

Aggressive Lymphoma Panel by FISH

DETECTION OF SPECIFIC RECURRENT GENOMIC ABERRATIONS IN B-CELL LYMPHOMAS WITH AN AGGRESSIVE CLINICAL COURSE BY FLUORESCENCE IN SITU HYBRIDIZATION (FISH)

Test Highlights

- This test provides significant prognostic information for patients with B-cell lymphomas with features intermediate between diffuse large B-cell lymphoma (DLBCL) and Burkitt lymphoma (BL).
- FISH may detect specific genomic aberrations that are not detected by cytogenetics.
- This test aids in monitoring response to therapy or progression of disease.

Clinical Background

- The WHO category “B-cell lymphomas with features intermediate between diffuse large B-cell lymphoma (DLBCL) and Burkitt lymphoma (BL)” describes a lymphoma subtype with morphology, immunophenotypic, and genetic abnormalities, which cannot be definitively classified as DLBCL or BL. These lymphomas typically have a high proliferation index and are clinically aggressive.
- In both BL and DLBCL, translocations involving the immunoglobulin heavy chain (IGH) and/or immunoglobulin light chain (IG-kappa or IG-lambda) genes are observed, with the immunoglobulin gene promoter driving expression of genes involving cellular proliferation (*MYC*, *BCL6*) and/or apoptosis inhibiting genes (*BCL2*). So-called dual-hit lymphomas (DHL) are unusual in that these neoplasms show rearrangements of both *BCL2* (18q21.3) and *MYC* (8q24). Triple-hit lymphomas (THL) show simultaneous rearrangements of *BCL2*, *MYC*, and *BCL6* and are exceedingly rare. Both DHL and THL show morphologic features intermediate between DLBCL and BL, and both are characterized by a poor survival rate. THL shows the poorest survival rate.
- Standard chromosome analysis using metaphase cells requires dividing cells and remains the gold standard for the detection of cytogenetic abnormalities. However, cytogenetically visible rearrangements can be missed due to suboptimal chromosome morphology, lack of dividing neoplastic cells, or preferential growth of normal cells in culture.
- 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 be performed on non-dividing (interphase) cells. In addition, FISH can detect cryptic or subtle rearrangements that might be difficult to detect by routine karyotyping.

Indications for Ordering

- Mature B-cell lymphoma with features intermediate between DLBCL and Burkitt lymphoma; aggressive B-cell lymphomas.
- FISH testing is indicated at the time of diagnosis for proper classification. However, it may be also 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.
- Samples should be stored at room temperature and transported to the laboratory within 24 hours of draw.

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 IGH/*BCL2*, *MYC*, and *BCL6* 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 each case.
- 200 nuclei are evaluated for each probe.
- 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.

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.

Tests Available

FISH panel for B-cell lymphomas:

	Chromosome Abnormalities	Probe Names (Genes involved)	Probe Type
1.	IGH/ <i>BCL2</i> rearrangement	IGH@, <i>BCL2</i>	Dual color
2.	<i>MYC</i> rearrangement	<i>MYC</i>	Breakapart
3.	<i>BCL6</i> rearrangement	<i>BCL6</i>	Breakapart

References

1. Myelodysplastic syndromes. In *Cancer Cytogenetics*, 3rd ed. S Heim and F Mitelman, eds. 2009; Hoboken, NJ: Wiley-Blackwell.
2. Swerdlow SH, et al. 2008. *WHO classification of tumours of haematopoietic and lymphoid tissues*, 4th ed. Lyon, France: International Agency for Research on Cancer.
3. Tomita N, et al. Clinicopathological features of lymphoma/leukemia patients carrying both BCL2 and MYC translocations. *Haematologica* 2009;94(7):935–43.

Test Information

2002650 Lymphoma (Aggressive) 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.