Molecular In My Pocket™…

ONCOLOGY: Pediatric Brain Tumors

Prepared by the Association for Molecular Pathology Training and Education Committee

Abbreviations:

CGH	Comparative Genomic Hybridization	**CMA**	Chromosomal Microarray Analysis	**ddPCR**	Digital Droplet PCR
FISH	Fluorescent in situ Hybridization	**IHC**	Immunohistochemistry	**MLPA**	Multiplex Ligation-dependent Probe Amplification
NGS	Next Generation Sequencing	**PCR**	Polymerase Chain Reaction		

Tumor Type	Gene/Biomarker	Alteration	Significance	Primary Assays
Pleomorphic xanthoastrocytoma	*BRAF*	p.V600E mutation	diagnosis	NGS (DNA)
Pilocytic astrocytoma	*BRAF*	KIAA1549-BRAF fusion or p.V600E	diagnosis, prognosis	ddPCR, NGS (DNA or RNA), array CGH for duplication involving BRAF
Low grade glioma	*FGFR*	mutation, fusion	diagnosis	NGS (DNA), CMA
	NF1	loss or inactivating mutation, loss of heterozygosity (LOH)	diagnosis, familial cancer risk if germline	NGS (DNA), CMA
	RAF1	fusion	diagnosis	NGS (DNA)
	MYB	fusion, amplification	diagnosis, prognosis	NGS (DNA), CMA
	MYBL1	fusion, amplification	diagnosis, prognosis	NGS (DNA), CMA
	BRAF	p.V600E mutation	diagnosis, prognosis	NGS (DNA)
Diffuse midline glioma, H3 K27M-mutant	*H3F3A, HISTIH3B, HIST1H3C*	K27M (aka K28M)	diagnosis	NGS (DNA), IHC, ddPCR
Glioma, H3 G34-mutant	*H3F3A*	G34R (aka G35R)	diagnosis, prognosis	NGS (DNA), IHC, ddPCR
Glioma, NTRK alterations	*NTRK3, NTRK1, NTRK2*	fusion, mutation, amplification, mRNA overexpression	diagnosis, therapeutic (NTRK inhibitors)	NGS (RNA), NGS (DNA)
High grade glioma, IDH wildtype	*TERT*	mutation	prognosis	NGS (DNA)
	EGFR	amplification	prognosis	NGS (DNA), CMA, FISH
	CDKN2A/B	homozygous deletion	prognosis	CMA, NGS (DNA)
	TP53	Loss-of-function (LOF) and gain-of-function mutations, loss, LOH	prognosis	NGS (DNA), CMA
	PTEN	mutation	prognosis	NGS (DNA)
	NF1	loss or inactivating mutation, loss of heterozygosity (LOH)	prognosis	NGS (DNA), CMA
	PIK3CA	mutation	prognosis	NGS (DNA)
	PDGFRA	amplification	prognosis	CMA, NGS (DNA)
	RB1	loss or inactivating mutation, loss of heterozygosity (LOH)	prognosis	NGS (DNA), CMA
	PIK3R1	mutation	prognosis	NGS (DNA)
	MDM2	mutation	prognosis	NGS (DNA)
	MDM4	amplification	prognosis	NGS (DNA), CMA, FISH
	MET	amplification, fusion, mutation	prognosis	NGS (DNA), CMA, FISH
	Gain of chromosome 7	chromosomal abnormality (gain of 7)	prognosis	CMA
	10q loss	chromosomal abnormality (loss of 10)	prognosis	CMA
	High tumor mutational burden	mutations	diagnosis, therapeutic (immunotherapy), familial cancer risk if germline alterations in mismatch repair pathway	NGS (DNA)

Oligodendroglioma	***IDH1/2***	**mutation**	**diagnosis**	**NGS (DNA)**
	1p/19q codeletion	chromosomal abnormality (loss of 1p and 19q)	diagnosis	CMA, FISH
Ependymoma	*c11orf95-RELA, YAP1*	Fusions	diagnosis, prognosis	NGS (RNA or DNA)
	1q gain	chromosomal abnormality (gain of 1p)	prognosis	CMA, FISH
Medulloblastoma, WNT-activated	*CTNNB1*	mutation	Subtype- prognosis	NGS (DNA)
	Monosomy 6	chromosomal abnormality (loss)	Subtype-diagnosis	CMA, FISH
	DDX3X	mutation	diagnosis	NGS (DNA)
Medulloblastoma, SHH-activated	*PTCH1*	inactivating mutation, LOH	Subtype-diagnosis, familial cancer risk if germline	NGS (DNA), CMA
	SUFU	inactivating mutation, LOH	Subtype-diagnosis, familial cancer risk if germline	NGS (DNA), CMA
	TP53	Loss-of-function (LOF) and gain-of-function mutations, loss, LOH, structural alterations (rare)	prognosis	NGS (DNA), CMA
	10q loss or LOH	chromosomal abnormality (loss or LOH)	diagnosis	CMA, FISH
	TERT promoter	mutation	diagnosis	NGS (DNA)
	MYCN	amplification	diagnosis, prognosis	FISH, CMA, NGS (DNA)
Medulloblastoma, Group 3	*Isochromosome 17q*	chromosomal abnormality (loss of 17p and gain of 17q)	Subtype-diagnosis	CMA, FISH
	MYC	Amplification, fusion (PVT1)	prognosis	CMA, FISH
Medulloblastoma, Group 4	*Isochromosome 17q*	chromosomal abnormality (loss of 17p and gain of 17q)	Subtype-diagnosis	CMA, FISH
	MYCN	amplification	diagnosis, prognosis	FISH, CMA, NGS
	KDM6A	inactivating mutation	diagnosis	NGS (DNA)
Spindle Cell Sarcoma with rhabdomyosarcoma-like feature, DICER1 mutant	*DICER1*	sequence variants, deletions	diagnosis, familial cancer risk if germline	NGS (DNA)
Meningioma	*NF2*	Loss-of-function (LOF) and gain-of-function mutations, loss, LOH	diagnosis, familial cancer risk if germline	NGS, CMA, MLPA
Choroid plexus tumors	*TP53*	Loss-of-function (LOF) and gain-of-function mutations, loss, LOH, structural alterations (rare)	diagnosis, familial cancer risk if germline	NGS, CMA, MLPA
ETMR	*C19MC*	amplification and gain	diagnosis, prognosis	CMA, FISH
SEGA	*TSC1/TSC2*	loss-of-function mutation, loss, LOH	diagnosis, familial cancer risk if germline	NGS (DNA)
ATRT	*SMARCB1 (INI1)*	loss or inactivating mutation, loss, LOH	diagnosis, familial cancer risk if germline	NGS, MLPA, IHC