Test Definition: TALFP

Pediatric T-Lymphoblastic Leukemia/Lymphoma Panel, FISH, Varies

Overview

Useful For

Detecting, at diagnosis, recurrent common chromosome abnormalities associated with T-cell acute lymphoblastic leukemia/lymphoma (T-ALL) in pediatric/young adult patients using a laboratory-designated probe set algorithm

As an adjunct to conventional chromosome studies in pediatric/young adult patients with T-ALL

Evaluating specimens in which chromosome studies are unsuccessful

This test **should not be used** to screen for residual T-ALL

Testing Algorithm

This test includes a charge for the probe application, analysis, and professional interpretation of results for 7 probe sets (14 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** pediatric/young adult T-cell acute lymphoblastic leukemia/lymphoma FISH panel includes testing for the following abnormalities using the FISH probes listed:
ABL1 amplification or t(9;22)(q34;q11.2), ABL1/BCR probe set
t(11q23;var) or *KMT2A* rearrangement, KMT2A break-apart probe set
1p33 rearrangement or *STIL* deletion, TAL1/STIL probe set
t(5;14)(q35;q32) or *TLX3::BCL11B* fusion, TLX3/BCL11B probe set
t(7q34;var) or *TRB* rearrangement, TRB break-apart probe set
t(14q11.2;var) or *TRA* rearrangement, TRA break-apart probe set
t(10;11)(p12;q14) or *MLLT10::PICALM* fusion, MLLT10/PICALM fusion 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.

When a *KMT2A* rearrangement is identified, testing with 1 or more dual-fusion (D-FISH) probe sets may be performed in an attempt to identify the translocation partner for the following abnormalities:
t(4;11)(q21;q23) or *KMT2A::AFF1* fusion, AFF1/KMT2A probe set
t(6;11)(q27;q23) or *KMT2A::AFDN* ;fusion, AFDN/KMT2A probe set
t(9;11)(p22;q23) or *KMT2A::MLLT3* fusion, MLLT3/KMT2A probe set
t(10;11)(p12;q23) or *KMT2A::MLLT10* fusion, MLLT10/KMT2A probe set

t(11;19)(q23;p13.1) or *KMT2A::MLLT1* fusion, KMT2A/ELL probe set
t(11;19)(q23;p13.3) or *KMT2A::ELL* fusion, KMT2A/MLLT1 probe set

When a *TRA* rearrangement is identified, testing in an attempt to identify the translocation partner may be performed. Probes include identification of t(10;14)(q24;q11.2) *TRA::TLX1* fusion or t(11;14)(p13;q11.2) *TRA::LMO2* fusion.

When a *TRB* rearrangement is identified, testing in an attempt to identify the translocation partner may be performed. Probes include identification of t(7;10)(q34;q24) *TRB::TLX1* fusion or t(7;11)(q34;p13) *TRB::LMO2* fusion.

In the absence of *BCR::ABL1* fusion or apparent episomal amplification of *ABL1*, when an extra or atypical ABL1 signal is identified, testing using the ABL1 break-apart probe set to identify a potential variant translocation involving *ABL1,* t(9;var)(q34;?) may be performed.

For more information see 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/lymphoma (T-ALL/LBL) who are 30 years 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.

This test **should NOT be used** to screen for residual T-ALL/LBL. At follow-up, or if the patient clinically relapses, conventional cytogenetic studies (CHRBM / Chromosome Analysis, Hematologic Disorders, Bone Marrow) is useful to identify cytogenetic changes in the neoplastic clone or the possible emergence of a new therapy-related myeloid clone. Additionally, targeted T-ALL FISH probes can be evaluated based on the abnormalities identified in the diagnostic study.

If targeted T- ALL FISH probes are preferred, order TALMF / T-Cell Acute Lymphoblastic Leukemia/Lymphoma (ALL), Specified FISH, Varies and request specific probes for targeted abnormalities.

If this test is ordered on a patient older than 31 years of age or older, this test will be canceled and automatically

reordered by the laboratory as TALAF/ T-Cell Acute Lymphoblastic Leukemia/Lymphoma (ALL), 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 BALFP / Pediatric B-Lymphoblastic Leukemia/Lymphoma Panel, 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 TRA, MLLT10/PICALM, TAL1/STIL. If an abnormality is identified that would result in reflex testing in this test, the same reflex testing will be performed in the TALMF. This cancellation is necessary to avoid duplicate testing. Probes for ABL1/BCR and break-apart MLL will still be performed as part of the pediatric/young adult B-ALL FISH panel.

For patients with T-cell lymphoma, order TLPFD / T-cell Lymphoma BM/BL panel, Diagnostic, FISH, Varies.

For testing paraffin-embedded tissue samples from patients with T-cell lymphoblastic leukemia/lymphoma (T-LBL), order TLBLF / T-Cell Lymphoblastic Leukemia/Lymphoma, FISH, Tissue. If a paraffin-embedded tissue sample is submitted for this test, testing will be canceled and TLBLF will be added and performed as the appropriate test.

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 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: 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 specimen 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 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
Bone marrow: 1 mL; Whole blood: 2 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 (aged 0 to 19 years), making it the most common 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.

An abnormal karyotype is found in 50% to 70% of T-ALL cases, although many of the classic abnormalities are "cryptic" by conventional chromosome studies and must be identified by fluorescence in situ hybridization studies (FISH) and are associated with various prognoses. 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 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/Lymphoma**

Cytogenetic change	**Genes involved**
del(1p33)	*TAL1/STIL*
t(5;14)(q35;q32)	*TLX3::BCL11B*
t(5q32;var)	*PDGFRB*
t(10;11)(p13;q14)	*PICALM::MLLT10*
Episomal amplification	*ABL1*
t(9p24.1;var)	*JAK2*
t(9q34;var)	*ABL1*
t(11q23;var)	*KMT2A*
t(4;11)(q21;q23)	*KMT2A::AFF1*
t(6;11)(q27;q23)	KMT2A::*AFDN*
t(9;11)(p21.3;q23)	*KMT2A::MLLT3*
t(10;11)(p13;q23)	*KMT2A::MLLT10*
t(11;19)(q23;p13.1)	*KMT2A::ELL*
t(11;19)(q23;p13.3)	*KMT2A::MLLT1*
t(7q34;var)	*TRB*
t(6;7)(q23;q34)	*TRB::MYB*
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)	*TRA*
t(8;14)(q24.21;q11.2)	*TRA::MYC*
t(10;14)(q24;q11.2)	*TLX1*::*TRA*
t(11;14)(p15;q11.2)	*LMO1*::*TRA*
t(11;14)(p13;q11.2)	*LMO2* ::*TRA*
del(17p)	*TP53*
Complex karyotype (> or =4 abnormalities)	

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 existing 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 T-ALL 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 circulating malignant 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. WHO Classification of Tumours Editorial Board, eds. Haematolymphoid tumours. 5th ed. IARC Press; 2024. WHO Classification of Tumours, Volume 11
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. Rearrangements involving *TAL1/STIL, TRB, ABL1, KMT2A*, and *TRA* are detected using a dual-color break-apart (BAP) strategy probe set. 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 *KMT2A, TRB*, or *TRA* genes are detected. Amplification of the *ABL1* gene region 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
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
88271x14, 88275x7, 88291x1- FISH Probe, Analysis, Interpretation; 7 probe sets
88271x2, 88275x1-FISH Probe, Analysis; each additional probe set (if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
TALFP	Pediatric T-ALL/LBL panel, FISH	101663-3

Result ID	Test Result Name	Result LOINC® Value
622421	Result Summary	50397-9
622422	Interpretation	69965-2
622423	Result Table	93356-4
622424	Result	62356-1
GC159	Reason for Referral	42349-1
GC160	Specimen	31208-2
622425	Source	31208-2
622426	Method	85069-3
622427	Additional Information	48767-8
622428	Disclaimer	62364-5

622429	Released By	18771-6