Overview of selected molecular diagnostic markers for CNS tumours

The table below summarizes selected molecular diagnostic markers for CNS tumours; the list of tests is not exhaustive and other assays may be helpful in some diagnostic circumstances. In addition, the tests listed are those related to ruling in the corresponding diagnoses; however, it should be realized that the assays may also be used in particular diagnostic situations to rule out other diagnoses. An example of this would be ATRX immunohistochemistry, which is commonly used to support a diagnosis of IDH-mutant diffuse astrocytoma, but which is also used to evaluate a possible diagnosis of oligodendroglioma, IDH-mutant and 1p/19q-codeleted. Some specific tests recommended in the commentaries below represent one of several validated and equivalent approaches to the evaluation of the described molecular variable; for those tests that have multiple testing modalities (e.g., sequencing and immunohistochemistry for BRAF V600E), it is assumed that only one of these testing modalities would be used per case unless one test yields equivocal results (e.g., a result of weak immunohistochemical positivity versus nonspecific background staining should be followed by gene sequencing). For some tests, relevance may be related to the age of the patient (e.g., EGFR gene amplification in adult high-grade gliomas rather than paediatric ones) and *the reader is referred to the commentaries under each molecular parameter for further information.*

Summary of tests by tumour type

Note: this is a summary and the reader is referred to the specific notes for details on use of each test.

W = component of the 2016 CNS WHO diagnostic criteria and 2017 WHO diagnostic criteria for pituitary adenomas

D = commonly used to support or refine the diagnosis, or provide important ancillary information in the corresponding tumour type

D* = commonly used to rule out the diagnosis; see commentary for details

(D) = can be used to support or refine the diagnosis, or provide important ancillary information in specific tumour subtype(s); see commentary for details

DA = diffuse astrocytoma; AA = anaplastic astrocytoma; O = oligodendroglioma; AO = anaplastic oligodendroglioma; GBM = glioblastoma; PXA = pleomorphic xanthoastrocytoma; GG = ganglioglioma; AT/RT = atypical teratoid / rhabdoid tumour; ETMR = embryonal tumour with multilayered rosettes; SFT/HPC = solitary fibrous tumour / haemangiopericytoma; MPNST = malignant peripheral nerve sheath tumour

Test	Gliomas								Embryonal tumours			Other					
	DA, AA	O, AO	Diffuse midline glioma	GBM	Pilocytic astrocytoma	PXA, GG	Ependymoma - supratentorial	Ependymoma – posterior fossa	Medulloblastoma	AT/RT	ETMR	Extraventricular neurocytoma	Meningioma	SFT/HPC	Craniopharyngioma	MPNST	Pituitary tumours
***ATRX* mutation**																	
ATRX mutation	D			D													
ATRX loss of expression (immunohistochemistry)	D			D													
***BRAF* alterations**																	
BRAF mutation	(D)			(D)	D	D									D		
BRAF V600E expression (immunohistochemistry)	(D)			(D)	D	D									D		
BRAF rearrangement/duplication					D												
***CDKN2A/B* homozygous deletion**	(D)					(D)											
C19MC alteration											W						
Chromosomal arm 1p/19q codeletion		W															

Test	Gliomas								Embryonal tumours			Other					
	DA, AA	O, AO	Diffuse midline glioma	GBM	Pilocytic astrocytoma	PXA, GG	Ependymoma - supratentorial	Ependymoma – posterior fossa	Medulloblastoma	AT/RT	ETMR	Extraventricular neurocytoma	Meningioma	SFT/HPC	Craniopharyngioma	MPNST	Pituitary tumours
Chromosome 7 gain combined with chromosome 10 loss (see below)				D													
Chromosome 10q23 (PTEN locus) deletion and *PTEN* mutation																	
Chromosome 10q23 *(PTEN* locus) deletion or monosomy 10				D													
PTEN mutation				D													
***EGFR* amplification and EGFRvIII mutation**																	
EGFR amplification				D													
EGFRvIII mutation				D													
Histone H3 mutation and H3 K27 trimethylation (me3)																	
Histone H3 K27M mutation (sequencing) and expression (immunohistochemistry)	(D)		W	D													
Histone H3 G34 mutation (sequencing) and expression (immunohistochemistry)	(D)			D													
Histone H3 K27me3 expression (immunohistochemistry)			D					D								D	
***IDH1/IDH2* mutation**																	
IDH1/IDH2 mutation	W	W	D*	W	D*	D*						D*					
IDH1 R132H expression (immunohistochemistry)	W	W	D*	W	D*	D*						D*					
Ki-67 immunohistochemistry		D											D				D
L1CAM expression (immunohistochemistry)							D										
LIN28A expression (immunohistochemistry)											D						
Medulloblastoma immunohistochemistry																	
β-catenin nuclear expression (immunohistochemistry)									D						D		
GAB1 expression (immunohistochemistry)									D								

Test	Gliomas								Embryonal tumours			Other					
	DA, AA	O, AO	Diffuse midline glioma	GBM	Pilocytic astrocytoma	PXA, GG	Ependymoma - supratentorial	Ependymoma – posterior fossa	Medulloblastoma	AT/RT	ETMR	Extraventricular neurocytoma	Meningioma	SFT/HPC	Craniopharyngioma	MPNST	Pituitary tumours
YAP1 expression (immunohistochemistry)									D								
***MGMT* promoter methylation**				D													
Monosomy 6									D								
MYC gene family amplification																	
MYC amplification									D								
MYCN amplification									D								
***NAB2-STAT6* fusion**																	
NAB2-STAT6 fusion														D			
STAT6 nuclear expression (immunohistochemistry)														D			
Pituitary hormones and transcription factors immunohistochemistry																	W
***RELA* fusion**							W										
***SMARCA4/BRG1* alteration**																	
SMARCA4/BRG1 mutation									D	W							
BRG1 loss of expression (immunohistochemistry)									D	W							
***SMARCB1/INI1/HNSF5* alteration**																	
SMARCB1/INI1/HNSF5 mutation									D	W							
INI1 (BAF47) loss of expression (immunohistochemistry)									D*	W							
***TERT* promoter mutation**		D		D													
***TP53* mutation**																	
TP53 mutation	D								W								
p53 expression (immunohistochemistry)	D								W								
***YAP1* fusion**							D										