Molecular In My Pocket™…
ONCOLOGY: Pediatric Solid Tumors

Prepared by the Association for Molecular Pathology Training and Education Committee

Tissue Type	Tumor Type	Gene/Biomarker	Alteration	Significance	Primary Assays
Thyroid	Papillary Thyroid Carcinoma	*BRAF*	sequence variant (30%, mostly p.V600E), fusion (10%)	diagnosis, treatment	IHC (BRAF V600E), NGS (DNA, RNA), ddPCR
		RET (30%)	fusion	diagnosis, treatment	NGS (DNA, RNA)
		NTRK1, NTRK3 (10%)	fusion	diagnosis, treatment	IHC (pan-TRK; screening), NGS (DNA, RNA)
		ALK (5%)	fusion	diagnosis, treatment	IHC (ALK; screening), NGS (DNA, RNA), FISH
		HRAS, NRAS (<5%)	sequence variant	diagnosis	NGS (DNA)
		DICER1 (<10%)	sequence variant	familial cancer risk	NGS (DNA)
		TERT	sequence variant	diagnosis, prognosis	NGS (DNA)
		TP53	sequence variant	diagnosis, prognosis	NGS (DNA)
	Cribriform Morular Thyroid Carcinoma	*APC*	loss-of-function variant	diagnosis, familial cancer risk	NGS (DNA)
		CTNNB1	sequence variant, intragenic deletion	diagnosis	NGS (DNA)
	Follicular Thyroid Carcinoma	*PPARG*	fusion (typically with *PAX8*)	diagnosis	NGS (DNA, RNA)
		HRAS, KRAS, NRAS	sequence variant	diagnosis	NGS (DNA)
	With Multiple Adenomas/Adenomatous Nodules	*PTEN*	sequence variant	diagnosis, familial cancer risk	NGS (DNA)
	Medullary Thyroid Carcinoma	*RET* (>95%)	sequence variant	diagnosis, familial cancer risk, treatment	NGS (DNA)
	Non-invasive Follicular Thyroid Neoplasm with Papillary-like Nuclear Features (NIFTP)	*HRAS, KRAS, NRAS*	sequence variant	diagnosis	NGS (DNA)
Lung	Pleuropulmonary Blastoma	*DICER1*	loss-of-function sequence variant or deletion + hotspot sequence variant	diagnosis, familial cancer risk	NGS (DNA)
GI	Gastrointestinal Stromal Tumor	*SDHA, SDHB, SDHC, SDHD*	sequence variant, loss of protein expression	diagnosis, familial cancer risk	IHC (SDHB), NGS (DNA)
Liver	Hepatoblastoma	*CTNNB1* (90%)	activating sequence variant, deletion of exon 3	diagnosis (more common in hepatoblastoma than in hepatocellular carcinoma)	IHC (beta-catenin), NGS (DNA)
	Fibrolamellar Carcinoma	*DNAJB1::PRKACA*	fusion	diagnosis	FISH, NGS (DNA, RNA)
Kidney	Wilms Tumor	1q gain 1p/16q LOH	copy gain LOH	prognosis	CMA, NGS (DNA)
	Clear Cell Sarcoma of Kidney	*BCOR*	internal tandem duplication (ITD)	diagnosis	IHC (BCOR), NGS (DNA, RNA)
		YWHAE	fusion	diagnosis	NGS (DNA, RNA)
	Cellular Congenital Mesoblastic Nephroma	*NTRK3*	fusion (mostly *ETV6::NTRK3*)	diagnosis, treatment	FISH or RT-PCR for classic fusion; NGS (DNA, RNA) for classic or alternate fusions
	Renal Cell Carcinoma with MiT Translocation	*TFE3* (>90%), *TFEB*	fusion	diagnosis	IHC (TFE3, TFEB), FISH, NGS (DNA, RNA)

Kidney *(continued…)*	Metanephric Adenoma	*BRAF*	p.V600E, other exon 15 sequence variant	diagnosis	IHC (BRAF V600E), NGS (DNA), ddPCR
	Rhabdoid Tumor	*SMARCB1* (*INI1*; >90%), *SMARCA4* (*BRG1*)	loss (sequence variant, deletion)	diagnosis, familial cancer risk	IHC (INI1, BRG1), CMA, NGS (DNA), MLPA
	Pediatric Cystic Nephroma	*DICER1*	loss-of-function sequence variant	diagnosis, familial cancer risk	NGS (DNA)
Ovary	Juvenile Granulosa Cell Tumor	*AKT1* (60%)	in-frame duplication, sequence variant	diagnosis	NGS (DNA)
		GNAS (30%)	sequence variant	diagnosis	NGS (DNA)
Eye	Retinoblastoma	*RB1*	inactivating mutation, loss, or LOH	diagnosis, familial cancer risk	MLPA, CMA, NGS (DNA)
Neural Crest	Paraganglioma	*SDHA, SDHB, SDHC, SDHD*	sequence variant, loss of protein expression	diagnosis, familial cancer risk	IHC (SDHB), NGS (DNA)
	Neuroblastoma	*MYCN*	amplification	prognosis	FISH, CMA, NGS (DNA)
		ALK	sequence variant, amplification	prognosis, treatment	NGS (DNA)
		ATRX	loss-of-function sequence variant	prognosis	NGS (DNA)
		1p/11q LOH	LOH	prognosis	CMA, NGS (DNA)
Multi-system	*DICER1* Syndrome	*DICER1*	loss-of-function sequence variant or deletion (germline)	diagnosis, familial cancer risk	NGS (DNA)
	Constitutional Mismatch Repair Deficiency Syndrome (CMMRD)	*MLH1, MSH2, PMS2, MSH6*	loss-of-function sequence variant or deletion (germline, biallelic)	diagnosis, familial cancer risk, treatment	IHC (MLH1, MSH2, PMS2, MSH6), NGS (DNA), MSI
	Gorlin Syndrome	*SUFU, PTCH1*	loss-of-function sequence variant, deletion/duplication (germline)	diagnosis, familial cancer risk	NGS (DNA), CMA, MLPA
	Multiple Endocrine Neoplasia (MEN) 2A/2B	*RET*	gain-of-function sequence variant (germline)	diagnosis, familial cancer risk	NGS (DNA)
	Li-Fraumeni Syndrome	*TP53*	loss-of-function sequence variant (germline)	diagnosis, familial cancer risk	NGS (DNA)

Abbreviations:

CGH Comparative Genomic Hybridization
FISH Fluorescent *in situ* Hybridization
MLPA Multiplex Ligation-dependent Probe Amplification
PCR Polymerase Chain Reaction
CMA Chromosomal Microarray Analysis
IHC Immunohistochemistry
MSI Microsatellite Instability
RT-PCR Reverse Transcription PCR
ddPCR Digital Droplet PCR
LOH Loss of Heterozygosity
NGS Next Generation Sequencing

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