MAYO CLINIC LABORATORIES

Test Definition: NONCR

Neuro-Oncology Gene Panel, Rearrangements Only, Tumor

Overview

Useful For

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

Identifying rearrangements 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 somatic rearrangements (fusions and abnormal transcript variants) associated with tumors of the central nervous system. This RNA panel includes detection of rearrangements in 81 genes, including 104 known gene fusions and 29 known abnormal transcript variants. See RNA Targeted Gene Fusions and Abnormal Transcript Variants 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. This test only evaluates targeted rearrangements (fusions and abnormal transcript variants); this test does not detect somatic DNA mutations.

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

- RNA Targeted Gene Fusions and Abnormal Transcript Variants
- Tissue Requirements for Solid Tumor Next-Generation Sequencing

Highlights

This next-generation sequencing tumor profiling assay interrogates targeted rearrangements across 81 genes associated with central nervous system tumors to assess for the presence of somatic rearrangements, such as gene fusions including *KIAA1549::BRAF, ZFTA::RELA* (previously *C11orf95::RELA*), and *EGFR* transcript variants (eg, *EGFR* vIII).

Method Name

Targeted Polymerase Chain Reaction (PCR)-Based 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 10% 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)
-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 4 unstained slides is preferred: this is approximately equivalent to 144 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 followings 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: Unused unstained slides will not be returned.

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 fusions, 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 fusions. This test evaluates targeted regions across 81 genes associated with a variety of adult and pediatric-type CNS tumors for the presence of somatic rearrangements (fusions and abnormal transcript variants) including, but not limited to, *KIAA1549::BRAF* and *ZFTA::RELA* (previously *C11orf95::RELA*) fusions, and *EGFR* transcript variants (eg, *EGFR* vIII).

See RNA Targeted Gene Fusions and Abnormal Transcript Variants 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 somatic DNA mutations.

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 fusion that may be present below the limits of detection of this assay. The analytical sensitivity of this assay is a minimum coverage of 10 targeted fusion reads with 5 unique fusion molecules in a sample with 10% or greater tumor content.

Detection of fusion transcripts (RNA) is particularly labile and degrades quickly. Rapid preservation of the tumor sample after collection reduces the likelihood of degradation, but there are sometimes biological factors, such as tumor necrosis that interfere with obtaining a high-quality RNA specimen despite rapid preservation.

This panel can detect in-frame and out-of-frame fusions. There may be lower sensitivity in detecting out-of-frame fusions, such as exon-intron, intron-intron, or big insertions. This assay will only detect fusions involving at least one gene in the defined gene fusion target list of interest.

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.

Supportive Data

Performance Characteristics

Detection of fusion transcripts (RNA): The RNA fusion portion of the test exhibited 94.2% sensitivity (49/52) in detecting fusion transcripts (confirmed detection by reverse transcriptase polymerase chain reaction or chromosomal microarray). No fusion transcripts were detected in 25 unique samples (100% specificity compared to chromosomal microarray),

resulting in an overall concordance of 96.1%.

To ensure accuracy, this test will be performed on cases estimated by a pathologist to have at least 10% tumor cells.

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. 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

Polymerase chain reaction amplification-based next-generation sequencing is performed to test for the presence of rearrangements in 81 genes, including 104 known gene fusions and 29 known abnormal gene transcript variants.

See RNA Targeted Gene Fusions and Abnormal Transcript Variants 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: Unused slides are stored indefinitely and not returned

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

81456

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
NONCR	Neuro-Onc Panel, Fusions Only	73977-1

Result ID	Test Result Name	Result LOINC® Value
606325	Result Summary	50397-9
606326	Result	82939-0
606327	Interpretation	69047-9
606328	Additional Information	48767-8
606329	Method	85069-3
606330	Disclaimer	62364-5
606331	Specimen	31208-2
606332	Source	31208-2
606454	Tissue ID	80398-1
606333	Released By	18771-6