

LAB ALERT

Date: January 15, 2015

RE: New Test CALR Mutation Detection

Dear Regional Pathology Clients,

We are very excited to announce that the Nebraska Medicine Molecular Diagnostics Laboratory is now performing Calreticulin (CALR) mutation testing. Insertion and deletion mutations in the *CALR* gene are important in the evaluation of peripheral blood and bone marrow for chronic myeloproliferative neoplasms (MPN). CALR mutations are the second most frequent somatic mutation after the JAK2 p.V617F mutation in MPNs. *CALR* mutations have been described in the majority of Essential Thrombocythemia (ET) and Primary Myelofibrosis (PMF) cases that have non-mutated *JAK2* or *MPL* genes. CALR mutations are not identified in Polycythemia Vera. The most common two types of mutations are type 1 and type 2 mutations. Type 1, a 52 bp deletion, accounts for approximately 50% of CALR mutations; while type 2, a 5bp insertion, accounts for approximately 30%.

The new assay utilizes DNA amplification and capillary electrophoresis to discriminate between non-mutated and mutated sequences. Dideoxy sequencing of exon 9 of the *CALR* gene will be utilized to confirm the mutations if needed. The lower limit of detection is 15% mutant allele. This assay detects only insertions and deletions and will not detect single nucleotide variants in exon 9 of the *CALR* gene.

****Note:** In suspected cases of ET and PMF, a reflex strategy has been recommended in the literature to perform CALR mutation testing after a JAK2 assay is found to be negative.

Test Name: CALR Mutations

CPT Code: 81479

Specimen requirements: EDTA anticoagulated blood or bone marrow, unstained bone marrow smears, paraffin embedded clot sections and tissue biopsies of other organs. Transport is 4⁰C for outside specimens.

The assay will be performed at least once per week.

References

- 1) Klampf, T, *et. al.* "Somatic Mutations of Calreticulin in Myeloproliferative Neoplasms." (2013) N Engl J Med 369:2379-90.
- 2) Nangalia, J, *et. al.* "Somatic *CALR* mutations in Myeloproliferative Neoplasms with Nonmutated *JAK2*." (2013) N Engl J Med 369:2391-405.

Technical inquires may be called to the laboratory at 559 8556, Jill Branson, Mgr, 559 7611 or Allison Cushman-Vokoun, Laboratory Medical Director, 559-3512.

Regional Pathology Services Client Services 402.559.6420 or Toll free at 1-800-334-0459