MAYO CLINIC LABORATORIES

Test Definition: TERTD

TERT Promoter Mutation Analysis, Droplet Digital PCR, Tumor

Overview

Useful For

Identifying specific mutations within the *TERT* promoter that assist in tumor diagnosis/classification

Genetics Test Information

This test uses droplet digital PCR (ddPCR) to evaluate for the presence of the c.-124C>T (also known as C228T) and c.-146C>T (also known as C250T) somatic mutations in the promoter region of the *TERT* gene. *TERT* promoter analysis ddPCR is a highly sensitive testing platform that can detect the c.-124C>T (C228T) and c.-146C>T (C250T) hotspot mutations at low levels, which may be observed in specimens with low number or proportion (%) of tumor cells/cells of interest.

This test cannot differentiate between somatic and germline variant origin and is not intended to assess for germline risk.

Additional Tests

Test Id	Reporting Name	Available Separately	Always Performed
SLIRV	Slide Review in MG	No	Yes

Testing Algorithm

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

Method Name

Droplet Digital Polymerase Chain Reaction (ddPCR)

NY State Available

Yes

Specimen

Specimen Type

Varies

Ordering Guidance

For the preferred test to assess for somatic hotspot mutations in the *TERT*, *IDH1,* and *IDH2* genes, order IDTRT / *IDH1*, *IDH2* and *TERT* Mutation Analysis, Next-Generation Sequencing, Tumor.

If this test is ordered with IDHT / *IDH1* and *IDH2* Mutations Analyses, Next-Generation Sequencing, Tumor, this test will be canceled and ordered as IDTRT.

Necessary Information

1. A pathology report (final or preliminary) is required and must accompany specimen for testing to be performed.

2. The following information must be included in the report provided.

-Patient name

-Block number-**must be on all blocks, slides and paperwork** (can be handwritten on the paperwork)

-Date of tissue collection

-Source of the tissue

Specimen Required

This assay requires at least 5% nuclei of tumor cells/cells of interest.

-Preferred amount of tumor area with sufficient percent tumor nuclei: tissue144 mm(2)

-These amounts are cumulative over up to 10 unstained slides and must have adequate percent nuclei of tumor cells/cells of interest.

-Tissue fixation: 10% neutral buffered formalin, not decalcified

-Cytology fixatives: Cytology smears fixed in alcohol and thin preps fixed with CytoLyt.

Preferred:

Specimen Type: Tissue block

Collection Instructions: Submit a formalin-fixed, paraffin-embedded tissue block with acceptable percent nuclei of tumor cells/cells of interest.

Acceptable:

Specimen Type: Tissue slides

Slides: 1 Hematoxylin and eosin stained and 10 unstained

Collection Instructions: Submit 1 slide stained with hematoxylin and eosin and 10 unstained, nonbaked slides with 5-micron thick sections.

Note: The total amount of required cell 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 coverslipped with a preferred total of 3000 nucleated cells or a minimum of at least 350 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.

Specimen Minimum Volume

See Specimen Required

Reject Due To

Specimens that have been decalcified (all methods)	Reject

Specimens that have not been formalin-fixed, paraffin-embedded excluding cytology slides Extracted nucleic acid (DNA/RNA)	

Specimen Stability Information

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

Clinical & Interpretive

Clinical Information

The *TERT* gene encodes the catalytic subunit of telomerase, an enzyme complex that regulates telomere length. Mutations in the *TERT* promoter, primarily involving mutational hotspot positions c.-124 (also known as C228) and c.-146 (also known as C250), increase telomerase activity allowing tumor cells to overcome cellular senescence. In central nervous system (CNS) tumors, *TERT* promoter mutations are a diagnostic and grading molecular biomarker in diffuse gliomas and meningioma. *TERT* promoter mutations are observed in other CNS tumor types and are not seen in CNS reactive non-neoplastic processes. *TERT* promoter mutations are also a molecular biomarker in non-CNS tumors, including hepatocellular tumors, melanoma, myxoid liposarcoma, thyroid carcinoma and urothelial carcinoma.

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

A negative (wildtype) result does not rule out the presence of a mutation that may be present but below the limits of detection of this assay. The analytical sensitivity of this assay for mutation detection is 1% mutant copies in a sample with 5% or more tumor cells/cells of interest.

This test detects *TERT* promoter mutations in 2 hotspots (C228T and C250T) only. Other alterations within the *TERT* promoter are not detectable by this test.

Rare genetic alterations (ie, 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 or other treatment of tissues, such as decalcification, may cause droplet digital polymerase chain reaction failure.

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.

Supportive Data

The *TERT* C228T and C250T droplet digital polymerase chain reaction (ddPCR) assays were shown to be reproducible, with 100% concordance for intra/inter-assay reproducibility experiments. Concordance between results by ddPCR and next-generation sequencing (NGS) for formalin-fixed paraffin-embedded samples was 98% (52/53), with the single discordant result (positive by ddPCR and negative for NGS) explained by the increased sensitivity of ddPCR relative to NGS technology. The analytical sensitivity of these assays was shown to be 1% fraction abundance of mutant copies at 2.5 ng DNA input (equivalent to at least 495 wild-type copies). All expected negative samples tested negative, and there was no cross reactivity between *TERT* C228T and C250T assays.

Clinical Reference

1. WHO Classification of Tumours Editorial Board: Central nervous system tumours. 5th ed. World Health Organization; 2021. WHO Classification of Tumours, Vol. 6
2. 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
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;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. Huang FW, Hodis E, Xu MJ, et al. Highly recurrent TERT promoter mutations in human melanoma. Science. 2013;339(6122):957-959
7. Schulze K, Imbeaud S, Letouze E, et al. Exome sequencing of hepatocellular carcinomas identifies new mutational signatures and potential therapeutic targets. Nat Genet. 2015;47(5):505-511

Performance

Method Description

Droplet digital polymerase chain reaction method is performed to test for the presence of hotspot c.-124C>T (C228T) and c.-146C>T (C250T) mutations in the promoter region of the *TERT* gene.(Unpublished Mayo method)

Gene	GenBank Accession Number	Chromosome (Genome build)
TERT promoter	NM_198253	Chromosome 5 (GRCh37/hg19)

PDF Report

No

Day(s) Performed

Monday through Friday

Report Available

6 to 12 days

Specimen Retention Time

FFPE tissue block: Unused portions of blocks will be returned 10 to 14 days after testing is complete; FFPE tissue/cytology slides: Unused slides are stored indefinitely and not returned; Digital images are obtained and stored for all slides used in testing.

Performing Laboratory Location

Rochester

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

81345

88381-Microdissection, manual

LOINC® Information

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

Result ID	Test Result Name	Result LOINC® Value
618698	Result Summary	50397-9
618699	Result	82939-0
618700	Interpretation	69047-9
618701	Additional Information	48767-8
618704	Specimen	31208-2
618705	Source	31208-2
618706	Tissue ID	80398-1
618702	Method	85069-3
618703	Disclaimer	62364-5
618707	Released By	18771-6