MAYO CLINIC LABORATORIES

Test Definition: TALPF

T-Cell Acute Lymphoblastic Leukemia/Lymphoma (ALL), FISH, Pediatric, Varies

Overview

Useful For

Detecting a neoplastic clone associated with the common chromosome abnormalities and classic rearrangements seen in pediatric/young adult patients with T-cell acute lymphoblastic leukemia (T-ALL)

An adjunct to conventional chromosome studies in patients with T-ALL

Evaluating specimens in which standard cytogenetic analysis is unsuccessful

Reflex Tests

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

Testing Algorithm

This test includes a charge for the probe application, analysis, and professional interpretation of results for 9 probe sets (18 individual fluorescence in situ hybridization [FISH] probes). Additional charges will be incurred for all reflex or additional probe sets performed.

The diagnostic pediatric/young adult T-cell acute lymphoblastic leukemia (T-ALL) FISH panel includes testing for the following abnormalities using the FISH probes listed:
+9/9p-, CDKN2A::D9Z1
t(9;22) or ABL1 amplification, ABL1::BCR
11q23 rearrangement, MLL (KMT2A) break-apart
-17/17p-, TP53::D17Z1
t(5;14), TLX3::BCL11B
7q34 rearrangement, TRB break-apart
14q11.2 rearrangement, TRAD break-apart
t(10;11), MLLT10::PICALM
1p33 rearrangement, TAL1/STIL

When an MLL (KMT2A) rearrangement is identified, reflex testing will be performed to identify the translocation partner. Probes include identification of:
t(11;19)(q23;p13.3) MLL::MLLT1
t(6;11)(q27;q23) MLLT4(AFDN)::MLL
t(4;11)(q21;q23) AFF1::MLL
t(9;11)(p22;q23) MLLT3::MLL
t(10;11)(p12;q23) MLLT10::MLL

t(11;19)(q23;p13.1) MLL::ELL

When a TRAD rearrangement is identified, reflex testing will be performed to identify the translocation partner. Probes include identification of:
t(11;14)(p15;q11.2) LMO1::TRAD
t(8;14)(q24.1;q11.2) MYC::TRAD
t(10;14)(q24;q11.2) TLX1(HOX11)::TRAD
t(11;14)(p13;q11.2) LMO2::TRAD

When a TRB rearrangement is identified, reflex testing will be performed to identify the translocation partner. Probes include identification of:
t(7;10)(q34;q24) TRB::TLX1
t(7;11)(q34;p15) TRB::LMO1
t(7;11)(q34;p13) TRB::LMO2
t(6;7)(q23;q34) MYB::TRB

In the absence of BCR::ABL1 fusion or apparent episomal amplification of ABL1, when an extra ABL1 signal is identified, reflex testing will be performed using the ABL1 break-apart probe set to evaluate for the presence or absence of an *ABL1* rearrangement.

For more information See Acute Leukemias of Ambiguous Lineage Testing Algorithm.

Special Instructions

- Acute Leukemias of Ambiguous Lineage Testing Algorithm

Method Name

Fluorescence In Situ Hybridization (FISH)

NY State Available

Yes

Specimen

Specimen Type

Varies

Ordering Guidance

This test is only performed on specimens from patients with T-cell acute lymphoblastic leukemia (T-ALL) who are 30 years of age or younger.
This test is intended for instances when the entire T-ALL fluorescence in situ hybridization (FISH) panel is needed for a **pediatric** patient.

-If this test is ordered on a patient older than 30 years, this test will be canceled and automatically reordered by the laboratory as TALAF/ T-Cell Acute Lymphoblastic Leukemia/Lymphoma, FISH, Adult, Varies.
-If this test is ordered and the laboratory is informed that the patient is on a Children's Oncology Group (COG) protocol, this test will be canceled and automatically reordered by the laboratory as COGTF / T-Cell Acute Lymphoblastic Leukemia/Lymphoma (ALL), Children's Oncology Group Enrollment Testing, FISH, Varies.
-If BALPF / B-Cell Acute Lymphoblastic Leukemia/Lymphoma (ALL), Pediatric, FISH, Varies testing is ordered concurrently with this test, the laboratory may cancel TALPF and automatically reorder as TALMF / T-Cell Acute Lymphoblastic Leukemia/Lymphoma (ALL), Specified FISH, Varies with the following FISH probes: TLX3/BCL11B, break-apart TRB, break-apart TRAD, MLLT10/PICALM, TAL1/STIL. If an abnormality is identified that would result in reflex testing in TALPF, the same reflex testing will be performed in the TALMF. This cancellation is necessary to avoid duplicate testing. Probes for CDKN2A/D9Z1, ABL1/BCR, break-apart MLL, TP53/D17Z1 will still be performed as part of the pediatric B-ALL FISH panel.
If limited T-cell ALL FISH probes are preferred, order TALMF / T-Cell Acute Lymphoblastic Leukemia/Lymphoma (ALL), Specified FISH, Varies.

At follow-up, conventional cytogenetic studies (CHRBM / Chromosome Analysis, Hematologic Disorders, Bone Marrow) and targeted T-ALL FISH probes can be evaluated based on the abnormalities identified in the diagnostic study. Order TALMF / T-Cell Acute Lymphoblastic Leukemia/Lymphoma (ALL), Specified FISH, Varies and request specific probes or abnormalities.

If the patient clinically relapses, a conventional chromosome study is useful to identify cytogenetic changes in the neoplastic clone or the possible emergence of a new therapy-related myeloid clone.

For patients with T-cell lymphoma, order TLPDF / T-Cell Lymphoma, Diagnostic FISH, Varies.

For testing paraffin-embedded tissue samples from patients with T-cell lymphoblastic lymphoma, order TLBLF / T-Cell Lymphoblastic Leukemia/Lymphoma, FISH, Tissue.

Additional Testing Requirements

At diagnosis, conventional cytogenetic studies (CHRBM / Chromosome Analysis, Hematologic Disorders, Bone Marrow) and this fluorescence in situ hybridization (FISH) panel should be performed. If there is limited specimen available, only this FISH test will be performed.

Shipping Instructions

Advise Express Mail or equivalent if not on courier service.

Necessary Information

1. A reason for testing and 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. If this information is not provided, an appropriate indication for testing may be entered by Mayo Clinic Laboratories.
2. If the patient has received an opposite sex bone marrow transplant, note this information on the request.

Specimen Required

Submit only 1 of the following specimens:

Preferred
Specimen Type: Bone marrow
Container/Tube:
Preferred: Yellow top (ACD)
Acceptable: Green top (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 specimen in original tube. **Do not aliquot.**

Acceptable
Specimen Type: Blood
Container/Tube:
Preferred: Yellow top (ACD)
Acceptable: Green top (heparin) or lavender top (EDTA)
Specimen Volume: 6 mL
Collection Instructions: Invert several times to mix blood.
2. Send whole blood specimen 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
Blood: 2 mL
Bone Marrow: 1 mL

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

Specimen Stability Information

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

Clinical & Interpretive

Clinical Information

In the United States, the incidence of acute lymphoblastic leukemia (ALL) is roughly 6000 new cases per year (as of 2019). ALL accounts for approximately 70% of all childhood leukemia cases (ages 0 to 19 years), making it the most common type of childhood cancer.

Approximately 85% of pediatric cases of ALL are of B-cell lineage (B-ALL) and 15% are of 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 (LBL), approximately 90% are T-cell lineage versus only 10% B-cell lineage. T-LBL often present as a mediastinal mass in younger patients with or without concurrent bone marrow involvement.

Specific genetic abnormalities are identified in the majority of cases of T-ALL, although many of the classic abnormalities are "cryptic" 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 clone for the prognostic genetic subgroups. A summary of the characteristic chromosome abnormalities identified in T-ALL are listed in the following table.

Table. Common Chromosome Abnormalities in T-cell Acute Lymphoblastic Leukemia

Cytogenetic change	**Genes involved**
del(1p33)	*TAL1/STIL*
t(5;14)(q35;q32)	*TLX3*/*BCL11B*
t(10;11)(p12;q14)	*MLLT10*/*PICALM*
Episomal amplification	*ABL1*
del(9p)	*CDKN2A*(*p16*)
t(11q23;var)	*MLL*(*KMT2A*)
t(4;11)(q21;q23)	*AFF1*/*MLL*(*KMT2A*)
t(6;11)(q27;q23)	*MLLT4(AFDN)*/*MLL*(*KMT2A*)
t(9;11)(p22;q23)	*MLLT3*/*MLL*(*KMT2A*)
t(10;11)(p12;q23)	*MLLT10*/*MLL*(*KMT2A*)
t(11;19)(q23;p13.1)	*MLL*(*KMT2A*)/*ELL*
t(11;19)(q23;p13.3)	*MLL*(*KMT2A*)/*MLLT1*
t(7q34;var)	*TRB*
t(6;7)(q23;q34)	*MYB*/*TRB*
t(7;10)(q34;q24)	*TRB*/*TLX1*
t(7;11)(q34;p15)	*TRB*/*LMO1*
t(7;11)(q34;p13)	*TRB*/*LMO2*
t(14q11.2;var)	*TRAD*
t(8;14)(q24.1;q11.2)	*MYC*/*TRAD*

t(10;14)(q24;q11.2)	*TLX1/TRAD*
t(11;14)(p15;q11.2)	*LMO1/TRAD*
t(11;14)(p13;q11.2)	*LMO2/TRAD*
del(17p)	*TP53*

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.

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.

Fluorescence in situ hybridization (FISH) is not a substitute for conventional chromosome studies because the latter detects many chromosome abnormalities associated with other hematological disorders that would be missed by this FISH panel test.

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

Supportive Data

Each probe was independently tested and verified on unstimulated peripheral blood and bone marrow specimens. Normal cutoffs were calculated based on the results of 25 normal specimens. Each probe set was evaluated to confirm the probe set detected the abnormality it was designed to detect.

Clinical Reference

1. Swerdlow SH, Campo E, Harris NL, et al, eds: WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues. IARC Press; 2017
2. Gesk S, Martin-Subero JI, Harder L, et al. Molecular cytogenetic detection of chromosomal breakpoints in T-cell receptor gene loci. Leukemia. 2003;17(4):738-745
3. Chin M, Mugishima H, Takamura M, et al: Hemophagocytic syndrome and hepatosplenic (gamma)(delta) T-cell lymphoma with isochromosome 7q and 8 trisomy. J Pediatr Hematol Oncol. 2004;26(6):375-378
4. 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
5. Liu Y, Easton J, Shao Y, et al. The genomic landscape of pediatric and young adult T-lineage acute lymphoblastic leukemia. Nat Genet. 2017;49(8):1211-1218

Performance

Method Description

This test is performed using commercially available and laboratory-developed probes. Deletion of the *CDKN2A* locus on chromosome 9 and *TP53* on chromosome 17 are detected using enumeration strategy probes. Rearrangements involving *TAL1/STIL, TRB, MLL* (*KMT2A*), and *TRAD* are detected using dual-color break-apart (BAP) strategy probes. Dual-color, dual-fusion fluorescence in situ hybridization (D-FISH) strategy probe sets are used to detect t(5;14), t(9;22), t(10;11), and in reflex testing when rearrangements of *MLL, TRB*, or *TRAD* genes are detected. Amplification of the *ABL1* (9q34) is detected using a D-FISH probe strategy. 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

Rochester

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

88271x18, 88275x9, 88291x1- FISH Probe, Analysis, Interpretation; 9 probe sets
88271x2, 88275x1-FISH Probe, Analysis; each additional probe set (if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
TALPF	Pediatric ALL (T-cell), FISH	In Process

Result ID	Test Result Name	Result LOINC® Value
609568	Result Summary	50397-9
609569	Interpretation	69965-2
609570	Result Table	93356-4
609571	Result	62356-1
GC074	Reason for Referral	42349-1
GC075	Specimen	31208-2
609572	Source	31208-2
609573	Method	85069-3
609574	Additional Information	48767-8
609575	Disclaimer	62364-5
609576	Released By	18771-6