Molecular In My Pocket™
ONCOLOGY: *Molecular Biomarkers in Tumors of the Central Nervous System*

Samples to test: Primary or recurrent tumors; formalin-fixed paraffin-embedded tissue (FFPE)

Biomarker	Alteration/ Alternative terms	Indications	Significance	Common methods
IDH1 ***IDH2***	*IDH1*: Mutations in codon R132 *IDH2*: Mutations in codons R140, R172	Diagnosis Prognosis Therapeutic	Diagnostic biomarker of astrocytoma, *IDH*-mutant and oligodendroglioma, *IDH*-mutant and 1p/19q co-deleted. Associated with improved prognosis except when the tumor also has *CDKN2A/B* homozygous deletion (negative prognosis). *IDH1* and *IDH2* mutations are targetable.	NGS, genotyping, PCR-based assays, IHC (R132H only)
1p/19q co-deletion	Deletion	Diagnosis	1p/19q whole-arm co-deletion is a diagnostic molecular biomarker of oligodendroglioma.	FISH, array, NGS
BRAF	Mutations (particularly V600E); fusions	Diagnosis Therapeutic	Diagnostic biomarker and seen in a variety of tumors, such as pleomorphic xanthoastrocytoma, ganglioglioma, pilocytic astrocytoma, diffuse low-grade glioma, MAPK pathway-altered. V600 mutations and fusions are targetable.	NGS, genotyping, PCR-based assays, IHC, RT-PCR, AMP
***H3-3A* (*H3F3A*)** ***H3C2* (*HIST1H3B*)**	Alterations in codons K28 (K27) or G35 (G34)	Diagnosis	Diagnostic molecular biomarker of diffuse midline glioma, H3 K28M (K27M)-altered; and diffuse hemispheric glioma, H3 G35 (G34)-mutant.	NGS, genotyping, PCR-based assays, IHC
TERT	Promoter mutations	Diagnosis	Diagnostic biomarker for glioblastoma, *IDH*-wildtype and anaplastic meningioma. Present in almost all oligodendrogliomas, *IDH*-mutant and 1p/19q co-deleted.	NGS, genotyping, PCR-based assays
MGMT	Promoter methylation	Prognosis Therapeutic	Associated with more favorable prognosis and response to temozolomide in patients with glioblastoma, *IDH*-wildtype.	Methylation-specific PCR-based assays, array, sequencing
ATRX	Loss of function mutations; loss of protein expression	Diagnosis	Diagnostic molecular biomarker for astrocytoma, *IDH*-mutant. Associated with *IDH1* and *IDH2* mutations. Typically, mutually exclusive with 1p/19q co-deletion. Supportive diagnostic biomarker for diffuse hemispheric glioma, H3 G34-mutant, and high-grade astrocytoma with piloid features.	NGS, IHC
***ZFTA* (previously *C11orf95*)**	Fusion	Diagnosis Prognosis	Diagnostic molecular biomarker for supratentorial ependymoma, *ZFTA* fusion-positive. *ZFTA* fusion-positive ependymomas tend to show more aggressive behavior.	NGS, RT-PCR, AMP, FISH
EGFR **chromosome 7** **chromosome 10**	*EGFR* amplification Gain of chromosome 7 Loss of chromosome 10	Diagnosis	Diagnostic biomarkers for glioblastoma, *IDH*-wildtype.	FISH, array, NGS, PCR-based assays
CDKN2A/B	Deletion (homozygous)	Diagnosis Prognosis	Diagnostic molecular biomarker for CNS WHO grade 4 astrocytoma, *IDH*-mutant, CNS WHO grade 3 oligodendroglioma, *IDH*-mutant and 1p/19q-codeleted, and anaplastic meningioma	FISH, array, NGS, PCR-based assays

Abbreviations: NGS: next-generation sequencing; IHC: immunohistochemistry; FISH: fluorescence *in situ* hybridization; AMP: anchored multiplex PCR; RT-PCR: reverse transcription-polymerase chain reaction.

Where to test: Testing should be performed in the laboratories that are certified under clinical laboratory improvement amendments of 1988 (CLIA-88) as qualified to perform high complexity (molecular pathology) testing.

***References*: 1.** WHO Classification of Tumours Editorial Board. Central nervous system tumours. Lyon (France): International Agency for Research on Cancer; 2021. (WHO classification of tumours series, 5th ed.; vol. 6). https://publications.iarc.fr/601.

Revised 7/2025

Prepared by the Association for Molecular Pathology Training and Education Committee
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