Overview

Useful For
Assisting in central nervous system tumor classification

This test is not useful for hematological malignancies.

Additional Tests

<table>
<thead>
<tr>
<th>Test ID</th>
<th>Reporting Name</th>
<th>Available Separately</th>
<th>Always Performed</th>
</tr>
</thead>
<tbody>
<tr>
<td>SLIRV</td>
<td>Slide Review in MG</td>
<td>No, (Bill Only)</td>
<td>Yes</td>
</tr>
</tbody>
</table>

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: tissue 144 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 |

Document generated February 6, 2021 at 4:54am CST
**Specimen Stability Information**

<table>
<thead>
<tr>
<th>Specimen Type</th>
<th>Temperature</th>
<th>Time</th>
<th>Special Container</th>
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</thead>
<tbody>
<tr>
<td>Varies</td>
<td>Ambient (preferred)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Frozen</td>
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</tr>
<tr>
<td></td>
<td>Refrigerated</td>
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</table>

**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 oligodendroglomas"). 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 interpretative 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.
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**


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)

<table>
<thead>
<tr>
<th>Gene</th>
<th>GenBank Accession Number</th>
<th>Nucleotide Start</th>
<th>Nucleotide End</th>
<th>Chromosome</th>
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<tr>
<td>TERT promoter</td>
<td>NM_198253</td>
<td>1295170</td>
<td>1295296</td>
<td>Chromosome 5</td>
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PDF Report

No

Day(s) and Time(s) Test Performed

Monday through Friday; Varies

Analytic Time

12 days

Maximum Laboratory Time

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 U.S. Food and Drug Administration.

CPT Code Information
### LOINC® Information

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<th>Test Order Name</th>
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<table>
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