In AML patients, molecular genetic markers are clinically significant factors in response to therapy and survival.

Nucleophosmin (NPM1) mutation occurs in nearly one-third of adult AML.

NPM1 mutation analysis is prognostic in nature, especially in cases with a normal karyotype.

Patients with NPM1 mutations typically show a good response to induction therapy.

The order code is NPMMUT.

Quick Facts

NPM1 Mutation Analysis

CLINICAL APPLICATION

- AML with mutated nucleophosmin (NPM1) is now a provisional entity described in the 2008 World Health Organization classification for “AML with recurrent genetic abnormalities.”

- AML with mutated NPM1 typically shows a good response to induction therapy and has a good prognosis, especially in the absence of a concomitant FLT-3 mutation.

- NPM1 mutation occurs in about 30% of adult AML; in children the frequency is much less at about 6-8%.

- NPM1 mutation (and its immunohistochemical counterpart, cytoplasmic nucleophosmin or NPMc+) appears to be nearly exclusive to AML and is usually expressed in the entire leukemic population.

- NPM1 mutation is thought to be a primary genetic lesion, as it is stable over the course of disease and has been detected in AML at relapse.

CLINICAL BACKGROUND

- Nucleophosmin is an important nucleolar phosphoprotein that acts as a molecular chaperone to establish multiple protein-to-protein interactions.

- Mutated NPM1 protein results in abnormal cytoplasmic localization and probably disturbs multiple cellular pathways, resulting in a “loss of function” in some key interactions and a “gain of function” in others. The mechanism by which mutated NPM1 protein promotes leukemogenesis remains unclear.

- The majority of mutations (90-95%) are 4-base pair insertions at a specific location in exon 12 of the NPM1 gene, although other insertion/deletion mutations in exon 12 have also been observed.

- About 85% of NPM1-mutated AML is cytogenetically normal.

- NPM1-mutated AML exhibits a CD34-negative profile in 90%-95% of cases.

- NPM1-mutated AML is usually accompanied by a high white blood cell count and differs from AML with myelodysplasia-related changes because it does not usually evolve from previous myelodysplastic syndrome or MDS/myeloproliferative neoplasm.

TECHNICAL INFORMATION

- NPM1 mutation analysis employs genomic DNA amplification by PCR and fragment analysis detection by capillary electrophoresis to identify the presence of a 4-base-pair insertion in exon 12 of the nucleophosmin (NPM1) gene.

- The limit of detection of this assay is approximately 5% NPM1 mutation-positive cells in a background of NPM1 mutation-negative cells.

For more information, please contact your local marketing representative.

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## NPM1 Mutation Analysis

### Test Information

<table>
<thead>
<tr>
<th>Description</th>
<th>NPM1 Mutation Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Method</td>
<td>PCR and Fragment Analysis</td>
</tr>
<tr>
<td>Order Code</td>
<td>NPMMUT</td>
</tr>
<tr>
<td>CPT Code</td>
<td>83891, 83898, 83909, 83912</td>
</tr>
<tr>
<td>Specimen Requirements</td>
<td>Whole blood (1ml minimum, 5ml preferred) in edta, sodium citrate or acd tube or bone marrow (1ml preferred, 0.5ml minimum)</td>
</tr>
<tr>
<td>Comments</td>
<td>Unacceptable Conditions: No tumor in tissue. (Specimens that contain less than 20% tumor will be tested and reported with a disclaimer). Specimens fixed/processed in alternative fixatives (alcohol, Prefer®). Frozen specimens. Stability: Room Temp: Indefinitely; Refrigerated: Indefinitely; Frozen: Unacceptable.</td>
</tr>
<tr>
<td>Ranges</td>
<td>Mutation not detected</td>
</tr>
</tbody>
</table>

### Selected References


For more information, please contact your local marketing representative.