Test Definition: TERT

TERT Promoter Analysis, Tumor

Overview

Useful For

Assisting in central nervous system tumor classification

This test is **not useful for** hematological malignancies.

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

Method Name

Polymerase Chain Reaction (PCR)-Based Next-Generation Sequencing

NY State Available

Yes

Specimen

Specimen Type

Varies

Necessary Information

Pathology report (final or preliminary) at minimum containing the following information must accompany specimen in order 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: tissue144 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 Special Instructions. In this document, the sizes are given as 4mm x 4mm x 10 slides as preferred: approximate/equivalent to 144 mm(2) and the minimum as 3mm x 1mm x 10 slides: approximate/equivalent to 36mm(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 slide

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.

Specimen Type: Cytology slide (direct smears or ThinPrep)

Slides: 1 to 3 slides

Collection Instructions: Submit 1 to 3 slides stained and cover slipped 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

Other	Specimens that have been decalcified (all methods) Specimens that have not been formalin-fixed, paraffin-embedded

Specimen Stability Information

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

Clinical and Interpretive

Clinical Information

TERT gene encodes the catalytic subunit of telomerase, an enzyme complex that regulates telomere length. *TERT* promoter mutations in 2 hotspots (C228T and C250T) have been shown to increase telomerase activity and contribute to tumorigenesis by allowing cancer cells to overcome cellular senescence. Among central nervous system tumors, *TERT* promoter mutations have primarily been identified in adults, with highest frequencies in oligodendroglioma, primary glioblastoma, solitary fibrous tumor, and medulloblastoma. Although less frequent, *TERT* promoter mutations have also been observed in lower-grade infiltrating (diffuse and anaplastic) astrocytomas and ependymoma, and are rare or absent in other central nervous system tumor types. The presence of *TERT* promoter mutations have been associated with a less favorable prognosis in lower-grade (grade II/III) diffuse gliomas that lack IDH1/2 mutations and have intact 1p/19q ("IDH-wildtype astrocytomas"), and with a more favorable prognosis in prognosis in grade II/III IDH1/2-mutant and 1p/19q-codeleted diffuse gliomas ("IDH-mutant and 1p/19q codeleted oligodendrogliomas"). Assessment of *TERT* promoter mutation status in central nervous system tumors may assist in tumor classification and provide prognostically relevant information for subgroups of patients with lower-grade diffuse gliomas.

TERT gene mutations are also observed in a variety of non-central nervous system (CNS) tumor types. In hepatocellular neoplasms *TERT* promoter mutations occur frequently in hepatocellular carcinomas and are believed to be an early step in hepatocarcinogenesis. However, *TERT* promoter mutations are not specific to hepatocellular carcinoma and have been reported as a key alteration in the rare progression of hepatocellular adenomas to hepatocellular carcinomas. As such, identification of a *TERT* promoter mutation suggests a hepatocellular neoplasm with an increased risk for aggressive behavior.

Reference Values

An interpretative report will be provided.

Interpretation

An interpretive report will be provided.

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 (wild-type) result does not rule out the presence of a mutation that may be present but below the limits of detection of this assay.

Point mutations and small insertion/deletion mutations will be detected with in the promoter region of the *TERT* gene

only.

This test does not detect structural variants, genomic copy number variants, or large single or multiexon deletions or duplications in the *TERT* gene.

Rare polymorphisms may be present that could lead to false-negative or false-positive results. Test results should be interpreted in the context of clinical findings, tumor sampling, and other laboratory data. If results obtained do not match other clinical or laboratory findings, contact the laboratory for updated interpretation. Misinterpretation of results may occur if the information provided is inaccurate 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 PCR failure.

Supportive Data

We have developed a next-generation sequencing assay to detect somatic mutations that can be used to assist in the classification and prognostication of central nervous system tumors.

This assay has been shown to be very reproducible, having a 100% concordance for intra- and interassay reproducibility experiments. All somatic mutations that had been previously identified by various other molecular methods were detected by this assay during accuracy studies. No pathogenic variants were detected in known mutation negative samples.

Clinical Reference

1. Killela PJ, Reitman ZJ, Jiao Y, et al: TERT promoter mutations occur frequently in gliomas and a subset of tumors derived from cells with low rates of self-renewal. Proc Natl Acad Sci USA. 2013;110(15):6021-6026

2. Brennan CW, Verhaak RG, McKenna A, et al: The somatic genomic landscape of glioblastoma. Cell. 2013;155(2):462-477

3. Koelsche C, Sahm F, Capper D, et al: Distribution of TERT promoter mutations in pediatric and adult tumors of the nervous system. Acta Neuropathol. 2013 Dec;126(6):907-915

4. Eckel-Passow JE, Lachance DH, Molinaro AM, et al: Glioma Groups Based on 1p/19q, IDH, and TERT Promoter Mutations in Tumors. N Engl J Med. 2015;372(26):2499-2508

5. Cancer Genome Atlas Research Network, Brat DJ, Verhaak RG, et al: Comprehensive, Integrative Genomic Analysis of Diffuse Lower-Grade Gliomas. N Engl J Med. 2015;372(26):2481-2498

6. Bell RJ, Rube HT, Xavier-Magalhaes A, et al: Understanding TERT Promoter Mutations: A Common Path to Immortality. Mol Cancer Res. 2016;14(4):315-323

7. Horn S, Figl A, Rachakonda PS, et al: TERT promoter mutations in familial and sporadic melanoma. Science. 2013;339(6122):959-961

8. Huang FW, Hodis E, Xu MJ, et al: Highly recurrent TERT promoter mutations in human melanoma. Science. 2013;339(6122):957-959

9. Huang DS, Wang Z, He XJ, et al: Recurrent TERT promoter mutations identified in a large-scale study of multiple tumour types are associated with increased TERT expression and telomerase activation. Eur J Cancer. 2015 May;51(8):969-976

10. Pekmezci M, Rice T, Molinaro AM, et al: Adult infiltrating gliomas with WHO 2016 integrated diagnosis: additional prognostic roles of ATRX and TERT. Acta Neuropathol 2017

11. Nault JC, Zucman-Rossi J: TERT promoter mutations in primary liver tumors. Clin Res Hepatol Gastroenterol. 2016 Feb;40(1):9-14Epub 2015 Aug 31

12. Schulze K, Imbeaud S, LetouzÃ© E, et al: Exome sequencing of hepatocellular carcinomas identifies new mutational signatures and potential therapeutic targets. Nat Genet. 2015 May;47(5):505-511

Performance

Method Description

Targeted next-generation sequencing is performed to test for the presence of a mutation in the promoter region of the *TERT* gene.(Unpublished Mayo method)

Gene	GenBank Accession Number	Nucleotide Start	Nucleotide End	Chromosome
TERT promoter	NM_198253	1295170	1295296	Chromosome 5

PDF Report

No

Day(s) Performed

Monday through Friday

Report Available

12 to 20 days

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 US Food and Drug Administration.

CPT Code Information

81345

88381

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
TERT	TERT Promoter Analysis, Tumor	95778-7

Result ID	Test Result Name	Result LOINC Value
92389	Result Summary	50397-9
92390	Result	82939-0
92391	Interpretation	69047-9
92392	Additional Information	48767-8
92393	Specimen	31208-2
92394	Source	31208-2
92395	Tissue ID	80398-1
92396	Released By	18771-6