MAYO CLINIC LABORATORIES

Test Definition: MGMT

MGMT Promoter Methylation, Tumor

Overview

Useful For

Prognostication of newly diagnosed glioblastomas

Identifying newly diagnosed glioblastomas that may respond to alkylating chemotherapy (ie, temozolomide)

Guiding therapy decision making for newly diagnosed glioblastomas in elderly patients (>60 years)

Additional Tests

Test Id	Reporting Name	Available Separately	Always Performed
SLIRV	Slide Review in MG	No	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 **must** accompany specimen in order for testing to be performed.

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 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.

Reject Due To

Hemolysis	NA
Lipemia	NA
Icterus	NA
Other	Specimens that have been decalcified (all methods); specimens that have not been formalin-fixed, paraffin-embedded; bone marrow in EDTA

Specimen Minimum Volume

5 unstained slides at 5-microns thickness

Specimen Stability Information

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

Clinical & Interpretive

Clinical Information

Glioblastoma (WHO grade IV astrocytoma) is the most frequent malignant primary central nervous system tumor in adults. It has a very poor prognosis, with median survival of less than a year. Current standard of care consists of surgical resection followed by radiotherapy in addition to alkylating chemotherapy with temozolomide.

MGMT (O[6]-methylguanine-DNA methyltransferase) is a DNA repair enzyme. This enzyme rescues tumor cells from alkylating agent-induced damage, and this leads to resistance to chemotherapy with alkylating agents. Epigenetic silencing of the *MGMT* gene by promoter methylation results in decreased MGMT protein expression, reduced DNA repair activity, and potential increased sensitivity to therapy. *MGMT* promoter methylation status has been most widely evaluated by methylation-specific PCR method, which is both sensitive and specific.

In newly diagnosed glioblastomas, the presence of *MGMT* promoter methylation has been shown to be an independent favorable prognostic factor and a strong predictor of responsiveness to alkylating chemotherapy (ie, temozolomide). This is particularly relevant for elderly patients (>60 years), who usually have decreased tolerance for combined aggressive chemoradiation. For this group of patients, recent clinical trials have provided strong evidence supporting an alternative therapeutic strategy consisting of monotherapy with the alkylating agent temozolomide for patients whose tumors show *MGMT* promoter methylation and radiotherapy alone for patients whose tumors lack *MGMT* promoter methylation. Thus, in addition to the significant prognostic and predictive value, *MGMT* methylation status has emerged as a valuable biomarker to guide therapy decision making for newly diagnosed glioblastoma in elderly patients, preventing unnecessary treatment toxicities and costs.

MGMT promoter methylation has been reported to high rates in oligodendrogliomas and astrocytomas of lower grade, in which they variably correlate with 1p19q codeletion and *IDH* mutations. Prognostic and predictive significance of *MGMT* promoter methylation status in these tumors has been shown in some studies, but not in others.

Reference Values

An interpretive report will be provided.

Interpretation

An interpretive report will be provided.

Cautions

Not all patients whose tumors have *MGMT* promoter methylation will respond to alkylating chemotherapy.
MGMT promoter methylation status should not be used as the sole determinant of alkylating therapy eligibility.
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.

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;6:39-51
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;13:707-715
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;13:916-926
5. Wick W, Weller M, van den Bent M, et al: MGMT testing-the challenges for biomarker-based glioma treatment. Nat Rev Neurol 2014;10:372-385

Performance

Method Description

A modification of the real-time, methylation-specific PCR assay described by Kitange et al, is used to test tumor DNA for the presence of methylation of the promoter of the *MGMT* gene.(Kitange GJ, Carlson BL, Mladek AC, et al: Evaluation of MGMT promoter methylation status and correlation with temozolomide response in orthotopic glioblastoma xenograft model. J Neurooncol 2009 Mar;92[1]:23-31)

PDF Report

No

Specimen Retention Time

Unused portions of blocks will be returned.; Extracted (at Mayo) DNA: 3 months.; 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

81287

Slide Review

88381