Overview

Useful For

Detecting a neoplastic clone associated with the common chromosome abnormalities seen in patients with T-cell lymphoblastic leukemia or lymphoma

Reflex Tests

Test ID	Reporting Name	Available Separately	Always Performed
_I300	Interphases, >=100	No	No
_I099	Interphases, 25-99	No	No
_IL25	Interphases,	No	No
_PB03	Probe, +3	No	No
_PB02	Probe, +2	No	No
_PADD	Probe, +1	No	No
_PBCT	Probe, +2	No	No

Testing Algorithm

This test may be ordered in 2 distinct ways allowing different combinations of probes to be utilized based on the clinical question, including the standard (diagnostic) TLBL FISH panel and the individual TLBL FISH probes (per client request).

The specific TLBL FISH panel or probes requested must be noted on the request form or in the reason for referral. If no specific panel or FISH probes are indicated, the standard (diagnostic) panel will be performed.

The standard (diagnostic) panel includes testing for the following abnormalities, using the FISH probes listed:

-1p33 rearrangements, TAL1/STIL(SIL)

-t(5;14)(q35;q32), TLX3(HOX11L2)/BCL11B

-7q34 rearrangements, TRB(TCR beta)

-9p-, CDKN2A(p16)/D9Z1

-t(9;22)(q34;q11.2), ABL1 amplification, ABL1(ABL)/BCR

-t(10;11)(p12;q14), MLLT10(AF10)/PICALM

-11q23 rearrangements, MLL

-14q11.2 rearrangements, TRAD (TCR alpha delta)

-17p-, TP53/D17Z1

When an MLL rearrangement is identified, reflex testing will be performed with 1 or more dual-fusion probe sets (D-

FISH) in an attempt to identify the translocation partner. Probes include:

-t(4;11)(q21;q23), AFF1(AF4)/MLL

-t(6;11)(q27;q23), MLLT4(AF6)/MLL

-t(9;11)(p22;q23), MLLT3(AF9)/MLL

-t(10;11)(p12;q23), MLLT10(AF10)/MLL

-t(11;19)(q23;p13.1), MLL/ELL

-t(11;19)(q23;p13.3), MLL/MLLT1(ENL)

When an TRB(TCR beta) rearrangement is identified, reflex testing will be performed with a dual-fusion probe sets

(D-FISH) in an attempt to identify the translocation partner.

-t(7;10)(q34;q24), TRB(TCR beta)/TLX1(HOX11)

When an TRAD(TCR alpha delta) rearrangement is identified, reflex testing will be performed with a dual-fusion probe sets

(D-FISH) in an attempt to identify the translocation partner.

-t(10;14)(q24;q11.2), TLX1(HOX11)/TRAD(TCR alpha delta)

This test includes a charge for application of the first probe set (2 FISH probes) and professional interpretation of results. Additional charges will be incurred for all reflex probes 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.

Method Name

Fluorescence In Situ Hybridization (FISH)

NY State Available

Yes

Specimen

Specimen Type

Tissue

Shipping Instructions

Advise Express Mail or equivalent if not on courier service.

Necessary Information

A reason for referral and pathology report are required in order for testing to be performed. Send information with specimen. Acceptable pathology reports include working drafts, preliminary pathology or surgical pathology reports.

Specimen Required

Submit only 1 of the following specimens:

Specimen Type: Tissue

Container/Tube: Formalin-fixed, paraffin-embedded tumor tissue block

Specimen Type: Slides

Specimen Volume: 19 Consecutive, unstained, 5 micron-thick sections placed on positively charged slides and 1 hematoxylin and eosin-stained slide

Forms

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

Specimen Minimum Volume

Formalin-fixed paraffin-embedded tissue block or for each probe set ordered, 9 unstained consecutive tissue sections cut at 5 microns and placed on positively charged microscope slides. Include 1 hematoxylin and eosin (H and E) stained slide.

Reject Due To

All specimens will be evaluated at Mayo Clinic Laboratories for test suitability.

Specimen Stability Information

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

Clinical and Interpretive

Clinical Information

T-lymphoblastic lymphoma (T-LBL) is the non-leukemic form of T-acute lymphoblastic leukemia (T-ALL). In the United States, the incidence of ALL is roughly 6,000 new cases per year (as of 2009), or approximately 1 in 50,000. ALL accounts for approximately 70 percent of all childhood leukemia cases (ages 0 to 19 years), making it the most common type of childhood cancer. Approximately 85% of pediatric ALL cases are B-cell lineage (B-ALL) and 15% are T-cell lineage (T-ALL). T-ALL is more common in adolescents than younger children and accounts for 25% of adult ALL. When occurring as a primary lymphoblastic lymphoma, approximately 90% are T-cell lineage versus only 10% B-cell lineage. T-LBL characteristically presents in adolescents and young adults as a mediastinal mass with or without concurrent bone marrow involvement. It is not uncommon that the only sample available with T-LBL involvement is a paraffin-embedded mediastinal or lymph node biopsy specimen.

Specific genetic abnormalities can be identified in the majority of T-ALL/LBL cases, although many of the classic abnormalities are â€œcrypticâ€• by conventional chromosome studies and must be identified by fluorescence in situ hybridization (FISH) studies. Each of the genetic subgroups are important to detect and can be critical prognostic markers. One predictive marker, amplification of the *ABL1* gene region, has been identified in 5% of T-ALL, and these patients may be responsive to targeted tyrosine kinase inhibitors. A combination of cytogenetic and FISH

testing is currently recommended in all pediatric and adult patients to characterize the T-ALL/LBL clone for prognostic genetic subgroups.

Reference Values

An interpretive report will be provided.

Interpretation

A positive result is detected when the percent of cells with an abnormality exceeds the normal cutoff for the probe set.

A positive result is not diagnostic for T-lymphoblastic lymphoma (T-LBL), but may provide relevant prognostic information.

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

Cautions

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

Fixatives other than formalin (eg, Prefer, Bouin) may not be successful for FISH assays. Although FISH testing will not be rejected due to nonformalin fixation, results may be compromised.

Paraffin-embedded tissues that have been decalcified are generally unsuccessful for FISH analysis. The pathologist reviewing the hematoxylin and eosin-stained slide may find it necessary to cancel testing.

Supportive Data

For each probe set, blinded FISH analysis was performed on 25 normal paraffin-embedded, formalin-fixed tissue controls and 32 to 36 paraffin-embedded, formalin-fixed tissue samples from patients diagnosed with T-cell lymphoblastic leukemia or lymphoma. Results from the 25 controls were used to generate the normal cutoff values.

Clinical Reference

1. Graux C, Cools J, Michaux L, et al: Cytogenetics and molecular genetics of T-cell acute lymphoblastic leukemia: from thymocyte to lymphoblast. Leukemia 2006;20:1496-1510

2. Swerdlow SH, Campo E, Stefano PA, et al: The 2016 revision of the World Health Organization classification of lymphoid neoplasms. Blood 2016;127(20):2375-2390

3. van Grotel M, Meijerink JP, Beverloo HB, et al: The outcome of molecular-cytogenetic subgroups in pediatric T-cell acute lymphoblastic leukemia: a retrospective study of patients treated according to DCOG or COALL protocols. Haematologica 2006;91:1212-1221

4. World Health Organization Classification of Tumours of Haematopoietic and Lymphoid Tissues. Edited by SH Swerdlow, E Campo, NL Harris, et al. Lyon, IARC Press, 2017

Performance

Method Description

This test uses FISH enumeration strategy probes to detect deletions of *CDKN2A(p16)* on chromosome 9p and *TP53* on chromosome 17p. Dual-color, break-apart (BAP) probes are used to detect rearrangements of the *TAL1*/*STIL(SIL), TRB(TCR* beta*), MLL,* and *TRAD(TCR* alpha delta*)* locus on 1p33, 7q34, 11q23, and 14q11.2, respectively. Dual-color, dual-fusion strategy (D-FISH) probe sets are used to detect fusions of the

TLX3(HOX11L2)/*BCL11B, ABL1(ABL)*/*BCR,* and *MLLT10(AF10)*/*PICALM* Â locus on (5;14)(q35;q32), (9;22)(q34;q11.2), and (10;11)(p12;q14) respectively. D-FISH probe sets are also used in reflext testing when rearrangements of *MLL*, *TRAD(TCR* alpha delta*)* and *TRB(TCR* beta*)* gene loci are detected. Amplification of the *ABL1* gene is detected using a D-FISH probe strategy. Paraffin-embedded tissues are cut at 5 microns and mounted on positively charged glass slides. The selection of tissue and the identification of target areas on the hematoxylin and eosin- (H and E) stained slide are performed by a pathologist. Using the H and E-stained slide as a reference, target areas are etched with a diamond-tipped etcher on the back of the unstained slide to be assayed. For each probe set, the probes are hybridized to the appropriate target areas and 2 technologists each analyze 50 interphase nuclei (100 total) per probe set with the results expressed as the percent abnormal nuclei.(Unpublished Mayo method)

PDF Report

No

Day(s) and Time(s) Test Performed

Specimens are processed Monday through Sunday.

Results reported Monday through Friday, 8 a.m.-5 p.m.

Analytic Time

7 days

Maximum Laboratory Time

10 days

Specimen Retention Time

Slides and H&E used for analysis are retained by the laboratory in accordance to CAP and NYS requirements. Client provided paraffin blocks and extra unstained slides (if provided) will be returned after testing is complete.

Performing Laboratory Location

Rochester

Fees and 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 Regional Manager. For assistance, contact Customer Service.

Test Classification

This test was developed using an analyte specific reagent. Its performance characteristics were determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the U.S. Food and Drug Administration.

CPT Code Information

88271 x 2, 88291-DNA probe, each (first probe set), Interpretation and report

88271 x 2-DNA probe, each; each additional probe set (if appropriate)

88271-DNA probe, each; coverage for sets containing 3 probes (if appropriate)

88271 x 2-DNA probe, each; coverage for sets containing 4 probes (if appropriate)

88271 x 3-DNA probe, each; coverage for sets containing 5 probes (if appropriate)

88274 w/modifier 52-Interphase in situ hybridization, <25 cells, each probe set (if appropriate)

88274-Interphase in situ hybridization, 25 to 99 cells, each probe set (if appropriate)

88275-Interphase in situ hybridization, 100 to 300 cells, each probe set (if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
TLBLF	T-Lymphoblastic Leuk/Lymph, FISH,Ts	In Process

Result ID	Test Result Name	Result LOINC Value
113467	Result Summary	50397-9
113468	Interpretation	69965-2
113626	Result Table	93356-4
113469	Result	62356-1
GC005	Reason for Referral	42349-1
113470	Specimen	31208-2
113471	Source	31208-2
113472	Tissue ID	80398-1
113473	Method	49549-9
113474	Additional Information	48767-8
113475	Disclaimer	62364-5
113476	Released By	18771-6