tissue. The assay is sensitive to variants above 5% allele frequency (10% clonal cells). This test is NOT appropriate for MRD monitoring. For patients with known JAK2 p.V617F positive disease, the quantitative JAK2 p.V617F assay should be used for monitoring.

Gene Regions Tested: CALR (exon 9), JAK2 (exons 12,14), and MPL (exon 10)

Limitations:
Gene amplifications, translocations, and insertions or deletions over 90 bases in length are not reliably detected by this assay. Variants predicted to be non-deleterious (synonymous coding changes and population variants) are not reported. Lack of mutation does not exclude myeloid neoplasia. Presence of clonality does not establish a diagnosis of malignancy.

References:

Questions?
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University of North Carolina Molecular Genetics Laboratory: March 1, 2019