Technical Brief

FISH for Acute Lymphoblastic Leukemia

Background Information
Using current World Health Organization (WHO) criteria, the diagnosis and classification of acute lymphoblastic leukemia (ALL) involves the correlation of morphologic findings with ancillary data, including cytogenetic findings. Several recurrent cytogenetic abnormalities occur in ALL that have direct implications on diagnosis or prognosis.1-3 Interphase fluorescence in situ hybridization (FISH) studies offer the ability to rapidly detect these cytogenetic abnormalities in nondividing cells. FISH studies are, therefore, an important adjunct to traditional banded karyotyping.3 FISH analysis can clarify suspected abnormalities identified in banded karyotypes, identify the presence of complex or cryptic cytogenetic abnormalities, or provide cytogenetic information even when banded karyotype data is not available.

Clinical Indications
Approximately 13,000 new cases of acute leukemia occur in the United States annually. Of these, approximately 70% are AML and occur primarily in adults, while 30% are ALL and occur predominantly in children.

Cleveland Clinic Laboratories offers FISH analysis for the following cytogenetic abnormalities in ALL:

1. **t(9;22)(q34;q11) (BCR/ABL):** Cases of precursor B-cell ALL with t(9;22) are associated with a poor prognosis.

2. **11q23 (MLL) abnormalities:** Translocations involving the MLL gene, which may involve one of many partner genes, are associated with a poor prognosis in precursor B-cell ALL.

3. **t(12;21)(p13;q22) (TEL/AML1):** This abnormality cannot be detected by traditional banded karyotyping. Cases of precursor B-cell ALL with t(12;21) are associated with a favorable prognosis.

4. **Trisomy 4/10/17:** Trisomy of chromosomes 4, 10 and 17 is associated with a hyperdiploid karyotype and favorable prognosis in precursor B-cell ALL.

Interpretation
At least 100 cells are analyzed.
- **Positive:** >10% of nuclei examined exhibit a positive signal pattern
- **Negative:** <10% of nuclei examined exhibit a positive signal pattern

Limitations of the Assays
False negative results will occur if the malignant cells represent <10% of the cells present in the specimen.

Methodology
FISH can be performed on peripheral blood or bone marrow aspirate specimens. Hybridizations are performed using the appropriate two-color or three-color probe set (Abbott Molecular, Des Plaines, IL), and cells are examined using fluorescence microscopy. The FISH reagents employed are either dual-fusion (DF) probes (e.g. t(8;21), t(15;17), t(9;22)) that specifically identify a particular translocation, or are break-apart (BA) probes (e.g. RARA, MLL) that identify the presence of a translocation involving one gene but do not specifically identify the partner gene.

Probes Available

<table>
<thead>
<tr>
<th>Probe</th>
<th>Abnormality</th>
<th>Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>BCR/ABL</td>
<td>t(9;22)(q34;q11.2) BCR/ABL</td>
<td>SF</td>
</tr>
<tr>
<td>MLL</td>
<td>11q23 (MLL) rearrangement</td>
<td>BA</td>
</tr>
<tr>
<td>TEL/AML1</td>
<td>t(12;21)(p13;q22) TEL/AML1</td>
<td>DF</td>
</tr>
<tr>
<td>Trisomy 4/10/17</td>
<td>Trisomy of chromosomes 4, 10, or 17</td>
<td>CN</td>
</tr>
</tbody>
</table>

SF – single fusion; BA – break-apart; DF – dual fusion; CN – copy number

08.03.11
Test Overview

FISH for Acute Lymphoblastic Leukemia

Specific testing collection, transport and ordering information is available at clevelandcliniclabs.com.

References


Technical Information Contact:
James Pettay, MT(ASCP)
216.444.2130
pettayj@ccf.org

Scientific Information Contacts:
James Cook, MD, PhD
216.444.4061
cookj2@ccf.org
Raymond Tubbs, DO
216.444.2844
tubbsr@ccf.org