Molecular In My Pocket…

Solid Tumors (Hereditary)

Prepared by the Association for Molecular Pathology
Training and Education Committee

Abbreviations

CA	Carcinoma	GI	Gastrointestinal	MMR	Mismatch Repair	SGA	Single Gene Assay
CGX	Cytogenetics	MEN	Multiple Endocrine Neoplasia	MSI	Microsatellite Instability	TKI	Tyrosine Kinase Inhibitor
IHC	Immunohistochemistry	LOF	Loss of Function	NGS	Next-Generation Sequencing		

Tissue Type	Disease	Gene	Common Genomic Variant(s)	Significance	Primary Assays
Adrenal	Hereditary Paraganglioma / Pheochromocytoma	*SDHA, SDHB, SDHC, SDHD*	LOF	risk of hereditary cancer	IHC, SGAs, NGS
Breast	Hereditary Breast and Ovarian Cancer	*BRCA1 / BRCA2*	LOF	risk of hereditary cancer; responsiveness to PARP inhibitor	SGAs, NGS
Endometrium	Lynch Syndrome	*MLH1, MSH2, MSH6, PMS2* (germline)	LOF	40-60% lifetime risk of endometrial cancer	SGAs, NGS
	Cowden Syndrome	*PTEN*	LOF	25% risk of endometrial cancer development	SGAs, NGS
Eye	Retinoblastoma	*RB1*	LOF	risk of hereditary cancer	SGAs, NGS
GI Tract	Hereditary Diffuse Gastric CA	*CDH1* (E-Cadherin)	LOF	risk of hereditary cancer	SGAs, NGS
	Gastrointestinal Stromal Tumor (GIST)	*SDHA, SDHB, SDHC, SDHD; KIT, PDGFRA*	LOF; Activating	response to TKIs, risk of hereditary cancer	SGAs, NGS, IHC for *SDHB*
	Colorectal CA (Lynch Syndrome)	Most commonly *MLH1, MSH2, MSH6, PMS2, EPCAM*	LOF	risk of hereditary cancer; prognosis, responsiveness to immunotherapy	MMR IHC, NGS
		MSI testing	MSI-High, Low, or Stable	risk of hereditary cancer; prognosis, responsiveness to immunotherapy	MSI testing
	Colorectal CA (FAP)	*APC*	LOF	risk of hereditary cancer	SGAs, NGS
Kidney	Birt-Hogg-Dube syndrome	*FLCN*	LOF	germline diagnosis; risk of hereditary cancer	SGAs, NGS
	Clear Cell Renal Cell CA	*VHL*	3p deletion	germline diagnosis; risk of hereditary cancer	CGX
	Polycystic Kidney Disease (Dominant / Recessive)	*PKD1 / PKHD1*	LOF	germline diagnosis	SGAs, NGS
	Hereditary Leiomyomatosis and Renal Cell CA Syndrome	*FH*	LOF	adverse prognosis; risk of hereditary cancer	IHC, SGAs, NGS
	Renal Cell CA; Von Hippel Lindau Syndrome	*VHL*	LOF	germline diagnosis; risk of hereditary cancer	SGAs, NGS
	Rhabdoid Sarcoma	*SMARCB1* (INI1), *SMARCA4* (BRG1)	LOF	risk of hereditary cancer	IHC, NGS
	Wilms Tumor	*WT1*	LOF	germline diagnosis; risk of hereditary cancer	SGAs, NGS
Ovary	Ovarian CA	*PTEN*	LOF	germline diagnosis; risk of hereditary cancer	SGAs, NGS
	Small cell CA, hypercalcemic type	*SMARCA4* (BRG1)	LOF	diagnosis; risk of hereditary cancer	SGAs, NGS
	Hereditary Breast and Ovarian Cancer	*BRCA1 / BRCA2*	LOF	risk of hereditary cancer; responsiveness to PARP inhibitor	SGAs, NGS
Soft Tissue	Epithelioid Sarcoma	*SMARCB1* (INI1)	LOF	diagnosis, risk of hereditary cancer; responsiveness to tazemetostat	IHC, NGS
Multi-System Syndromes	Cowden Syndrome	*PTEN*	LOF	germline diagnosis; risk of hereditary cancer	SGAs, NGS
	DICER1 Syndrome	*DICER1*	LOF	germline diagnosis; risk of hereditary cancer	SGAs, NGS
	Li-Fraumeni Syndrome	*TP53*	LOF	risk of hereditary cancer	SGAs, NGS
	McCune Albright Syndrome	*GNAS*	SNVs	germline diagnosis; risk of hereditary cancer	SGAs, NGS
	MEN Types 1 / 2A & 2B / 4	*MEN1 / RET / CDKN1B*	SNVs	germline diagnosis; risk of hereditary cancer	SGAs, NGS
	Neurofibromatosis	*NF1 / NF2*	LOF	germline diagnosis; risk of hereditary cancer	SGAs, NGS
	Peutz-Jeghers Syndrome	*STK11*	LOF	germline diagnosis; risk of hereditary cancer	SGAs, NGS
	Tuberous Sclerosis	*TSC1 / TSC2*	LOF	germline diagnosis; risk of hereditary cancer	SGAs, NGS

Revised 7/2023