FISH for Acute Myeloid Leukemia

Background Information

Using current World Health Organization (WHO) criteria, the diagnosis and classification of acute myeloid leukemia (AML) involves the correlation of morphologic findings with ancillary data, including cytogenetic findings. Several recurrent cytogenetic abnormalities occur in AML 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 AML. We also offer a FISH for Acute Myeloid Leukemia panel that includes: t(8;21), inv(16), t(15;17) and MLL.

1. t(9;22)(q32;q11) *BCR/ABL1*: The *BCR/ABL1* translocation is present in cases of chronic myeloid leukemia in blast crisis and occasionally in cases of apparently de novo AML.
2. t(8;21)(q22;q22) *RUNX1/RUNX1T1 (AML1/ETO)*: Cases of AML with t(8;21) constitute a distinct subtype in the WHO classification. The presence of t(8;21) is associated with a favorable prognosis.
3. Inv(16)(p13q22) *CBFB/MYH11*: Cases of AML with inv(16) or the related t(16;16)(p13;q22) represent a distinct subtype of AML in the WHO classification. Cases of AML with inv(16) display a favorable prognosis.
4. t(15;17)(q22;q12) *PML/RARA*: Translocations involving the retinoic acid receptor alpha gene *(RARA)* are present in all cases of acute promyelocytic leukemia and are associated with a favorable prognosis when treated with specific therapy. In most cases, the translocation is t(15;17)(q22;q12), although rare variant translocations involving *RARA* and other genes may also occur.
5. 11q23 (MLL) abnormalities: Translocations involving the *MLL* gene are associated with poor prognosis in AML. Cases with t(9;11)(p22;q23) *MLLT3/MLL* represent a distinct subtype of AML in the WHO classification.
6. Myelodysplasia-associated abnormalities: Cases of AML with loss of chromosomes 5/5q or 7/7q are classified as a distinct subtype of AML in the WHO classification.

Probes Available

Probe	Abnormality	Type
BCR/ABL1	t(9;22)(q34;q11.2) *BCR/ABL1*	SF
RUNX1/RUNX1T1	t(8;21)(q22;q22) *RUNX1/RUNX1T1*	DF
CBFB/MYH11	inv(16)(p13.1q22) or t(16;16)(p13.1;q22)	BA
PML/RARA	t(15;17)(q22;q12) *PML/RARA*	DF
RARA	17q12 *(RARA)* rearrangement	BA
MLL	11q23 *(MLL)* rearrangement	BA
MDS Panel	-5/5q-, -7/7q-, +8, 20q-	CN

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

Limitations of the Assay

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.

References

1. Arber DA, Brunning RD, LeBeau MM, *et al*. Acute myeloid leukemia 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 reivision of the World Health Organization (WHO) classification of myeloid neoplasms and acute leukemia: rationale and important changes. *Blood.* 2009;114:937-51.
3. Coleman JF, Theil KS, Tubbs RR, *et al*. Diagnostic yield of bone marrow and peripheral blood FISH panel testing in clinically suspected myelodysplastic syndromes and/or acute myeloid leukemia: a prospective analysis of 433 cases. *Am J Clin Pathol*. 2011;135:915-20.

Test Overview

FISH for Acute Myeloid Leukemia

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

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