FISH for Non-Hodgkin Lymphoma

Background Information

Using current World Health Organization criteria, the diagnosis and classification of non-Hodgkin lymphoma (NHL) requires correlation of morphologic findings with other ancillary data that may include cytogenetic findings. Several types of non-Hodgkin lymphoma are associated with specific, recurring cytogenetic abnormalities that are of diagnostic significance.[1-3]

Interphase fluorescence *in situ* hybridization (FISH) studies offer the ability to detect cytogenetic abnormalities in non-dividing cells. FISH studies are especially valuable in lymph node or other solid tissue biopsies because they can be performed on formalin-fixed, paraffin-embedded tissues and can, therefore, provide cytogenetic information even when material is not available for traditional banded karyotyping studies.

Clinical Indications

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

1. **t(14;18)(q32;q21) (*IGH*/*BCL2*):** The *IGH/BCL2* translocation is present in approximately 70-95% of cases of follicular lymphoma and 30% of diffuse large B-cell lymphomas (1,2). Analysis for t(14;18)(q32;q21) or variant *BCL2* translocations is useful in distinguishing these lymphomas from other types of NHL.
2. **t(11;14)(q13;q32) (*CCND1*/*IGH*):** This translocation or another rare variant *CCND1* translocation is present in the large majority of cases of mantle cell lymphoma.
3. **t(8;14)(q24;q32) (*MYC*/*IGH*) and variants:** By definition, all cases of Burkitt lymphoma contain a *MYC* rearrangement, usually t(8;14). In some cases, the translocations involve *IGK* (2p12), *IGL* (22q11), or other loci, instead of *IGH*. Translocations involving *MYC* also may be present in other forms on NHL including diffuse large B-cell lymphoma.

Probes Available

Probe	Abnormality	Type
IGH/BCL2	t(14;18)(q32;q21) *IGH/BCL2*	DF
BCL2	18q21 (*BCL2*) rearrangement	BA
IGH/CCND1	t(11;14)(q13;q32) *IGH/CCND1*	DF
CCND1	11q13 (*CCND1*) rearrangement	BA
IGH/MYC	t(8;14)(q24;q32) *IGH/MYC*	DF
MYC	8q24 (*MYC*) rearrangement	BA
BIRC3(API2)/MALT1	t(11;18)(q21;q21) *BIRC3(API2)/MALT1*	DF
IGH/MALT1	t(14;18)(q32;q21) *IGH/MALT1*	DF
MALT1	18q21 (*MALT1*) rearrangement	BA
IGH	14q32 (*IGH*) rearrangement	BA
ALK	2p23 (*ALK*) rearrangement	BA
BCL6	3q26 (*BCL6*) rearrangement	BA

DF – dual fusion; BA – break-apart

4. 18q21 (*MALT1*) translocations: Two translocations involving the *MALT1* gene, t(11;18)(q21;21) (*BIRC3*(*API2*)/*MALT1*) and t(14;18)(q21;q21) (*IGH*/*MALT1*) are associ-ated with extra-nodal MALT lymphomas. In some settings, such as gastric MALT lymphomas, the presence of a *MALT1* translocation has prognostic significance.
5. 14q32 (*IGH*) translocations: Translocations involving the *IGH* locus may be seen in various B-cell non-Hodgkin lymphomas.
6. 2p23 (*ALK*) translocations: Translocations involving the *ALK* gene may be seen in T-cell anaplastic large cell lymphomas.
7. 3q26 (*BCL6*) translocation: Translocations involving the *BCL6* locus may be seen in various non-Hodgkin lymphomas, especially in diffuse large B-cell lymphoma and grade 3B follicular lymphomas.

Interpretation

At least 100 cells are analyzed.

Positive: >10% of the 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. Paraffin-embedded material should be formalin-fixed. Material fixed in B5 or other fixatives is not acceptable for analysis.

Methodology

FISH can be performed on formalin-fixed, paraffin-embedded tissue sections. Peripheral blood or bone marrow aspirate specimens are also suitable for most probes. Hybridizations are performed using the appropriate two-color probe set (Abbott Molecular, Des Plains, IL), and cells are examined using fluorescence microscopy.

The FISH reagents employed are either dual-fusion (DF) probes (e.g. t(14;18), t(11;14)) that specifically identify a particular translocation, or are break-apart (BA) probes (e.g. CMYC) that identify the presence of a translocation involving one gene but do not identify the partner gene specifically.

References

1. Swerdlow SH, Campo E, Harris NL, *et al*. (eds). WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues. IARC Press: Lyon 2008.
2. Campo E, Swerdlow SH, Harris NL, *et al*. The 2008 WHO classification of lymphoid neoplasms and beyond: evolving concepts and practical applications. *Blood*. 2001;117:5019-32.
3. Cook JR. Paraffin section interphase fluorescence *in situ* hybridization in the diagnosis and classification of non-Hodgkin lymphomas. *Diagn Mol Pathol*. 2008;13:197-206.

Test Overview

FISH for non-Hodgkin Lymphoma

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

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