

Acute Myeloid Leukemia (AML) Panel by FISH

DETECTION OF SPECIFIC RECURRENT GENOMIC ABERRATIONS IN ACUTE MYELOID LEUKEMIA (AML) BY FLUORESCENCE IN SITU HYBRIDIZATION (FISH)

Test Highlights

- This test allows for classification of AML with recurrent cytogenetic abnormalities, provides significant prognostic information, and is suitable for widespread use.
- FISH is more sensitive than conventional cytogenetics in detecting particular genomic aberrations.
- This test can be used to monitor response to therapy or progression of disease.

Clinical Background

- AML represents a group of hematopoietic neoplasms derived from the bone marrow precursors of myeloid lineage.
- AML is the most common type of acute leukemia in adults.
- Incidence is two to three in 100,000 individuals per year.
- AML peaks in the fifth and sixth decade.
- Males are more affected than females (minimal difference).
- Classification of AML is based on blast count (>20 percent), cytogenetic features, cell of origin, and morphology.
- Recurrent specific chromosomal abnormalities have played an important role in the classification of AML. They also provide significant prognostic information.
- AML with recurrent genetic changes is a subtype of AML as per the WHO classification and is described as follows:
 - AML with t(8;21)(q22;q22)—*RUNX1T1/RUNX1* (ETO/AML1)
 - Acute promyelocytic leukemia (APL) with t(15;17)(q22;q12)—*PML/RARA*
 - AML with inv(16)(p13.1q22) or t(16;16)(p13.1;q22)—*MYH11/CBFB*
 - AML with t(9;11)(p22;q23)—*MLLT3/MLL*
 - AML with t(6;9)(p23;q34)—*DEK/NUP214*
 - AML with inv(3)(q21q26.2) or t(3;3)(q21;q26.2)—*RPN1/EVII*
 - AML with t(1;22)(p13;q13)—*RBM15/MKLI*
- Standard chromosome analysis (karyotypic analysis) using metaphase cells requires dividing cells and remains the gold standard for the detection of cytogenetic abnormalities. However, AML with t(15;17), inv(16), and t(11q23:var) involving the MLL locus on chromosome 11 may be either cryptic, subtle, or masked by complex rearrangements or deletions. Therefore, it may be difficult to detect using standard cytogenetic techniques, especially in metaphase cells with suboptimal chromosome morphology.
- In a diagnostic cytogenetics laboratory, FISH analysis has several advantages over chromosome studies. It has a rapid turnaround time, detects small numbers of abnormal cells, and can also be performed on nondividing or interphase cells. In addition, FISH can detect cryptic or subtle rearrangements that might be difficult to detect by routine karyotyping.

Indications for Ordering

- Acute myeloid leukemia.
- FISH testing is indicated at the time of diagnosis for proper classification. However, it may also be used for follow-up studies, either to monitor response to therapy or progression of the disease.

Additional Ordering Notes

- A sodium-heparin (green-top) tube with 3–4 mL of bone marrow is required (can be performed on peripheral blood).
- Samples should be stored at room temperature and transported to the laboratory within 24 hours of draw.

Limitations

- This probe panel only detects specific aberrations in the chromosomes of interest for diagnosis and prognosis.
- Chromosome alterations outside the regions complementary to these FISH probes will not be detected.

Methodology

- Bone marrow cells on unstimulated cultures, either from direct harvest or 24-hour culture, are analyzed by FISH using a set of commercially available FISH probes.
- Each probe can be run as a part of the panel or individually.
- The FISH probes for t(8;21), inv(16) or t(16;16), t(15;17), and 11q23 (MLL locus) are set up separately for each patient.
- Hybridization and detection of hybridization signals are performed according to the manufacturer's protocols.
- At least two technologists score the same case.
- For each probe, 200 nuclei are evaluated.
- Bone marrow samples from 20 individuals without apparent hematological diseases and with normal karyotype are used as controls for each probe to determine the cutoff value for normal variation of the probe signal patterns.

- Tests available
 - FISH Panel for AML with Recurrent Genetic Abnormalities:

	Chromosome Abnormalities	Probe Names (Genes Involved)	Probe Type
1.	t(8;21)	ETO/AML1 (<i>RUNX1T1/RUNX1</i>)	Dual fusion
2.	t(15;17)	PML/RARA fusion (<i>PML/RARA</i>)	Dual fusion
3.	Inv(16) or t(16;16)	CBFB rearrangement (<i>MYH11/CBFB</i>)	Breakapart
4.	t(11q23:var)	MLL rearrangement (<i>MLL/var</i>)*	Breakapart

*The *MLL* gene on 11q23 has multiple translocation partners, and FISH probe for *MLL* is a breakapart probe that can detect only rearrangement of the *MLL* locus. To identify the translocation partner, correlation with chromosome studies is recommended.

References

1. McKenna RW. Acute myeloid leukemia. In *Practical diagnosis of hematologic disorders*, 4th ed. C Kjeldsberg, ed. 2006; Chicago: ASCP Press, 457–98.
2. Chromosomal and molecular genetic aberrations of tumor cells. In *Cancer cytogenetics*, 3rd ed. S Heim and F Mitelman, eds. 2009; Hoboken, New Jersey: Wiley-Blackwell.
3. Swerdlow SH, et al. *WHO classification of tumours of haematopoietic and lymphoid tissues*, 4th ed. 2008; Lyon, France: International Agency for Research on Cancer, 109–47.

Test Information

2002384 Acute Myelogenous Leukemia Panel by FISH

For specific collection, transport, and testing information, refer to the ARUP Web site at www.aruplab.com.

For information on test selection, ordering, and interpretation, refer to ARUP Consult® at www.arupconsult.com.