MAYO CLINIC LABORATORIES

Test Definition: NONCM

Neuro-Oncology Gene Panel, Mutations Only, Tumor

Overview

Useful For

Identifying mutations that may support a diagnosis or help determine prognosis for patients with central nervous system tumors

Identifying specific mutations within genes known to be associated with response or resistance to specific cancer therapies

This test is **not intended** for use for hematological malignancies.

Genetics Test Information

This test uses next-generation sequencing to evaluate for microsatellite instability (MSI) status and somatic mutations involving 89 genes associated with tumors of the central nervous system. See Targeted DNA Gene Regions Interrogated by Neuro-Oncology Panel for details regarding the targeted gene regions identified by this test.

Of note, this test is performed to evaluate for somatic (ie, tumor-specific) mutations within the genes listed. Although germline (ie, inherited) alterations may be detected, this test cannot distinguish between germline and somatic alterations with absolute certainty. Follow-up germline testing using non-neoplastic (normal) tissue can be performed for confirmation of suspected clinically relevant germline alterations. Germline testing should be performed along with genetic counseling.

This test only evaluates MSI status and somatic mutations; this test does not evaluate for rearrangements (fusions and abnormal transcript variants).

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

- Targeted DNA Gene Regions Interrogated by Neuro-Oncology Panel
- Tissue Requirements for Solid Tumor Next-Generation Sequencing

Highlights

This next-generation sequencing tumor profiling assay interrogates targeted gene regions across 89 genes associated with central nervous system tumors to assess for the presence of somatic mutations, such as mutations in *IDH1/2, TERT* promoter*, ATRX, TP53, H3-3A* (previously *H3F3A*)*, H3C2/H3C3 (previously HIST1H3B/C), BRAF, FGFR1, NF1, and SMARCB1*.

Microsatellite instability (MSI) status is also determined (MSS, MSI-H) as part of this test and is often clinically actionable for determining the efficacy of immunotherapy in solid tumors.

Method Name
Sequence Capture 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
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 288 mm(2)
-Minimum amount of tumor area: tissue 36 mm(2)
-If ordered in conjunction with CMAPT / Chromosomal Microarray, Tumor, Formalin-Fixed Paraffin-Embedded, the preferred amount of tissue is 430 mm(2), the minimum amount is 180 mm(2).
-These amounts are cumulative over up to 15 unstained slides and must have adequate percent tumor nuclei.
-Tissue fixation: 10% neutral buffered formalin, not decalcified
- For this test, at least 6 mm x 6 mm areas on 8 unstained slides is preferred: this is approximately equivalent to 288 mm(2). The minimum acceptable area is 6 mm x 6 mm on 1 unstained slides: approximately equivalent to 36 mm(2). For specimen preparation guidance, see Tissue Requirement for Solid Tumor Next-Generation Sequencing.

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 Hematoxylin and eosin-stained and 15 unstained
Collection Instructions:
Submit the following slides:
1 Slide stained with hematoxylin and eosin
AND
15 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 15 slides from the same block.
Additional Information: Hematoxylin and eosin-stained and unstained 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 Extracted nucleic acid (DNA/RNA)	Reject

Specimen Stability Information

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

Clinical & Interpretive

Clinical Information

Molecular biomarkers, including clinically relevant gene mutations (ie, sequence variants), have been incorporated in the World Health Organization classification of central nervous system (CNS) tumors. Additionally, there are clinically available targeted therapies for patients with certain CNS tumor types harboring specific mutations. This test evaluates targeted regions across 89 genes associated with a variety of adult and pediatric-type CNS tumors for the presence of somatic mutations including, but not limited to, mutations in *IDH1/2, TERT* promoter*, ATRX, TP53, H3-3A* (previously *H3F3A*)*, H3C2/H3C3* (previously *HIST1H3B/C*)*, BRAF, FGFR1*, *NF1* and *SMARCB1*.

See Targeted DNA Gene Regions Interrogated by Neuro-Oncology Panel for details regarding the targeted gene regions identified by this test.

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 does not include evaluation of rearrangements (fusions and abnormal transcript variants).

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.

Variants of uncertain significance may be identified.

A negative result does not rule out the presence of a variant that may be present 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 89 genes. This test may detect single exon deletions but does not detect multi-exon deletions, duplications, or genomic copy number variants in any of the genes tested

The presence or absence of a variant may not be predictive of response to therapy in all patients.

Rare 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, 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 or incomplete.

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

Genes may be added or removed based on updated clinical relevance. Refer to the Targeted DNA Gene Regions Interrogated by Neuro-Oncology Panel for the most up to date list of genes included in this test.

Supportive Data

Performance Characteristics

The limit of detection for calling a somatic variant (single nucleotide variants [SNV] and deletions-insertions [delins]) is 5% variant allele frequency (VAF) 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% (226/234) of variants, respectively. Concordance for the detection of delins was 98.9% (186/188) in variants 1 to 10 base pairs (bp) in size, 95.8% (23/24) in variants 11 to 50 bp in size, and 88.9% (8/9) in variants 51 to 200 bp in size.

Microsatellite instability (MSI) evaluation is accurate at a tumor purity of at least 10% for colorectal tumors and 20% for other tumor types. During verification studies, 98% (200/204) concordance for MSI status was observed between this test and the reference method.

To ensure accuracy, this test will be performed on cases estimated by a pathologist to have at least 20% tumor cells.

Clinical Reference

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2. Zhang J, Wu G, Miller CP, et al. Whole-genome sequencing identifies genetic alterations in pediatric low-grade gliomas. Nat Genet. 2013;45(6):602-612
3. Jones DT, Hutter B, Jager N, et al. Recurrent somatic alterations of FGFR1 and NTRK2 in pilocytic astrocytoma. Nat Genet. 2013;45(8):927-932
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5. Brastianos PK, Horowitz PM, Santagata S, et al. Genomic sequencing of meningiomas identifies oncogenic SMO and AKT1 mutations. Nat Genet. 2013;45(3):285-289
6. Clark VE, Erson-Omay EZ, Serin A, et al. Genomic analysis of non-NF2 meningiomas reveals mutations in TRAF7, KLF4, AKT1, and SMO. Science. 2013;339(6123):1077-1080
7. Wu G, Diaz AK, Paugh BS, et al. The genomic landscape of diffuse intrinsic pontine glioma and pediatric non-brainstem high-grade glioma. Nat Genet. 2014;46(5):444-450
8. 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
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10. Ceccarelli M, Barthel FP, Malta TM, et al. Molecular profiling reveals biologically discrete subsets and pathways of progression in diffuse glioma. Cell. 2016;164(3):550-563
11. Pajtler KW, Mack SC, Ramaswamy V, et al. The current consensus on the clinical management of intracranial ependymoma and its distinct molecular variants. Acta Neuropathol. 2017;133(1):5-12
12. Northcott PA, Buchhalter I, Morrissy AS, et al. The whole-genome landscape of medulloblastoma subtypes. Nature. 2017;547(7663):311-317

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14. Nabors LB, Portnow J, Ammirati M, et al. Central nervous system cancers version 1.2015. J Natl Compr Canc Netw. 2015;13(10);1191-1202

Performance

Method Description

Hybridization and capture-based next-generation sequencing (NGS) are performed to determine microsatellite instability (MSI) status and evaluate the presence of a mutation in targeted regions of 89 genes.

See Targeted DNA Gene Regions Interrogated by Neuro-Oncology Panel for details regarding the targeted gene regions identified by this test.(Unpublished Mayo method)

A pathology review and macro dissection to enrich for tumor cells is 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 10 to 14 days after testing is complete; FFPE tissue slides: Tissue slides: Hematoxylin and eosin-stained and unstained slides will not be returned. Unused slides are stored for at least 5 years.

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

Test Definition: NONCM

Neuro-Oncology Gene Panel, Mutations Only, Tumor

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

81457

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
NONCM	Neuro-Onc Panel, Mutations Only	73977-1

Result ID	Test Result Name	Result LOINC® Value
622296	Result Summary	50397-9
622297	Result	82939-0
622298	Interpretation	69047-9
622299	Additional Information	48767-8
622300	Method	85069-3
622301	Disclaimer	62364-5
622302	Specimen	31208-2
622303	Source	31208-2
622304	Tissue ID	80398-1
622305	Released By	18771-6