

## Molecular In My Pocket...

# ONCOLOGY: Molecular Biomarkers in Tumors of the Central Nervous System

### **Molecular Biomarkers in Tumors of the Central Nervous System**

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

Biomarker	Specific alterations Alternative terms	Indications	Result interpretation significance	Assays Techniques
<b>IDH1 IDH2</b>	IDH1: Mutations in codon R132 IDH2: Mutations in codons R140, R172	Diagnosis Prognosis	Can be seen in astrocytoma, glioblastoma, oligodendroglioma. Associated with improved prognosis except when the tumor also has a homozygous deletion of <i>CDKN2A/B</i>	NGS, pyrosequencing, Sanger sequencing, genotyping, PCR-based assays, IHC
<b>1p/19q co-deletion</b>	Deletion	Diagnosis Prognosis	Co-deletion of 1p/19q is seen in oligodendrogliomas and is associated with improved prognosis.	FISH, array, NGS
<b>BRAF</b>	Mutations in codon V600; fusions	V600 mutations are therapeutic: Fusions such as BRAF-KIAA1549 are more diagnostic	Seen in tumors such as pilocytic astrocytoma, pleomorphic xanthoastrocytoma, ganglioglioma. Activating mutations or fusions are potentially targetable.	NGS, pyrosequencing, Sanger sequencing, genotyping, PCR-based assays, IHC, RT-PCR, AMP
<b>H3F3A HIST1H3B</b>	Mutations in codon K27, G34	Diagnosis	Seen in diffuse midline glioma, H3 K27M-mutant G34 mutations can be seen in pediatric cortical gliomas	NGS, pyrosequencing, Sanger sequencing, genotyping, PCR-based assays, IHC
<b>TERT</b>	Promoter mutation	Prognosis	Associated with less favorable prognosis in IDH-wild type astrocytomas and present in almost all oligodendrogliomas.	NGS, pyrosequencing, Sanger sequencing, genotyping, PCR-based assays
<b>MGMT</b>	Promoter methylation	Therapeutic	Associated with response to temozolomide	Methylation-specific PCR, bisulfite real-time PCR, bisulfite sequencing
<b>ATRX</b>	Loss of function mutations	Diagnosis	Associated with the presence of IDH1 or IDH2 mutations. Typically mutually exclusive with 1p/19q co-deletion	NGS, pyrosequencing, Sanger sequencing, IHC
<b>RELA</b>	Fusion	Diagnosis Prognosis	RELA-fusion positive ependymomas (usually supratentorial) tend to show more aggressive behavior.	RT-PCR, AMP, FISH

**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. Louis DN, *et al.* (Eds). WHO Classification of Tumours of the Central Nervous System. Vol 1. 4th ed. Geneva, Switzerland: World Health Organization; 2016. 2. Brat DJ, *et al.* cIMPACT-NOW update 5: recommended grading criteria and terminologies for IDH-mutant astrocytomas. *Acta Neuropathol.* 2020 Mar;139(3):603-608. doi: 10.1007/s00401-020-02127-9. Epub 2020 Jan 29. PMID: 31996992.

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