Test Definition: BLPMF

B-Cell Lymphoma, Specified FISH, Varies

Overview

Useful For

Detecting common chromosome abnormalities associated with specific B-cell lymphoma subtypes using **client** specified FISH probes

This test **should not be used** to screen for residual B-cell lymphoma

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
BLPMB	Probe, Each Additional (BLPMF)	No, (Bill Only)	No

Testing Algorithm

This test includes a charge for probe application, analysis, and professional interpretation of results for one probe set (2 individual fluorescence in situ hybridization [FISH] probes). Additional charges will be incurred for additional probe sets performed. Analysis charges will be incurred based on the number of cells analyzed per probe set. If no cells are available for analysis, no analysis charges will be incurred.

This test is performed using client-specified FISH probes and is not intended as a panel test. Specific probes or suspected B-cell lymphoma subtype must be listed in the probe request field. Reflex probes can be performed when appropriate if specified in the order request field.

When specified, any of the following probes for the following known subtypes of B-cell lymphoma will be performed:

Pediatric Burkitt lymphoma testing (aged 18 years or younger):
-Recommended probe request = 5'/3' MYC, MYC/IGH, MYC/IGK, MYC/IGL, 3'/5' BCL2, 3'/5' BCL6
*If reflex is included in the probe request, IGH/BCL2 reflex testing would occur if an unbalanced *BCL2* disruption is observed.

Diffuse large B-cell, "double-hit", "triple hit" lymphoma testing:
-Recommended probe request = 5'/3' MYC, MYC/IGH, reflex with 3'/5' BCL2, 3'/5' BCL6
*If reflex is included in the probe request, break-apart BCL2 and BCL6 reflex testing would occur when a *MYC* disruption is observed. IGH/BCL2 reflex testing would occur if an unbalanced *BCL2* disruption is observed.

Follicular lymphoma testing:
-Recommended probe request = 3'/5' BCL2, 3'/5' BCL6
*If reflex is included in the probe request, IGH/BCL2 reflex testing would occur if an unbalanced *BCL2* disruption is observed.

Mantle cell lymphoma (MCL) testing:
-Recommended probe request = CCND1/IGH, 5'/3' CCND1 as reflex

*If reflex is included in the probe request, break-apart CCND1 reflex testing would occur when an additional CCND1 FISH signal is detected to rule out a *CCND1* gene disruption.
*To rule out a *CCND2* gene disruption in *CCND1*-negative MCL, request FISH probe 5'/3' CCND2.

Blastoid Mantle cell lymphoma testing:
-Recommended probe request = CCND1/IGH, TP53, 5'/3' MYC, MYC/IGH, 5'/3' CCND1 as reflex
*If reflex is included in the probe request, break-apart CCND1 reflex testing would occur when an additional CCND1 FISH signal is detected to rule out a *CCND1* gene disruption

Splenic marginal zone lymphoma testing:
-Recommended probe request = D7Z1/7q32, TP53/D17Z1

See **Common Chromosome Abnormalities in B-cell Lymphomas** in Clinical Information for specific gene locations associated with these B-cell lymphoma subtypes.

If the laboratory is not provided with a specific probe request or an appropriate B-cell lymphoma subtype, the following probes will be performed.
t(3q27;var) rearrangement, BCL6 break-apart
7q-, D7Z1/7q32
8q24.21 rearrangement, MYC break-apart
t(8;14)(q24.21;q32), MYC/IGH fusion
t(11;14)(q13;q32), CCND1/IGH fusion
-17/17p-, TP53/D17Z1
t(18q21;var) rearrangement, BCL2 break-apart

When this test and flow cytometry testing for leukemia/lymphoma are ordered concurrently, the flow cytometry result will be utilized to determine if sufficient clonal B-cells are available for FISH testing. If the result does not identify a sufficient clonal B-cell population, this FISH test order will be canceled, and no charges will be incurred. The B-cell lymphoma subtype will be used by the laboratory to determine appropriate FISH probes, if determined and applicable.

Appropriate ancillary probes may be performed at consultant discretion to render comprehensive assessment. Any additional probes will have the results included within the final report and will be performed at an additional charge.

For more information see Bone Marrow Staging for Known or Suspected Malignant Lymphoma Algorithm.

Special Instructions

- Bone Marrow Staging for Known or Suspected Malignant Lymphoma Algorithm

Method Name

Fluorescence In Situ Hybridization (FISH)

NY State Available

Yes

Specimen

Specimen Type
Varies

Ordering Guidance
This test should only be ordered if the sample is known to have a sufficient clonal B-cell population. If a flow cytometry result is available and does not identify a sufficient clonal B-cell population, this test order will be canceled, and no charges will be incurred.

This test **should NOT be used** to screen for residual B-cell lymphoma.

This assay detects chromosome abnormalities observed in blood or bone marrow samples of patients with B-cell lymphoma. If a paraffin-embedded tissue specimen is submitted, the test will be canceled and BLYM / B-Cell Lymphoma, FISH, Tissue will be added and performed as the appropriate test.

For patients with B-cell acute lymphoblastic leukemia/lymphoma (B-ALL/LBL), order either BALAF / B-Cell Acute Lymphoblastic Leukemia/Lymphoma (ALL), FISH, Adult, Varies or BALFP / Pediatric B-Lymphoblastic Leukemia/Lymphoma panel, FISH, Varies, depending on the age of the patient.

For testing paraffin-embedded tissue samples from patients with B-cell lymphoblastic Lymphoma, see BLBLF / B-Cell Lymphoblastic Leukemia/Lymphoma, FISH, Tissue.

Additional Testing Requirements
Microarray testing for Burkitt-like lymphoma with 11q aberration is available, order CMAH / Chromosomal Microarray, Hematologic Disorders, Varies.

Shipping Instructions
Advise Express Mail or equivalent if not on courier service.

Necessary Information
1. A list of probes requested for analysis is required. Probes available for this test are listed in the Testing Algorithm section.
2. A reason for testing must be provided. If this information is not provided, an appropriate indication for testing may be entered by Mayo Clinic Laboratories.
3. A flow cytometry and/or a bone marrow pathology report should be submitted with each specimen. The laboratory will not reject testing if this information is not provided, but appropriate testing and interpretation may be compromised or delayed.

Specimen Required
Submit only 1 of the following specimens:

Preferred
Specimen Type: Bone marrow

Container/Tube:
Preferred: Yellow top (ACD)
Acceptable: Green top (sodium heparin) or lavender top (EDTA)
Specimen Volume: 2 to 3 mL
Collection Instructions:
1. It is preferable to send the first aspirate from the bone marrow collection.
2. Invert several times to mix bone marrow.
3. Send bone marrow in original tube. **Do not aliquot.**

Acceptable
Specimen Type: Whole blood
Container/Tube:
Preferred: Yellow top (ACD)
Acceptable: Green top (sodium heparin) or lavender top (EDTA)
Specimen Volume: 6 mL
Collection Instructions:
1. Invert several times to mix blood.
2. Send whole blood in original tube. **Do not aliquot.**

Forms
If not ordering electronically, complete, print, and send a Hematopathology/Cytogenetics Test Request (T726) with the specimen.

Specimen Minimum Volume
Bone marrow: 1 mL; Whole blood: 2 mL

Reject Due To

Fresh tissue	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Varies	Ambient (preferred)		
	Refrigerated		

Clinical & Interpretive

Clinical Information
Mature B-cell lymphoma can be low grade, intermediate grade, or high grade, and the prognosis and clinical course are highly variable. Genetic abnormalities can assist diagnosis and have served as important prognostic markers in B-cell lymphomas. Fluorescence in situ hybridization (FISH) permits the detection of recurrent gene rearrangements associated with various chromosomal abnormalities in specific B-cell lymphoma subtypes (see Table).

Table. **Common Chromosome Abnormalities in B-cell Lymphomas**

Lymphoma type	Chromosome abnormality	FISH probe
Burkitt (pediatric, aged 18 or younger)	8q24.21 rearrangement	5'/3' MYC
	t(2;8)(p11;q24.21)	IGK/MYC
	t(8;14)(q24.21;q32)	MYC/IGH
	t(8;22)(q24.21;q11.2)	MYC/IGL
	3q27 rearrangement	3'/5' BCL6
	18q21 rearrangement	3'/5' BCL2
Diffuse large B-cell, "double-hit"	8q24.21 rearrangement	5'/3' MYC
	t(8;14)(q24.21;q32)	MYC/IGH
	Reflex: t(8;22)(q24.21;q11.2)	MYC/IGL
	Reflex: t(2;8)(p12;q24.21)	IGK/MYC
	Reflex: 3q27 rearrangement	3'/5' BCL6
	Reflex: 18q21 rearrangement	3'/5' BCL2
Follicular	18q21 rearrangement	3'/5' BCL2
	3q27 rearrangement	3'/5' BCL6
Mantle cell	t(11;14)(q13;q32)	CCND1/IGH
	Reflex: 11q13 rearrangement	5'/3' CCND1
	Cyclin D1-negative MCL subtype only: 12p13.32 rearrangement	5'/3' CCND2
	Blastoid subtype only: deletion of 17p	TP53/D17Z1
	Blastoid subtype only: 8q24.21 rearrangement	5'/3' MYC
Splenic marginal zone	Deletion of 7q	D7Z1/7q32
	Deletion of 17p	TP53/D17Z1

Reference Values

An interpretive report will be provided.

Interpretation

A neoplastic clone is detected when the percent of cells with an abnormality exceeds the normal reference range for any given probe set.

The absence of an abnormal clone does not rule out the presence of lymphoma or another neoplastic disorder.

Detection of an abnormal clone supports a diagnosis of B-cell lymphoma. The specific abnormality detected may help to determine a specific B-cell lymphoma subtype.

Cautions

This test is not approved by the US Food and Drug Administration and is best used as an adjunct to existing clinical and pathologic information.

Bone marrow is the preferred sample type for this fluorescence in situ hybridization test (FISH). If bone marrow is not available, a blood specimen may be used if there are neoplastic cells in the blood specimen (as verified by a hematopathologist).

If no FISH signals are observed post-hybridization, the case will be released indicating a lack of FISH results.

Clinical Reference

1. Swerdlow SH, Campo E, Harris NL, et al, eds. WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues. 4th ed. IARC Press; 2017. WHO Classification of Tumours. Vol 2
2. King RL, McPhail ED, Meyer RG, et al. False-negative rates for MYC fluorescence in situ hybridization probes in B-cell neoplasms. Haematologica. 2019;104(6):e248-e251
3. Pophali PA, Marinelli LM, Ketterling RP, et al. High level MYC amplification in B-cell lymphomas: is it a marker of aggressive disease?. Blood Cancer J. 2020;10(1):5

Performance

Method Description

This test is performed using commercially available and laboratory-developed fluorescence in situ hybridization (FISH) probes. Deletion of the 7q32 locus from chromosome 7 and the *TP53* locus from chromosome 17 are detected using enumeration strategy probe sets. Rearrangements involving *MYC, BCL2, BCL6, CCND1 or CCND2* are detected using dual-color break-apart (BAP) strategy probe sets. Dual-color, dual-fusion fluorescence in situ hybridization (D-FISH) strategy probe sets are used to detect t(2;8), t(8;14), t(8;22), and t(11;14). For enumeration and BAP strategy probe sets, 100 interphase nuclei are scored; 200 interphase nuclei are scored when D-FISH probes are used, and results are expressed as the percent abnormal nuclei.(Unpublished Mayo method)

PDF Report

No

Day(s) Performed

Monday through Friday

Report Available

7 to 10 days

Specimen Retention Time

4 weeks

Performing Laboratory Location

Mayo Clinic Laboratories - Rochester Main Campus

Fees & Codes

Fees

- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact Customer Service.

Test Definition: BLPMF

B-Cell Lymphoma, Specified FISH, Varies

Test Classification

This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. It has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information

88271 x 2, 88275, 88291-FISH Probe, Analysis, Interpretation; 1 probe set
88271 x 2, 88275-FISH Probe, Analysis; each additional probe set (if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
BLPMF	B-cell Lymphoma, Specified FISH	101920-7

Result ID	Test Result Name	Result LOINC® Value
614229	Result Summary	50397-9
614230	Interpretation	69965-2
614231	Result Table	93356-4
614232	Result	62356-1
GC105	Reason for Referral	42349-1
GC106	Probes Requested	78040-3
GC107	Specimen	31208-2
614233	Source	31208-2
614234	Method	85069-3
614235	Additional Information	48767-8
614236	Disclaimer	62364-5
614237	Released By	18771-6