Overview

Useful For

Detecting a neoplastic clone associated with the common chromosome abnormalities seen in patients with T-cell acute lymphoblastic leukemia (T-ALL)

Identifying and tracking known chromosome abnormalities in patients with T-ALL and tracking response to therapy

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

Reflex Tests

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

Testing Algorithm

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.

We recommend the following testing algorithm for patients with T-cell acute lymphoblastic leukemia (T-ALL):

-At diagnosis, conventional cytogenetic studies (CHRBM / Chromosome Analysis, Hematologic Disorders, Bone Marrow) and a complete T-ALL FISH panel should be performed.

-At follow-up, conventional cytogenetic studies (CHRBM / Chromosome Analysis, Hematologic Disorders, Bone Marrow) and targeted T-ALL FISH probes based on the abnormalities identified in the diagnostic study can be evaluated.

-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.

Panel includes testing for the following abnormalities using the probes listed:

1p33 rearrangement, *TAL1/STIL*

t(5;14) *TLX3/BCL11B*

7q34 rearrangement, *TRB*

9p-,*CDKN2A*/*D9Z1*

t(9;22) or *ABL1* amplification, *BCR*/*ABL1*

t(10;11), *MLLT10*/*PICALM*

11q23 rearrangement, *MLL* (*KMT2A*)

14q11.2 rearrangement, *TRAD*

17p-, *TP53*/*D17Z1*

When an *MLL* (*KMT2A*) rearrangement is identified, reflex testing will be performed to identify the translocation partner. Probes include identification of t(4;11)(q21;q23) *AFF1*/*MLL,* t(6;11)(q27;q23) *MLLT4*/*MLL,* t(9;11)(p22;q23) *MLLT3*/*MLL,* t(10;11)(p13;q23) *MLLT10*/*MLL,* t(11;19)(q23;p13.1) *MLL*/*ELL* or t(11;19)(q23;p13.3) *MLL*/*MLLT1.*

When a *TRAD* rearrangement is identified, reflex testing will be performed to identify the translocation partner. Probes include identification of 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 or 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*/*HOX11,* t(7;11)(q34;p15) *TRB*/*LMO1*, t(7;11)(q34;p13) *TRB*/*LMO2*, or t(6;7)(q27;q34) *TRB*/*MYB.*

In the absence of *BCR/ABL1* fusion, when an extra signal for *ABL1* 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.

If this test is ordered and the laboratory is informed that the patient is on a COG protocol, this test will be canceled and automatically reordered by the laboratory as COGTF / T-Cell Acute Lymphoblastic Leukemia (T-ALL), Childrenâ€™s Oncology Group Enrollment Testing, FISH, Varies.

Method Name

Fluorescence In Situ Hybridization (FISH)

NY State Available

Yes

Specimen

Specimen Type

Varies

Advisory Information

For diagnosis or follow-up testing for T-cell acute lymphoblastic leukemia, order CHRBM / Chromosome Analysis, Hematologic Disorders, Bone Marrow) and a complete T-ALL FISH panel should be performed.

For patients with T-cell lymphoma, order TLPF / T-Cell Lymphoma, FISH, Blood or Bone Marrow.

Shipping Instructions

Advise Express Mail or equivalent if not on courier service.

Necessary Information

1. Provide a reason for referral 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.

2. A pathology and/or flow cytometry report may be requested by the Genomics Laboratory to optimize testing and aid in interpretation of results.

Specimen Required

Submit only 1 of the following specimens:

Specimen Type: Whole blood

Container/Tube: Green top (sodium heparin)

Specimen Volume: 7-10 mL

Collection Instructions:

1. Invert several times to mix blood.

2. Other anticoagulants are not recommended and are harmful to the viability of the cells.

Specimen Type: Bone marrow

Container/Tube: Green top (sodium heparin)

Specimen Volume: 1-2 mL

Collection Instructions:

1. Invert several times to mix bone marrow.

2. Other anticoagulants are not recommended and are harmful to the viability of the cells.

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 and Interpretive

Clinical Information

In the United States, the incidence of acute lymphoblastic leukemia (ALL) is roughly 6,000 new cases per year (as of 2009), or approximately 1 in 50,000. 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 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 (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 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.

Common Chromosome Abnormalities in

T-cell Acute Lymphoblastic Leukemia

Cytogenetic change	Genes involved
del(1p33)	*TAL1/STIL*
t(5;14)(q35;q32)	*TLX3*(*HOX11L2*)/*BCL11B*
t(10;11)(p13;q14)	*MLLT10*(*AF10*)/*PICALM*
Episomal amplification	*ABL1*
del(9p)	*CDKN2A*(*p16*)
t(11q23;var)	*MLL*(*KMT2A*)
t(4;11)(q21;q23)	*AFF1*(*AF4*)/*MLL*(*KMT2A*)
t(6;11)(q27;q23)	*MLLT4*(*AF6*)/*MLL*(*KMT2A*)
t(9;11)(p22;q23)	*MLLT3*(*AF9*)/*MLL*(*KMT2A*)
t(10;11)(p13;q23)	*MLLT10*(*AF10*)/*MLL*(*KMT2A*)
t(11;19)(q23;p13.1)	*MLL*(*KMT2A*)/*ELL*
t(11;19)(q23;p13.3)	*MLL*(*KMT2A*)/*MLLT1*(*ENL*)
t(7q34;var)	*TRB*

t(6;7)(q23;q34)	*MYB*/*TRB*
t(7;10)(q34;q24)	*TRB*/*TLX1*(*HOX11*)
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*(*HOX11*)/*TRAD*
t(11;14)(p15;q11.2)	*LMO1*/*TRAD*
t(11;14)(p13;q11.2)	*LMO2*/*TRAD*
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.

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

Cautions

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

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 hematopathology).

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. For each probe set a series of chromosomally abnormal specimens was evaluated to confirm each probe set detected the abnormality it was designed to detect.

Clinical Reference

1. World Health Organization Classification of Tumours. Pathology and Genetics of Tumours of Haematopoietic and Lymphoid Tissues. Edited by ES Jaffe, NL Harris, H Stein, JW Vardiman. Lyon, IARC Press, 2001

2. Gesk S, Martin-Subero JI, Harder L, et al: Molecular cytogenetic detection of chromosomal breakpoints in T-cell receptor gene loci. Leukemia 2003;17:738-745

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. Cayuela JM, Madani A, Sanhes L, et al: Multiple tumor-suppressor gene 1 inactivation is the most frequent genetic alteration in T-cell acute lymphoblastic leukemia. Blood 1996;87:2180-2186

6. Hayette S, Tigaud I, Maguer-Satta V, et al: Recurrent involvement of the *MLL* gene in adult T-lineage acute lymphoblastic leukemia. Blood 2002;99:4647-4649

7. Graux C, Cools J, Melotte C, et al: Fusion of *NUP214* to *ABL1* on amplified episomes in T-cell acute lymphoblastic leukemia. Nat Genet 2004;36:1084-1089

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 (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, 200 interphase nuclei are scored; 500 interphase nuclei are scored when D-FISH probes are used. Two technologists analyze each probe set and all results are 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

4 weeks

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
TALLF	ALL (T-cell), FISH	In Process

Result ID	Test Result Name	Result LOINC Value
51924	Result Summary	50397-9
51926	Interpretation	69965-2
51925	Result Table	93356-4
54551	Result	62356-1
CG692	Reason for Referral	42349-1
CG693	Specimen	31208-2
51927	Source	31208-2
51928	Method	49549-9
55117	Additional Information	48767-8
53863	Disclaimer	62364-5
51929	Released By	18771-6