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/ABL1)***: 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.

We also offer a FISH for B lymphoblastic leukemia panel which includes all of the probes listed above.

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 Assay

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

Probes Available

Probe	Abnormality	Type
BCR/ABL1	*t(9;22)(q34;q11.2) BCR/ABL1*	SF
MLL	*11q23 (MLL) rearrangement*	BA
TEL/AML1	*t(12;21)(p13;q22) TEL/AML1*	DF
Trisomy 4/10/17	*Trisomy of chromosome 4, 10, or 17*	CN

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

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.

References

1. Borowitz MJ and Chan JKC. B lymphoblastic leukemia/ lymphoma with recurrent genetic abnormalities. IN: WHO Classification of Haematopoietic and Lymphoid Tissues. Swerdlow SH, Campo E, Harris NL, *et al*. (eds). IARC Press:Lyon 2008:171-175.
2. Vardiman JW, Thiele J, Arber DA, *et al*. The 2008 revision of the World Health Organization (WHO) classifi-cation of myeloid neoplasms and acute leukemia: rationale and important changes. *Blood.* 2009;114:937-51.
3. Avet-Loiseau H. FISH analysis at diagnosis in acute lymphoblastic leukemia. *Leuk Lymphoma*. 1999;33:441-9.

Test Overview

FISH for Acute Lymphoblastic Leukemia

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

Technical Information Contact:

James Pettay, MT(ASCP)
216.444.9486
pettayj@ccf.org

Scientific Information Contact:

James Cook, MD, PhD
216.444.4435
cookj2@ccf.org