

NPM1 Mutation Assay

Indications for Testing

- Stratifying high and low risk AML
- At initial diagnosis of AML
- Reoccurrence of leukemia after induction therapy on patients not initially screened for *NPM1* mutations.

Test Code

NPM1

Specimen Requirements

5 ml of Peripheral Blood in EDTA or ACD
3 ml of bone marrow in EDTA or ACD
1 µg of previously isolated DNA

Specimen Transport

Ambient or Cool
Do not Freeze

CPT Codes

83891, 83898, 83909, 83912

Turn-Around-Time

3-5 Days

Description of Testing

Primers targeting the area surrounding exon 12 of the *NPM1* gene are used to amplify the patient's DNA. The size of the *NPM1* PCR product is determined by capillary electrophoresis.

References

1. Acute Myeloid Leukemia, Clinical Practice Guidelines in Oncology, (V.1.2010) National Comprehensive Cancer Network.
2. Wertheim G, et al. (2008) Nucleophosmin (NPM1) mutations in acute myeloid leukemia: an ongoing (cytoplasmic) tale of dueling mutations and duality of molecular genetic testing methodologies. *J Mol Diagn* 10(3):198-202.
3. Gale R, et al. (2008) The impact of FLT3 internal tandem duplication mutant level, number, size and interaction with NPM1 mutations in a large cohort of young adult patients with acute myeloid leukemia. *Blood* 111:2776-2784.
4. Falini B, et al. (2007) Translocations and mutations involving the nucleophosmin (NPM1) gene in lymphomas and leukemias. *Haematologica* 92(4):519-532.
5. Thiede C, et al. (2006) Prevalence and prognostic impact of NPM1 mutations in 1485 adult patients with acute myeloid leukemia (AML). *Blood* 107:4011-4020.
6. Döhner K, et al. (2005) Mutant nucleophosmin (NPM1) predicts favorable prognosis in younger adults with acute myeloid leukemia and normal cytogenetics: interaction with other gene mutations. *Blood* 106(12):3740-3746.
7. Gallagher R, et al. (2005) Dueling mutations in normal karyotype AML. *Blood* 106:3681-3682.

* *NPM1* testing is covered by a United States patent licensed from Xenomics, Inc.

Clinical Utility of *NPM1* Mutation Assay

The Nucleophosmin (*NPM1*) gene is one of the most commonly mutated genes in acute myeloid leukemia (AML), occurring in about 35% of AML patients at diagnosis and in approximately 60% of adult cytogenetically normal AML (CN-AML). The CN-AML group is collectively the most common AML group and assigned an intermediate prognostic category. However studies have shown that the CN-AML group is not homogenous and significant diversity has been shown to exist within this population of AML patients. The vast majority of *NPM1* mutations are insertions in exon 12 occurring near the C-terminus of the protein resulting in cytoplasmic localization. Currently there are over 40 known *NPM1* mutations, most of which will be detected with our assay.

Clinical studies have found that *NPM1* mutations are associated with increased blast counts, higher extramedullary involvement and increased platelet counts in AML. *NPM1* mutations, in the absence of the *FLT3* mutation, are associated with a good response to induction therapy and have a 60% improved 5 year survival. It has been suggested that the identification of mutations in both *NPM1* and *FLT3* genes allows for the stratification of the CN-AML patients into three different prognostic groups. A favorable prognosis is associated with *NPM1+* and *FLT3-*, an intermediate prognosis with *NPM1+* and *FLT3+* or *NPM1-* and *FLT3-*, and a poor prognosis with *NPM1-* and *FLT3+*.

It is recommended that patients who are CN-AML should be screened for *NPM1* mutations in efforts to assess prognosis and aid in treatment decisions. Utilizing both *NPM1* and *FLT3* mutations status is the most common method in stratification of the CN-AML population.