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 Hostpot 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:
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3. Klampfl T, et al. Somatic mutations of calreticulin in myeloproliferative neoplasms. N Engl J Med. 2013 Dec 19;369(25):2379-90. PMID: 24325356
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5. Pardanani DA et al. MPL515 mutations in myeloproliferative and other myeloid disorders: a study of 1182 patients. Blood. 2006; 108(10):3472-3476. PMID: 16868251
6. McClure, Rebecca F. et al. Clinical Significance of DNA Variants in Chronic Myeloid Neoplasms. The Journal of Molecular Diagnostics, Volume 20 , Issue 6 , 717 - 737

Questions?
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