Test Definition: CLLDF

Chronic Lymphocytic Leukemia, Diagnostic FISH, Varies

Overview

Useful For

Detecting recurrent common chromosome abnormalities in patients with chronic lymphocytic leukemia (CLL) using a laboratory-designated probe set algorithm

Distinguishing patients with 11;14 translocations who have the leukemic phase of mantle cell lymphoma from patients who have CLL

Detecting patients with atypical CLL with translocations between *IGH* and *BCL3*

Evaluating specimens in which chromosome studies are unsuccessful

Reflex Tests

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

Testing Algorithm

This test includes a charge for the probe application, analysis, and professional interpretation of results for 6 probe sets (12 individual fluorescence in situ hybridization [FISH] probes). Additional charges will be incurred for all reflex or 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 as panel testing only using the following analysis algorithm.

The diagnostic chronic lymphocytic leukemia (CLL) FISH panel includes testing for the following abnormalities using the FISH probes listed:
6q-, D6Z1/MYB probe set
11q-, D11Z1/ATM probe set
+12, D12Z3/MDM2 probe set
13q-, D13S319/LAMP1 probe set
-17/17p-, TP53/D17Z1 probe set
t(11;14)(q13;q32) or *IGH::CCND1* fusion, CCND1/IGH probe set

Appropriate ancillary probes may be performed at consultant discretion to render comprehensive assessment. Any additional probes used will have the results included within the final report and will be performed at an additional charge. In the following situations, additional (reflex) testing may be performed at the laboratory's discretion and may be influenced by available karyotype results or other FISH testing.

In the absence of *IGH::CCND1* fusion, when an extra IGH signal is identified, testing using the IGH/BCL3 probe set to

identify a potential *IGH::BCL3* fusion, t(14;19)(q32;q13) may be performed.

In the absence of *IGH::CCND1* fusion, when an extra or atypical CCND1 signal is identified, testing using the CCND1 break-apart probe set to identify a potential variant translocation involving *CCND1,* t(11;var)(q13;?) may be performed.

Method Name
Fluorescence In Situ Hybridization (FISH)

NY State Available
Yes

Specimen

Specimen Type
Varies

Ordering Guidance
This test is intended for instances when the entire chronic lymphocytic leukemia (CLL) fluorescence in situ hybridization (FISH) panel is needed.

If targeted CLL FISH probes are preferred, order CLLMF / Chronic Lymphocytic Leukemia, Specified FISH, Varies and request specific probes for targeted abnormalities.

For testing paraffin-embedded tissue specimens from patients with CLL or small lymphocytic lymphoma, order SLL / Small Lymphocytic Lymphoma, FISH, Tissue. If a paraffin-embedded tissue sample is submitted for this test, this test will be canceled and SLL will be added and performed as the appropriate test.

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

Necessary Information
1. 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.
2. 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: 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.**

Acceptable
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.**

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

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

Reject Due To

Fresh tissue	Reject

Specimen Stability Information

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

Clinical & Interpretive

Clinical Information
Chronic lymphocytic leukemia (CLL) is one of the most common leukemias in adults. The most frequently seen cytogenetic abnormalities in CLL involve chromosomes 6, 11, 12, 13, and 17. These are detected and quantified using the CLL fluorescence in situ hybridization (FISH) panel.

Use of CpG-oligonucleotide mitogen will identify an abnormal CLL karyotype in at least 80% of cases. This mitogen is

added to cultures when chromosome analysis is ordered and the reason for testing is B-cell lymphoproliferative disorders (CHRBM / Chromosome Analysis, Hematologic Disorders, Bone Marrow and CHRHB / Chromosome Analysis, Hematologic Disorders, Blood).

This FISH test detects an abnormal clone in approximately 70% of patients with indolent disease and in greater than 80% of patients who require treatment. At least 5% of patients referred for CLL FISH testing have translocations involving the *IGH* locus. Fusion of *IGH* with *CCND1* is associated with t(11;14)(q13;q32), and fusion of *IGH* with *BCL3* is associated with t(14;19)(q32;q13.3). Patients with t(11;14) usually have the leukemic phase of mantle cell lymphoma. Patients with t(14;19) may have an atypical form of B-CLL or the leukemic phase of a lymphoma.

The prognostic associations for chromosome abnormalities detected by this FISH assay are, from best to worst: 13q-, normal, +12, 6q-, 11q- and 17p-.

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 a neoplastic disorder.

Cautions

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

Fluorescence in situ hybridization (FISH) is not a substitute for conventional chromosome studies because the latter detects chromosome abnormalities associated with other hematological disorders that would go undetected in a targeted chronic lymphocytic leukemia FISH panel test.

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

Clinical Reference

1. Dewald GW, Brockman SR, Paternoster SF, et al. Chromosome anomalies detected by interphase FISH: correlation with significant biological features of B-cell chronic lymphocytic leukemia. Br J Haematol. 2003;121:287-295
2. Dohner H, Stilgenbauer S, Benner A, et al. Genomic aberrations and survival in chronic lymphocytic leukemia. N Engl J Med. 2000;343(26):1910-1916
3. Van Dyke DL, Shanafelt TD, Call TG, et al. A comprehensive evaluation of the prognostic significance of 13q deletions in patients with B-chronic lymphocytic leukaemia. Br J Haematol. 2010;148:544-550
4. Shanafelt TD. Predicting clinical outcome in CLL: how and why. Hematology Am Soc Hematol Educ Program. 2009;421-429
5. Van Dyke DL, Werner L, Rassenti LZ, et al. The Dohner fluorescence in situ hybridization prognostic classification of chronic lymphocytic leukaemia (CLL): the CLL Research Consortium experience. Br J Haematol. 2016;173(1):105-113
6. Fang H, Reichard KK, Rabe KG, et al. IGH translocations in chronic lymphocytic leukemia: Clinicopathologic features and clinical outcomes. Am J Hematol. 2019;94(3):338-345

7. Huh YO, Schweighofer CD, Ketterling RP, et al. Chronic lymphocytic leukemia with t(14;19)(q32;q13) is characterized by atypical morphologic and immunophenotypic features and distinctive genetic features. Am J Clin Pathol. 2011;135(5):686-696

Performance

Method Description

This test is performed using commercially available and laboratory-developed probes. Deletion of chromosomes 6q, 11q, 13q and 17p, and trisomy of chromosome 12 are detected using enumeration strategy probes. Rearrangements involving CCND1 are detected using a dual-color break-apart (BAP) strategy probe. A dual-color, dual-fusion fluorescence in situ hybridization (D-FISH) strategy probe set is used to detect *IGH::CCND1* rearrangements and for reflex testing to identify *IGH*::*BCL3* rearrangements. For enumeration and BAP strategy probe sets, 100 interphase nuclei are scored; 200 interphase nuclei are scored when D-FISH probes are used. All 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 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

88271x12, 88275x6, 88291-FISH Probe, Analysis, Interpretation; 6 probe sets
88271x2, 88275-FISH Probe, Analysis; each additional probe set (if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
CLLDF	CLL, Diagnostic FISH	101788-8

Result ID	Test Result Name	Result LOINC® Value
610714	Result Summary	50397-9
610715	Interpretation	69965-2
610716	Result Table	93356-4
610717	Result	62356-1
GC088	Reason for Referral	42349-1
GC089	Specimen	31208-2
610718	Source	31208-2
610719	Method	85069-3
610720	Additional Information	48767-8
610721	Disclaimer	62364-5
610722	Released by	18771-6