

# *NPM1* Mutations in Acute Myelogenous Leukemia

## *DETECTS MUTATED NUCLEOPHOSMIN GENE IN ACUTE MYELOGENOUS LEUKEMIA CELLS*

### Clinical Background

- Acute myelogenous leukemia (AML) is a heterogeneous disease clinically, molecularly, and cytogenetically. Approximately 30 percent of cases display recurrent cytogenetic abnormalities, typically reciprocal translocations, that help define distinct entities and often confer a favorable prognosis. However, approximately 40–50 percent of AML cases have normal karyotypes with variable prognoses.
- Several genetic changes have been identified in karyotypically normal AML that can aid in prediction of clinical outcome.<sup>1</sup> One class of mutations was detected in exon 12 of the nucleophosmin (*NPM1*) gene. These mutations consist of small insertions that alter the reading frame of translation at the C-terminus of *NPM1*. As a result, a nucleolar localization motif is lost and a nuclear export signal is gained in the new reading frame of translation, causing delocalization of the NPM1 protein into the cytoplasm.<sup>2</sup> *NPM1* mutations are thought to be an early event in leukemogenesis, and once present, appear stable.
- *NPM1* mutations in AML have been reported to confer a more favorable disease outcome, especially in the absence of FLT-3 mutations.<sup>3</sup> This test detects all reported *NPM1* mutations.

### Indications For Use

The principal use for this test is the detection of mutations in the *NPM1* gene associated with AML prognosis.

### Interpretation

- Positive: An NPM1c mutation was detected.
- Not Detected: There is no evidence of a NPM1c mutation. This result does not rule out the possibility of a mutation below the detectable limit of the assay.

### Limitations

- This test requires that at least one mutated AML cell is present per 20 white cells for detection.
- Results of this test should always be interpreted in the context of clinicopathologic and other relevant data, and should not be used alone for a diagnosis of malignancy. A negative result does not preclude the presence of *NPM1* mutations in rare AML cells below the detection limit of this test.

### Methodology

Genomic DNA is prepared from whole blood or bone marrow, and a fragment containing exon 12 of *NPM1* is PCR-amplified. Small insertional NPMc+ mutations are then identified by analysis of the PCR product by capillary electrophoresis.

### References

1. Mrozek K, et al. Clinical relevance of mutations and gene-expression changes in adult acute myeloid leukemia with normal cytogenetics: are we ready for a prognostically prioritized molecular classification? *Blood* 2007; 109:431–48.
2. Falini B, et al. Acute myeloid leukemia carrying cytoplasmic/mutated nucleophosmin (NPMc+ AML): biologic and clinical features. *Blood* 2007; 109:874–85.
3. Thiede C, et al. Prevalence and prognostic impact of *NPM1* mutations in 1,485 adult patients with acute myeloid leukemia. *Blood* 2006; 107:4011–20.
4. Szankasi P, Jama M, Bahler DW. A new DNA based test for detection of Nucleophosmin exon 12 mutations by capillary electrophoresis. *J Mol Diagn* 2008; 10:236–41.

### Test Information

0040174

*NPM1* Mutation by PCR and Fragment Analysis, Fluid

0040179

*NPM1* Mutation by PCR and Fragment Analysis, Paraffin

For specific collection, transport, and testing information, refer to the ARUP Web site at [www.aruplab.com](http://www.aruplab.com).

For information on test selection, ordering, and interpretation, refer to ARUP Consult<sup>®</sup> at [www.arupconsult.com](http://www.arupconsult.com).