Molecular In My Pocket™...

ONCOLOGY: *Breast Cancer*

Tumor Group	Gene/Biomarker	Alterations	Indications	Result Interpretation/Significance	Assay Techniques
Invasive Ductal/Lobular Carcinoma	*BRCA1/2***	Inactivating variants	Germline testing, therapeutic	Hereditary breast cancer, predicts response to PARP-inhibitors	CMA, MLPA, NGS, PCR, Sanger
	*CDH1***	Inactivating variants	Germline testing, diagnostic	Inactivated in lobular carcinomas (*in-situ* and invasive), germline pathogenic variants associated with susceptibility to ILC and hereditary diffuse gastric cancer	CMA, IHC (E-cadherin), MLPA, NGS, PCR, Sanger
	ERBB2	Amplification, activating variants	Therapeutic	Molecular/intrinsic subtype classification, predicts response to anti-HER2 therapies	FISH, IHC, NGS
	ER/PR	Increased expression	Prognostic, therapeutic	Molecular/intrinsic subtype classification, predicts response to endocrine therapy	IHC
	IDH2	p.Arg172 hotspot variants	Diagnostic, possibly therapeutic in the future	Associated with tall cell carcinoma with reversed polarity	NGS, PCR, Sanger
	PIK3CA	Activating variants	Therapeutic	Predicts response to alpelisib; enriched in luminal A tumors	NGS, PCR, Sanger
	*PTEN***	Inactivating variants	Germline testing	Cowden syndrome	CMA, MLPA, NGS, PCR, Sanger
	*STK11***	Inactivating variants	Germline testing	Peutz-Jeghers syndrome	CMA, MLPA, NGS, PCR, Sanger
	*TP53***	Inactivating variants	Germline testing	Li-Fraumeni syndrome, enriched in basal-like tumors	CMA, MLPA, NGS, PCR, Sanger
Salivary Gland-Type Neoplasms	*CRTC1::MAML2* *CRTC3:MAML2*	Fusion	Diagnostic	Associated with mucoepidermoid carcinoma	FISH, NGS, RT-PCR
	ETV6::NTRK3	Fusion	Diagnostic, therapeutic	Associated with secretory carcinoma, predicts response to larotrectinib and entrectinib	FISH, IHC (pan-TRK), NGS, RT-PCR
	HMGA2 or *PLAG1*	Fusion	Diagnostic	Associated with pleomorphic adenoma	FISH, IHC (HMGA2, PLAG1), NGS, RT-PCR
	HRAS	p.Gly12, p.Gly13, p.Gln61 hotspot variants	Diagnostic, possibly therapeutic in the future	Associated with adenomyoepithelioma	IHC, NGS, PCR, Sanger
	MYB::NFIB and *MYBL1::NFIB*	Fusion	Diagnostic	Associated with adenoid cystic carcinoma	FISH, IHC/ISH (MYB), NGS, RT-PCR

Mesenchymal Neoplasms	*ALK*	Fusions	Diagnostic, therapeutic	Associated with inflammatory myofibroblastic tumor	IHC, FISH, NGS, RT-PCR
	CTNNB1	Activating variants	Diagnostic	Associated with desmoid fibromatosis	IHC, NGS, PCR, Sanger
	EWSR1::DDIT3 and FUS::DDIT3	Fusion	Diagnostic	Associated with myxoid round cell liposarcoma	FISH, NGS, RT-PCR
	MDM2 or *CDK4*	Amplification	Diagnostic	Associated with well-differentiated liposarcoma and de-differentiated liposarcoma	FISH, NGS
	MYC	Amplification	Diagnostic	Associated with postradiation angiosarcoma	IHC, FISH, NGS
	TERT	Promoter variants	Diagnostic	Presence favors phyllodes tumor over fibroadenoma (both with *MED12* mutations)	NGS, PCR, Sanger
	USP6	Fusions	Diagnostic	Associated with nodular fasciitis	FISH, NGS, RT-PCR
	13q14	Deletion	Diagnostic	Associated with myofibroblastoma	FISH
Tumor-Agnostic Molecular Markers	Microsatellite instability (MSI)/mismatch repair (MMR) deficiency	Loss of MLH1, PMS2, MSH2, MSH6 expression and/or MSI-high status	Germline testing, therapeutic	Lynch syndrome, predicts response to immune checkpoint inhibitor (pembrolizumab; for unresectable/metastatic tumors)	IHC, PCR, NGS
	Tumor mutational burden (TMB)	SNVs and indels	Therapeutic	TMB ≥ 10 variants/Mb eligible for immune checkpoint inhibitor (pembrolizumab for unresectable/metastatic tumors)	NGS

*Legend: ** - germline risk factor; CMA - chromosomal microarray; FISH - fluorescence in situ hybridization; IHC - immunohistochemistry; indel - insertion-deletion; ISH - in-situ hybridization; LCIS - lobular carcinoma in situ; ILC - invasive lobular carcinoma; MLPA - multiplex ligation-dependent probe amplification; MMR - mismatch repair; MSI - microsatellite instability; NGS - next-generation sequencing; PARP - poly(ADP-ribose) polymerase; PCR - polymerase chain reaction; RT-PCR - reverse transcription polymerase chain reaction; SNV - single nucleotide variant*

Multi-Gene Expression Assays

Tumor Requirements	Assay Name	Assay Composition	Assay Results	Therapeutic Value	Prognostic Value
HR-positive, HER2-negative, 0-3 positive LNs, early stage IBC	Oncotype DX	16 cancer-related genes and 5 reference genes	Recurrence score (RS; 0-100)	Predictive for benefit of chemotherapy added to endocrine therapy	Prognostic for recurrence risk
	MammaPrint/BluePrint	70 genes (Mammaprint) and/or 80 genes (BluePrint)	MammaPrint index (MPI; -1.0 to +1.0) and low/high risk of recurrence; BluePrint molecular subtype result	Not determined	Prognostic for recurrence risk
	Prosigna	50 test genes and 8 housekeeping genes plus tumor size and nodal status	Risk of recurrence (ROR; 0-100)	Not determined	Prognostic for recurrence risk
	Breast Cancer Index	Ratio between *HOXB13:IL17BR* plus expression of 5 cell cycle-related genes	BCI Prognostic - low/high risk of recurrence; BCI Predictive - low/high likelihood of benefit	Predictive for extended endocrine therapy (beyond 5 years)	Prognostic for recurrence risk
	EndoPredict	8 target genes, 3 normalization genes, 1 control gene plus tumor size and nodal status	EPclin risk score (1.0-6.0), percent likelihood distant recurrence	Not determined	Prognostic for recurrence risk

Legend: HR - hormone receptor; IBC - invasive breast cancer; LN - lymph node