MAYO CLINIC LABORATORIES

Test Definition: IDH12

IDH1/IDH2 Mutation Analysis, Tumor

Overview

Useful For

Supporting a morphological diagnosis of a diffuse glioma

Assisting in central nervous system tumor classification

Stratifying prognosis of diffuse gliomas

Supporting the differential diagnosis of chondroid bone tumors

Stratifying prognosis of acute myeloid leukemia

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 minimum of 5000 total nucleated cells, minimum of 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.

Reject Due To

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

Specimen Minimum Volume

See Specimen Required

Specimen Stability Information

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

Clinical & Interpretive

Clinical Information

IDH1 and *IDH2* (*IDH*) genes encode dehydrogenase enzymes that are involved in cellular glucose metabolism and oxidative damage control. *IDH* variants, primarily involving codons R132 in *IDH1* and R172 in *IDH2*, result in reduction of the enzyme physiological activity and gain of a neomorphic ability to generate oncometabolite R(-)-2-hydroxyglutarate, which contribute to tumorigenesis by altering numerous cellular responses, including genome-wide epigenetic changes that characterize the glioma CpG island methylator phenotype (G-CIMP). *IDH* variants seem to be an early event in gliomagenesis and have been identified in over 70% of lower-grade (grades II/III) diffuse gliomas and secondary glioblastoma. These variants are rarely seen in other central nervous system tumors and are not seen in reactive non-neoplastic processes, and define a group of lower and high-grade diffuse gliomas associated with a more favorable prognosis. Assessment of *IDH* variant status in central nervous system tumors may assist in tumor classification and provide prognostically relevant information for subgroups of patients with diffuse gliomas.

IDH1 and *IDH2* gene variants are also observed in a variety of non-CNS tumor types. Assessment of *IDH* variant status may assist in the differential diagnosis of chondroid bone tumors and provide prognostically relevant information in other contexts, such as in the setting of acute myeloid leukemia (AML).

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 variant that may be present but below the limits of detection of this assay.

Point mutations and small insertion/deletion mutations will be detected within targeted regions of the *IDH1*, and *IDH2* genes only. This test does not detect structural variants, genomic copy number changes, or large single or multiexon deletions or duplications in the *IDH1* and *IDH2* genes.

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, please 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 tumor classification and prognostication of patients with 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. Parsons DW, Jones S, Zhang X, et al: An integrated genomic analysis of human glioblastoma multiforme. Science. 2008 Sep 26;321(5897):1807-1812

2. Yan H, Parsons DW, Jin G, et al: *IDH1* and *IDH2* mutations in gliomas. N Engl J Med. 2009 Feb 19;360(8):765-773

3. Hartmann C, Meyer J, Balss J, et al: Type and frequency of *IDH1* and *IDH2* mutations are related to astrocytic and oligodendroglial differentiation and age: a study of 1,010 diffuse gliomas. Acta Neuropathol. 2009 Oct;118(4):469-474

4. 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 Jun 25;372(26):2481-2498

5. 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 Jun 25;372(26):2499-2508

6. Chotirat S, Thongnoppakhun W, Wanachiwanawin W, Auewarakul CU: Acquired somatic mutations of isocitrate dehydrogenases 1 and 2 (IDH1 and IDH2) in preleukemic disorders. Blood Cells Mol Dis. 2015 Mar;54(3):286-291

Performance

Method Description

Next-generation sequencing is performed to test for the presence of a mutation in targeted regions of the *IDH1* and *IDH2* genes, including exon 4 (codons 113-138) of *IDH1* and exon 4 (codons 137-174) of *IDH2*.(Unpublished Mayo method)

Gene	GenBank Accession Number	Nucleotide Start	Nucleotide End	Chromosome	Exon	Codons
IDH1	NM_005896	209113084	209113170	Chromosome 2	Exon 4	113-138
IDH2	NM_002168	90631831	90631945	Chromosome 15	Exon 4	136-174

PDF Report

No

Specimen Retention Time

Unused portions of blocks will be returned to the client. Unused slides are stored indefinitely.

Performing Laboratory Location

Rochester

Fees & Codes

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

IDH1:

81120

88381

IDH2:

81121

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
IDH12	IDH1/IDH2 Mutation Analysis, Tumor	95772-0

Result ID	Reporting Name	LOINC®
92397	Result Summary	50397-9
92398	Result	82939-0
92399	Interpretation	69047-9
92400	Additional Information	48767-8
92401	Specimen	31208-2
92402	Source	31208-2

92403	Tissue ID	80398-1
92404	Released By	18771-6