MAYO CLINIC LABORATORIES

Test Definition: MGMT

MGMT Promoter Methylation, Tumor

Overview

Useful For

Prognostication of newly diagnosed patients with glioblastoma, IDH-wildtype

Identifying newly diagnosed glioblastoma, IDH-wildtype patients that may respond to alkylating chemotherapy (ie, temozolomide)

Guiding therapy decision making for newly diagnosed glioblastoma, IDH-wildtype in older patients (>60-65 years)

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.

Highlights

MGMT promoter methylation status has prognostic and predictive value for glioblastoma patients.

Method Name

Methylation-Specific Polymerase Chain Reaction (PCR) Analysis

NY State Available

Yes

Specimen

Specimen Type

Varies

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

Preferred:
Specimen Type: Tissue
Container/Tube: Tissue block
Collection Instructions: Submit a formalin-fixed, paraffin-embedded tissue block. At least 40% tumor is required for this assay. In general, a 6 mm x 3 mm area of tissue cut at 5-micron thickness is the minimum amount of tissue needed; this could be collected over multiple slides.

Acceptable:
Specimen Type: Tissue sections
Slides: 1 Stained and 5 unstained
Collection Instructions: Submit 1 slide stained with hematoxylin and eosin and 5 unstained, nonbaked slides with 5-micron thick sections of the tumor. At least 40% tumor is required for this assay. In general, a 6 mm x 3 mm area of tissue cut at 5-micron thickness is the minimum amount of tissue needed; this could be collected over multiple slides.

Forms

If not ordering electronically, complete, print, and send an Oncology Test Request (T729) with the specimen.

Specimen Minimum Volume

5 Unstained slides at 5-microns thickness

Reject Due To

Specimens that have been decalcified (all methods) Specimens that have not been formalin-fixed, paraffin-embedded Bone marrow in EDTA	Reject

Specimen Stability Information

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

Clinical & Interpretive

Clinical Information

Glioblastoma is the most frequent malignant primary central nervous system (CNS) tumor in adults as originally defined based on morphology. Based on the 2021 World Health Organization (WHO) classification of CNS tumors, the original glioblastoma is now divided in "glioblastoma, IDH-wildtype, CNS WHO grade 4" (most cases) and "astrocytoma, IDH-mutant, CNS WHO grade 4." Current standard of care in both tumor types consists of surgical resection followed by radiotherapy in addition to alkylating chemotherapy with temozolomide.

MGMT (O[6]-methylguanine-DNA methyltransferase) encodes a DNA repair enzyme. This enzyme rescues tumor cells from alkylating agent-induced damage and confers tumor resistance to chemotherapy with alkylating agents. Epigenetic silencing of *MGMT* by promoter methylation of upstream and downstream CpG sites within differentially methylated regions results in decreased *MGMT* expression and presumably reduces MGMT-mediated DNA repair of alkylating agent-induced DNA damage in tumor cells.

In newly diagnosed original glioblastoma patients, *MGMT* promoter methylation has been shown to be a favorable prognostic biomarker and a strong predictor of responsiveness to alkylating chemotherapy. This is particularly relevant for older patients (>60-65 years), who may have decreased tolerance for combined chemoradiation. For this group of patients, *MGMT* promoter methylation status guides therapy decision making, as *MGMT* promoter methylation identifies patients who would benefit from monotherapy with the alkylating agent temozolomide instead of radiotherapy alone.

In IDH-mutant diffuse gliomas, *MGMT* promoter methylation is very frequent and occurs as part of the IDH mutation-induced glioma CpG island methylation phenotype; in infratentorial IDH-mutant astrocytomas, however, *MGMT* promoter methylation is less common. The prognostic and predictive significance of *MGMT* promoter methylation status in the context of IDH-mutant tumors is unclear. *MGMT* promoter methylation is also frequent in "diffuse hemispheric glioma, H3 G34-mutant" and limited data suggest that it is also a favorable prognostic marker in this tumor context.

MGMT promoter methylation status may be evaluated by multiple methods, and the testing platform with most prospective clinical trial validation is methylation-specific polymerase chain reaction evaluating downstream CpG sites.

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

Test results should be interpreted in 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 possible 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 formalin-fixed, paraffin-embedded tissues; other types of fixatives are discouraged. Improper treatment of tissues, such as decalcification, may cause polymerase chain reaction failure.

Clinical Reference

1. Hegi ME, Diserens AC, Gorlia T, et al. MGMT gene silencing and benefit from temozolomide in glioblastoma. N Engl J Med. 2005;352(10):997-1003
2. Weller M, Stupp R, Reifenberger G, et al. MGMT promoter methylation in malignant gliomas: ready for personalized medicine? Nat Rev Neurol. 2010;6(1):39-51
3. Wick W, Platten M, Meisner C, et al. Temozolomide chemotherapy alone versus radiotherapy alone for malignant astrocytoma in the elderly: The NOA-08 randomised, phase 3 trial. Lancet Oncol. 2012;13(7):707-715
4. Malmstrom A, Gronberg BH, Marosi C, et al. Temozolomide versus standard 6-week radiotherapy versus hypofractionated radiotherapy in patients older than 60 years with glioblastoma: the Nordic randomised, phase 3 trial. Lancet Oncol. 2012;13(9):916-926
5. Korshunov A, Capper D, Reuss D, et al. Histologically distinct neuroepithelial tumors with histone 3 G34 mutation are molecularly similar and comprise a single nosologic entity. Acta Neuropathol. 2016;131(1):137-146
6. Korshunov A, Casalini B, Chavez L, et al. Integrated molecular characterization of IDH-mutant glioblastomas. Neuropathol Appl Neurobiol. 2019;45(2):108-118
7. Mansouri A, Hachem LD, Mansouri S, et al. MGMT promoter methylation status testing to guide therapy for glioblastoma: refining the approach based on emerging evidence and current challenges. Neuro Oncol. 2019;21(2):167-178
8. Banan R, Stichel D, Bleck A, et al. Infratentorial IDH-mutant astrocytoma is a distinct subtype. Acta Neuropathol. 2020;140(4):569-581
9. Wen PY, Weller M, Lee EQ, et al. Glioblastoma in adults: a Society for Neuro-Oncology (SNO) and European Society of Neuro-Oncology (EANO) consensus review on current management and future directions. Neuro Oncol. 2020;22(8):1073-1113
10. WHO Classification of Tumours Editorial Board. Central Nervous System Tumours. 5th ed. IARC Press; 2021. WHO Classification of Tumours, Vol 6
11. Brat DJ, Aldape K, Bridge JA, et al. Molecular biomarker testing for the diagnosis of diffuse gliomas. Arch Pathol Lab Med. 2022;146(5):547-574

Performance

Method Description

A real-time methylation-specific polymerase chain reaction assay that evaluates 8 CpG sites (79-86) within the downstream differentially methylated region of the *MGMT* promoter region.(Ida CM, Butz ML, Jenkins RB, et al. Real-time methylation-specific polymerase chain reaction for MGMT promoter methylation clinical testing in glioblastoma: An alternative detection method for a heterogeneous process. Am J Clin Pathol. 2017;148[4]:296-307)

PDF Report

No

Day(s) Performed

Varies

Report Available

7 to 10 days

Specimen Retention Time

FFPE tissue block: Unused portions of FPPE blocks will be returned; Unused, unstained slides: 5 years; Stained slides: Indefinitely

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

81287
88381

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
MGMT	MGMT Promoter Methylation, Tumor	60252-4

Result ID	Test Result Name	Result LOINC® Value
36734	Result Summary	50397-9
36735	Result	60252-4
36736	Interpretation	69047-9
36737	Additional Information	48767-8
36738	Specimen	31208-2
36739	Source	31208-2
36740	Tissue ID	80398-1
36741	Released by	18771-6