Overview

Useful For
Evaluating chronic lymphocytic leukemia patients at diagnosis or during disease course for the presence of TP53 gene variants indicating high risk of disease progression and adverse outcomes.

This test is not intended for the evaluation of patients suspected of having an inherited or germline TP53 cancer syndrome (eg, Li Fraumeni syndrome).

Highlights
This test is complementary to fluorescence in situ hybridization (FISH) analysis for the 17p- abnormality but more appropriately identifies the presence of variant alteration and gene inactivation in tumor cells.

Reflex Tests

<table>
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<tr>
<th>Test ID</th>
<th>Reporting Name</th>
<th>Available Separately</th>
<th>Always Performed</th>
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<tbody>
<tr>
<td>CSP53</td>
<td>TP53 Pre-Analysis Cell Sorting, V</td>
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Testing Algorithm
Flow cytometry will be performed on peripheral blood samples to verify diagnosis of chronic lymphocytic leukemia (CLL) and to selectively enrich for B-cells in samples with a clonal population.

See TP53 Sequencing Testing Algorithm in Special Instructions.

Special Instructions
- TP53 Mutation Testing Algorithm
- Molecular Hematopathology Patient Information

Method Name
Polymerase Chain Reaction (PCR) and Sanger Sequencing

NY State Available
Yes

Specimen

Specimen Type
Varies

Advisory Information
For the evaluation of patients suspected of having an inherited or germline TP53 cancer syndrome (eg, Li Fraumeni syndrome), order TP53Z / TP53 Gene, Li Fraumeni Syndrome, Full Gene Analysis, Varies.

Shipping Instructions
Blood and bone marrow specimens must arrive within 10 days of collection.
Necessary Information
The following information is required:

1. Pertinent clinical history
2. Clinical or morphologic suspicion
3. Date of collection
4. Specimen source

Specimen Required
Submit only 1 of the following specimens:

Specimen Type: Blood (preferred)
Container/Tube: Lavender top (EDTA) or yellow top (ACD solution B)
Specimen Volume: 3 mL
Collection Instructions:
1. Invert several times to mix blood.
2. Send specimen in original tube.
3. Label specimen as blood.

Specimen Stability Information: Ambient/Refrigerate <10 days

Specimen Type: Bone marrow
Container/Tube: Lavender top (EDTA), yellow top (ACD solution B), or green top (heparin)
Specimen Volume: 3 mL
Collection Instructions:
1. Invert several times to mix bone marrow.
2. Send specimen in original tube.
3. Label specimen as bone marrow.

Specimen Stability Information: Ambient/Refrigerate <10 days

Specimen Type: Tissue
Container/Tube: Plastic container
Specimen Volume: 100 mg
Test Definition: P53CA
TP53 gene somatic mutation analysis

Collection Instructions: Stabilize fresh tissue in tissue culture medium or freeze immediately after collection.

Specimen Stability Information: Refrigerate 24 hours/ Frozen

Forms
1. Molecular Hematopathology Patient Information: B-Cell Chronic Lymphocytic Leukemia (CLL) for IGVH and/or TP53 Somatic Mutation Testing in Special Instructions

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

Specimen Minimum Volume
Blood, bone marrow: 1 mL

Reject Due To

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<tbody>
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<tr>
<td>Extracted DNA</td>
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Specimen Stability Information

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Clinical and Interpretive

Clinical Information
Patients with chronic lymphocytic leukemia (CLL) have variable disease course influenced by a series of tumor biologic factors. The presence of chromosomal 17p- or a TP53 gene variant confers a very poor prognosis to a subset of CLL patients, both at time of initial diagnosis, as well as at disease progression, or in the setting of therapeutic resistance. TP53 gene variant status in CLL has emerged as the single most predictive tumor genetic abnormality associated with adverse outcome and poor response to standard immunochemotherapy; however, patients can be managed with alternative therapeutic options.

Although the prognostic relevance of an acquired TP53 gene variant is best studied for CLL, similar findings are also reported for other hematologic malignancies including low-grade B-cell lymphoma, diffuse large B-cell lymphoma, and some types of myelodysplastic syndromes (MDS) and acute myeloid leukemia (AML). Therefore, while this test has been developed to be primarily focused on high-risk CLL patients, TP53 gene sequencing analysis can also be performed in additional neoplasms, as clinically indicated.

Reference Values
Genetic variants present or absent as compared to a reference sequence of the normal TP53 gene

Interpretation
Results are reported in standard nomenclature according to the most recent Human Genome Variation Society (HGVS) recommendations and an interpretive comment regarding the nature of the sequence variant (eg, known deleterious, suspected deleterious, synonymous change) will be included to complete the clinical report.
Cautions

This test will not detect all possible acquired variants in the TP53 gene because it is restricted to analyzing exons 4 to 9. However, this region encompasses more than 90% of described pathologic variants and covers the coding exons of the critical DNA binding regions.

The analytical sensitivity of the assay can be affected by the absolute B-cell number in the peripheral blood or tissue sample, as well as the often subclonal nature of this tumor genetic abnormality. The assay attempts to compensate in part for this by performing an initial screening flow cytometry to assess B-cell quantity and by performing the cell enrichment step (for the peripheral blood specimens only) to isolate relatively pure CD19+ B-cells for analysis. Nevertheless, the nature of the Sanger sequencing method is such that typical reproducible analytic sensitivity will be in the order of 25% variant allele burden.

Because optimal cell enrichment is dependent on the absolute B-cell quantity, samples with a very low WBC or initial percentage of B cells (determined from flow cytometry or WBC automated cell count) will likely result in poor assay performance and inability to detect possible TP53 gene variants in the tumor population.

Clinical Reference


Performance

Method Description

Peripheral blood specimens from chronic lymphocytic leukemia (CLL) patients only will be analyzed by a screening flow cytometry method to determine B-cell content and confirm the presence of a clonal B-cell population. Blood samples (but not bone marrows) from patients with CLL are enriched for B-lymphocytes by cell sorting and DNA is extracted from the B-cell fraction. For other sample types (bone marrow, fresh or frozen tissues) DNA is extracted directly without prior enrichment. Polymerase chain reaction (PCR) and Sanger sequencing of TP53 exons 4 to 9 is performed. Sequence analysis is performed using Mutation Surveyor and Alamut software. The presence of a detected variant is then assessed using curated public databases of known TP53 gene mutations. (The TP53 Web
Test Definition: P53CA
TP53 gene somatic mutation analysis


PDF Report
No

Day(s) and Time(s) Test Performed
Monday through Friday

Analytic Time
7 days

Maximum Laboratory Time
14 days

Specimen Retention Time
DNA 3 months

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 and its performance characteristics 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
81352-TP53 (tumor protein 53) (eg, tumor samples), full gene sequence or targeted sequence analysis of >5 exons

LOINC® Information

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