Test Definition: TP53

TP53 Mutation Analysis, Next-Generation Sequencing, Tumor

Overview

Useful For

Assisting in the clinical management of patients with cancer

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

Genetics Test Information

This test uses targeted next-generation sequencing to evaluate for somatic mutations within the *TP53* gene. See Targeted Genes and Methodology Details for TP53 Mutation Analysis for details regarding the targeted gene regions evaluated by this test.

This test is performed to evaluate for somatic mutations within solid tumor samples. It **does not assess** for germline alterations within the TP53 gene.

Additional Tests

Test Id	Reporting Name	Available Separately	Always Performed
SLIRV	Slide Review in MG	No, (Bill Only)	Yes

Testing Algorithm

When this test is ordered, slide review will always be performed at an additional charge.

Special Instructions

- Tissue Requirements for Solid Tumor Next-Generation Sequencing
- Targeted Genes and Methodology Details for TP53 Mutation Analysis

Method Name

Sequence Capture and Targeted Next-Generation Sequencing (NGS)

NY State Available

Yes

Specimen

Specimen Type

Varies

Ordering Guidance

Multiple oncology (cancer) gene panels are available. For more information see Hematology, Oncology, and Hereditary Test Selection Guide.

Necessary Information

A pathology report (final or preliminary), at minimum containing the following information, **must accompany specimen for testing to be performed**:

1. Patient name
2. Block number-must be on all blocks, slides, and paperwork (can be handwritten on the paperwork)
3. Tissue collection date
4. Source of the tissue

Specimen Required

This assay requires at least 20% tumor nuclei.

-Preferred amount of tumor area with sufficient percent tumor nuclei: tissue 216 mm(2)
-Minimum amount of tumor area: tissue 36 mm(2)
-These amounts are cumulative over up to 10 unstained slides and must have adequate percent tumor nuclei.
-Tissue fixation: 10% neutral buffered formalin, not decalcified
-For specimen preparation guidance, see Tissue Requirement for Solid Tumor Next-Generation Sequencing. In this document, the sizes are given as 4 mm x 4 mm x 10 slides as preferred: approximate/equivalent to 144 mm(2) and the minimum as 3 mm x 1 mm x 10 slides: approximate/equivalent to 36 mm(2).

Preferred:
Specimen Type: Tissue block
Collection Instructions: Submit a formalin-fixed, paraffin-embedded tissue block with acceptable amount of tumor tissue.

Acceptable:
Specimen Type: Tissue slides
Slides: 1 Stained and 10 unstained
Collection Instructions: Submit 1 slide stained with hematoxylin and eosin and 10 unstained, nonbaked slides with 5-micron thick sections of the tumor tissue.
Note: The total amount of required tumor nuclei can be obtained by scraping up to 10 slides from the same block.
Additional Information: Unused unstained slides will not be returned.

Specimen Type: Cytology slides (direct smears or ThinPrep)
Slides: 1 to 3 Slides
Collection Instructions: Submit 1 to 3 slides stained and coverslipped with a preferred total of 5000 nucleated cells, or a minimum of at least 3000 nucleated cells.
Note: Glass coverslips are preferred; plastic coverslips are acceptable but will result in longer turnaround times.
Additional Information: Cytology slides will not be returned.

Forms

If not ordering electronically, complete, print, and send an Oncology Test Request (T729) with the specimen.

Specimen Minimum Volume

See Specimen Required

Reject Due To

Specimens that have been decalcified (all methods) Specimens that have not been formalin-fixed, paraffin-embedded, except for cytology slides Extracted nucleic acid (DNA/RNA)	Reject

Specimen Stability Information

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

Clinical & Interpretive

Clinical Information

The *TP53* gene is a tumor suppressor gene that regulates expression of genes involved in cell cycle arrest, apoptosis, DNA repair, and changes in metabolism. Somatic mutations in the *TP53* gene are the most common genetic alteration seen in human cancers, with over 50% of adult human tumors bearing inactivating mutations, insertions, and deletions in the *TP53* gene. Somatic mutations in the *TP53* gene usually correlate with poor outcome and early recurrence in cancer. In central nervous system (CNS) tumors, *TP53* mutations are a diagnostic molecular biomarker for medulloblastoma, SHH-activated tumors, and a supporting molecular biomarker for IDH (isocitrate dehydrogenase)-mutant astrocytoma and choroid plexus carcinoma.

The results of this test can be useful for predicting prognosis for breast cancer, cervical cancer, melanoma, and other cancers, and for diagnosis/classification of CNS tumors.

Reference Values

An interpretive report will be provided.

Interpretation

The interpretation of molecular biomarker analysis includes an overview of the results and the associated diagnostic, prognostic, and therapeutic implications.

Cautions

This test cannot differentiate between somatic and germline alterations. Additional testing may be necessary to clarify the significance of results if there is a potential hereditary risk.

DNA variants of uncertain significance may be identified.

A negative result does not rule out the presence of a variant that may be present but below the limits of detection of this assay. The analytical sensitivity of this assay for sequence reportable alterations is 5% mutant allele frequency with a minimum coverage of 500X in a sample with 20% or more tumor content.

Point mutations and small insertion/deletion mutations will be detected in the *TP53* gene only. This test may detect single exon deletions but does not detect multiexon deletions, duplications, or genomic copy number variants.

Variant allele frequency (VAF) is the percentage of sequencing reads supporting a specific variant divided by the total sequencing reads at that position. In somatic testing, VAF should be interpreted in the context of several factors including, but not limited to, tumor purity/heterogeneity/copy number status (ploidy, gains/losses, loss of heterozygosity) and sequencing artifact/misalignment.(1,2)

Rare polymorphisms may be present that could lead to false-negative or false-positive results.

The presence or absence of a variant may not be predictive of response to therapy in all patients.
Test results should be interpreted in the context of clinical, tumor sampling, histopathological, and other laboratory data. If results obtained do not match other clinical or laboratory findings, contact the laboratory for discussion. Misinterpretation of results may occur if the information provided is inaccurate and/or incomplete.

Reliable results are dependent on adequate specimen collection and processing. This test has been validated on cytology slides and formalin-fixed, paraffin-embedded tissues; other types of fixatives are discouraged. Improper treatment of tissues, such as decalcification, may cause polymerase chain reaction failure.

Supportive Data

Performance Characteristics
The limit of detection for calling a somatic variant (single nucleotide variants [SNV] and deletions-insertions [delins, formerly indels]) is 5% variant allele frequency and having at least 500x deduplicated coverage.

Verification studies demonstrated concordance between this test and the reference method for detection of SNV and delins is 99.7% (699/701) and 96.6% (226/237) of variants, respectively. Concordance for the detection of delins was 98.9% (186/188) in variants 1-10 base pairs (bp) in size, 95.8% (23/24) in variants 11-50 bp in size, and 88.9% (8/9) in variants 51-200 bp in size.

Clinical Reference

1. Strom SP. Current practices and guidelines for clinical next-generation sequencing oncology testing. Cancer Biol Med. 2016;13(1):3-11. doi:10.28092/j.issn.2095-3941.2016.0004

2. Spurr L, Li M, Alomran N, et al. Systematic pan-cancer analysis of somatic allele frequency. Sci Rep. 2018;8(1):7735. Published 2018 May 16. doi:10.1038/s41598-018-25462-0
3. Robels AI, Jen J, Harris CC. Clinical outcomes of TP53 mutations in cancers. Cold Spring Harb Perspect Med. 2016;6(9):a026294. doi:10.1101/cshperspect.a026294
4. Olivier M, Hollstein M, Hainaut P. TP53 mutations in human cancers: origins, consequences, and clinical use. Cold Spring Harb Perspect Biol. 2010;2(1): a001008
5. WHO Classification of Tumours Editorial Board: Central nervous system tumours. 5th ed. World Health Organization; 2021. WHO Classification of Tumours. Vol 6.

Performance

Method Description

Next-generation sequencing is performed to evaluate the presence of a mutation in all coding regions of the *TP53* gene. See Targeted Genes and Methodology Details for TP53 Mutation Analysis for details regarding the targeted gene regions evaluated by this test.(Unpublished Mayo method)

A pathology review and macro dissection to enrich for tumor cells are performed prior to slide scraping.

PDF Report

No

Day(s) Performed

Monday through Friday

Report Available

12 to 20 days

Specimen Retention Time

FFPE tissue block: Unused portions of blocks will be returned within 10-14 days after testing is complete; FFPE tissue/cytology slides: Unused slides are stored indefinitely; Digital images are obtained and stored for all slides used in testing.

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

88381-Microdissection, manual
81351

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
TP53	TP53 Mutation Analysis, Tumor	103680-5

Result ID	Test Result Name	Result LOINC® Value
617897	Result	82939-0
617898	Interpretation	69047-9
617899	Additional Information	48767-8
617900	Specimen	31208-2
617901	Tissue ID	80398-1
617902	Method	85069-3
617903	Disclaimer	62364-5
617904	Released By	18771-6