Comprehensive Tumor Profiling for New York State

CARIS LIFE SCIENCES

Caris Life Sciences' comprehensive molecular profiling approach to assess DNA, RNA and proteins reveals a molecular blueprint to guide more precise and individualized treatment decisions from among 60+ FDA-approved therapies.

DNA

Whole Exome Sequencing

SNVs, Indels & Copy Number Alterations

RNA

Whole Transcriptome Sequencing

Fusions & Variant Transcripts

Protein

Immunohistochemistry

Technical Specifications

Sufficient tumor content (>20% tumor nuclei) must be present to complete all analyses. If you have any questions, please contact Customer Support at (888) 979-8669.

Technical Information	IHC	CISH
Sample Requirements *(see requisition for full details)*	1 unstained slide at 4µm thickness from FFPE block, with evaluable tumor present, per IHC test	1 unstained slide at 4µm thickness from FFPE block, with at least 100 evaluable tumor cells present, per CISH test
Sensitivity/Specificity	>95%	>95%

Technical Information	NGS (Whole Exome – DNA)	NGS (Whole Transcriptome – RNA)
Sample Requirements	FFPE block or 10 unstained slides with a minimum of 20% malignant origin for DNA and 10% malignant origin for RNA. Needle biopsy is also acceptable (4-6 cores).	
Tumor Enrichment (when necessary)	Microdissection to isolate and increase the number of cancer cells to improve test performance and increase the chance for successful testing from small tumor samples	
Number of Genes	~22,000 genes	
Average Depth of Coverage (DNA) **Average Read Count (RNA)**	1,000x for 719+ clinical and research genes and 400-500x for all other genes	60 million
Positive Percent Agreement (PPA)	>95% for base substitutions at ≥ 5% mutant allele frequency; >99% for indels at ≥ 5% mutant allele frequency; >95% for copy number alterations (amplifications ≥ 6 copies)	>97%
Negative Percent Agreement (NPA)	>99%	>99%
Genomic Signatures	Loss of Heterozygosity (LOH) Microsatellite Instability (MSI) Tumor Mutational Burden (TMB)	

Caris Molecular Profiling Associations List

The list below details the biomarkers assessed, technology platforms utilized and associated therapies or clinical trials. **Biomarkers and therapy associations may vary by the tumor type submitted.** *Individual assay results are always included with the final report.*

Biomarker	Technology/Alteration	Agent
ALK	IHC, RNA Fusion	crizotinib, ceritinib, alectinib, brigatinib (NSCLC only), lorlatinib (NSCLC only)
	DNA Mutation	resistance to crizotinib, alectinib
AR	IHC	bicalutamide, leuprolide (salivary gland tumors only)
		enzalutamide, bicalutamide (TNBC only)
BRAF	DNA Mutation	vemurafenib, dabrafenib, cobimetinib, trametinib
		encorafenib + binimetinib (melanoma only)
		dabrafenib+trametinib (anaplastic thyroid and NSCLC only)
		atezolizumab + cobimetinib + vemurafenib (melanoma only)
		cetuximab + encorafenib (CRC only)
BRCA1/2	DNA Mutation, DNA Deletion	carboplatin, cisplatin, oxaliplatin
		niraparib (ovarian, prostate), olaparib (breast, cholangiocarcinoma, ovarian, pancreatic, prostate), rucaparib (ovarian, pancreatic, prostate), talazoparib (breast only), veliparib combination (pancreatic only)
		resistance to olaparib, niraparib, rucaparib with reversion mutation
COL1A1-PDGFB	RNA Fusion	imatinib (DFSP only)
EGFR	DNA Mutation	afatinib (NSCLC and CUP only)
		afatinib + cetuximab (T790M; NSCLC only)
		amivantamab, mobocertinib (Exon 20 insertion; NSCLC only)
		erlotinib, gefitinib (NSCLC and CUP only)
		osimertinib, dacomitinib (NSCLC and CUP only)
ER	IHC	endocrine therapies
		everolimus (breast only)
		palbociclib, ribociclib, abemaciclib (breast only)
ERBB2 (HER2)	IHC, CISH, DNA Mutation, CNA	trastuzumab, lapatinib, neratinib (breast only), pertuzumab, T-DM1, fam-trastuzumab deruxtecan-nxki, tucatinib, margetuximab
	DNA Mutation	T-DM1 (NSCLC only)
ER/PR/ERBB2 (HER2)	IHC, CISH	sacituzumab govitecan (TNBC only)
ESR1	DNA Mutation	exemestane + everolimus, fulvestrant, palbociclib combination therapy (breast only)
		resistance to aromatase inhibitors (breast only)
FGFR2/3	DNA Mutation, RNA Fusion	erdafitinib (urothelial bladder only), pemigatinib, infigratinib (biliary tract cancers only)
HRR	DNA Mutation, DNA Deletion	olaparib (prostate only)
IDH1	DNA Mutation	temozolomide (glioma only)
		ivosidenib (biliary tract cancers only)
KIT	DNA Mutation	imatinib
		regorafenib, sunitinib (both GIST only)
KRAS	DNA Mutation	resistance to cetuximab, panitumumab (CRC only)
		resistance to erlotinib/gefitinib (NSCLC only)
		resistance to trastuzumab, lapatinib, pertuzumab (CRC only)
		sotorasib (G12C-mutated, NSCLC only)
LOH (Genomic)	DNA Mutation	rucaparib (ovarian only)
MET	RNA Exon Skipping, DNA Exon Skipping, CNA	capmatinib, crizotinib, tepotinib (all NSCLC only)
MGMT	Pyrosequencing (Methylation)	temozolomide (glioma only)
MMR Deficiency	IHC, DNA Mutation	pembrolizumab, dostarlimab (pan-tumors)
MSI		pembrolizumab, nivolumab (CRC, small bowel adenocarcinoma), nivolumab+ipilimumab (CRC, small bowel adenocarcinoma)
MMR Proficiency	IHC, DNA Mutation	pembrolizumab + lenvatinib (endometrial only)
MSS		
NF1	DNA Mutation	selumetinib (neurofibroma only)
NRAS	DNA Mutation	resistance to cetuximab, panitumumab (CRC only)
		resistance to trastuzumab, lapatinib, pertuzumab (CRC only)
NTRK1/2/3	RNA Fusion	entrectinib, larotrectinib
	DNA Mutation	resistance to larotrectinib, entrectinib
PALB2	DNA Mutation	olaparib (pancreatic and prostate), veliparib combination (pancreatic only)
PDGFRA	DNA Mutation	imatinib, avapritinib (GIST only), sunitinib
PD-L1	IHC	pembrolizumab (22c3 TPS in NSCLC; 22c3 CPS in cervical, esophageal, head & neck, urothelial and non-urothelial bladder, vulvar)
		atezolizumab (SP142 IC urothelial bladder cancer; SP142 IC & TC, SP263 TC NSCLC)
		pembrolizumab + chemotherapy (22c3 CPS in TNBC only)
		nivolumab/ipilimumab combination (28-8 NSCLC only)
		nivolumab (28-8 gastric/GEJ only)
		cemiplimab (22c3 TPS NSCLC only)
PIK3CA	DNA Mutation	alpelisib + fulvestrant (breast only)
POLE	DNA Mutation	pembrolizumab (endometrial and CRC only)
PR	IHC	endocrine therapies
RET	RNA Fusion	cabozantinib, vandetanib, selpercatinib, pralsetinib (NSCLC only)
	DNA Mutation	vandetanib, cabozantinib, selpercatinib (thyroid only); resistance to vandetanib, cabozantinib
ROS1	IHC, RNA Fusion	crizotinib, ceritinib, entrectinib, lorlatinib (NSCLC only)
TMB	DNA Mutation	pembrolizumab
VHL	DNA Mutation	belzutifan (renal cell carcinoma, CNS hemangioblastomas, pancreatic neuroendocrine tumors)

IHC: Immunohistochemistry **CISH:** Chromogenic in situ Hybridization **CNA:** Copy Number Alteration (DNA)
HRR (Homologous Recombination Repair) genes: ATM, BARD1, BRCA1, BRCA2, BRIP1, CDK12, CHEK1, CHEK2, FANCL, PALB2, RAD51B, RAD51C, RAD51D, RAD54L
Note: in certain instances, some biomarkers included in MI Profile or genes ordered individually will not associate with commercially available cancer therapies or clinical trials.

Biomarker Analysis by Tumor Type

The information below details the biomarkers analyzed by technology for the tumor type submitted. Before ordering testing services, please refer to the profile menu online (www.CarisLifeSciences.com/profiling-menu) to view the most up-to-date listing of biomarkers that will be performed. Tests may vary if insufficient tumor samples are submitted.

MI Profile™					
Tumor Type	**Immunohistochemistry (IHC)**	**Other**	**MI Tumor Seek™**		
			Whole Exome Sequencing (WES)		**Whole Transcriptome Sequencing (WTS)**
			DNA Alterations	**Genomic Signatures**	**RNA Alterations**
Bladder	MMR, PD-L1 (SP142 and 22c3)		Mutations, Indels, CNA	LOH, MSI, TMB	Fusions, Variant Transcripts
Breast	AR, ER, Her2/Neu, MMR, PD-L1 (22c3), PR, PTEN		Mutations, Indels, CNA	LOH, MSI, TMB	Fusions, Variant Transcripts
Cancer of Unknown Primary – Female	AR, ER, Her2/Neu, MMR, PD-L1(SP142)		Mutations, Indels, CNA	LOH, MSI, TMB	Fusions, Variant Transcripts
Cancer of Unknown Primary – Male	AR, Her2/Neu, MMR, PD-L1 (SP142)		Mutations, Indels, CNA	LOH, MSI, TMB	Fusions, Variant Transcripts
Cervical	ER, MMR, PD-L1 (22c3), PR		Mutations, Indels, CNA	LOH, MSI, TMB	Fusions, Variant Transcripts
Cholangiocarcinoma/ Hepatobiliary	Her2/Neu, MMR, PD-L1 (SP142)	Her2 *(Chromogenic in situ Hybridization)*	Mutations, Indels, CNA	LOH, MSI, TMB	Fusions, Variant Transcripts
Colorectal and Small Intestinal	Her2/Neu, MMR, PD-L1 (SP142), PTEN		Mutations, Indels, CNA	LOH, MSI, TMB	Fusions, Variant Transcripts
Endometrial	ER, MMR, PD-L1 (SP142), PR, PTEN		Mutations, Indels, CNA	LOH, MSI, TMB	Fusions, Variant Transcripts
Esophageal Cancer	Her2/Neu, MMR, PD-L1 (22c3)	EBER *(Chromogenic in situ Hybridization)*	Mutations, Indels, CNA	LOH, MSI, TMB	Fusions, Variant Transcripts
Gastric/GEJ	Her2/Neu, MMR, PD-L1 (28-8)	EBER, Her2 *(Chromogenic in situ Hybridization)*	Mutations, Indels, CNA	LOH, MSI, TMB	Fusions, Variant Transcripts
GIST	MMR, PD-L1 (SP142), PTEN		Mutations, Indels, CNA	LOH, MSI, TMB	Fusions, Variant Transcripts
Glioma	MMR, PD-L1 (SP142)	MGMT Methylation *(Pyrosequencing)*	Mutations, Indels, CNA	LOH, MSI, TMB	Fusions, Variant Transcripts
Head & Neck	MMR, p16, PD-L1 (22c3)	EBER, HPV *(Chromogenic in situ Hybridization)*, HPV reflex to confirm p16 result	Mutations, Indels, CNA	LOH, MSI, TMB	Fusions, Variant Transcripts
Kidney	MMR, PD-L1 (SP142)		Mutations, Indels, CNA	LOH, MSI, TMB	Fusions, Variant Transcripts
Lymphoma/Leukemia			Mutations, Indels, CNA	TMB	Fusions, Variant Transcripts
Melanoma	MMR, PD-L1 (SP142)		Mutations, Indels, CNA	LOH, MSI, TMB	Fusions, Variant Transcripts
Merkel Cell	MMR, PD-L1 (SP142)		Mutations, Indels, CNA	LOH, MSI, TMB	Fusions, Variant Transcripts
Neuroendocrine	MMR, PD-L1 (SP142)		Mutations, Indels, CNA	LOH, MSI, TMB	Fusions, Variant Transcripts
Non-Small Cell Lung	ALK, MMR, PD-L1 (22c3, 28-8, SP263 and SP142)		Mutations, Indels, CNA	LOH, MSI, TMB	Fusions, Variant Transcripts
Ovarian	ER, MMR, PD-L1 (22c3), PR		Mutations, Indels, CNA	LOH, MSI, TMB	Fusions, Variant Transcripts
Pancreatic	MMR, PD-L1 (SP142)		Mutations, Indels, CNA	LOH, MSI, TMB	Fusions, Variant Transcripts
Prostate	AR, MMR, PD-L1 (SP142)		Mutations, Indels, CNA	LOH, MSI, TMB	Fusions, Variant Transcripts
Salivary Gland	AR, Her2/Neu, MMR, PD-L1 (SP142)		Mutations, Indels, CNA	LOH, MSI, TMB	Fusions, Variant Transcripts
Sarcoma	MMR, PD-L1 (SP142)		Mutations, Indels, CNA	LOH, MSI, TMB	Fusions, Variant Transcripts
Small Cell Lung	MMR, PD-L1(22c3)		Mutations, Indels, CNA	LOH, MSI, TMB	Fusions, Variant Transcripts
Thyroid	MMR, PD-L1 (SP142)		Mutations, Indels, CNA	LOH, MSI, TMB	Fusions, Variant Transcripts
Uterine Serous	ER, Her2/Neu, MMR, PD-L1 (SP142), PR, PTEN	Her2 *(Chromogenic in situ Hybridization)*	Mutations, Indels, CNA	LOH, MSI, TMB	Fusions, Variant Transcripts
Vulvar Cancer (SCC)	ER, MMR, PD-L1 (22c3), PR		Mutations, Indels, CNA	LOH, MSI, TMB	Fusions, Variant Transcripts
Other Tumors	MMR, PD-L1 (SP142)		Mutations, Indels, CNA	LOH, MSI, TMB	Fusions, Variant Transcripts

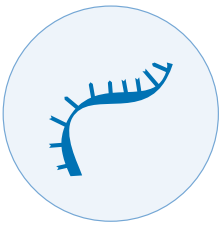
MMR = Mismatch Repair proteins: MLH1, MSH2, MSH6, PMS2

Caris Molecular Testing – Complete Gene Coverage

As the pioneer in precision medicine, Caris was the first to provide WES and WTS for every patient. All molecular profiling orders include next-generation sequencing of all 22,000 genes.

Whole Exome Sequencing (WES) DNA

- 22,000 genes
- 1,000x for 719+ clinical and research genes and 500x for all other genes
- SNVs, indels, and copy number alterations
- 250,000 evenly-spaced genomic SNP
- Genomic signatures:
  - Loss of Heterozygosity (LOH)
  - Microsatellite Instability (MSI)
  - Tumor Mutational Burden (TMB)



Whole Transcriptome Sequencing (WTS) RNA

- 22,000 genes
- 60 million read count
- Gene fusions and variant transcripts
- Novel translocation detection independent of intronic breakpoint

Gene List

Listed below are the genes most commonly associated with cancer. Full 22,000 genes search is available on CarisLifeSciences.com.

ABL1	*BCR*	*CSF1R*	*FANCC*	*GNAQ*	*LZTR1*	*MUTYH*	*PIK3CB*	*RAD51D*	*SOCS1*
ABL	*BLM*	*CTNNA1*	*FANCD2*	*GNAS*	*MAML2*	*MYB*	*PIK3R1*	*RAD54L*	*SPEN*
ACVR1	*BMPR1A*	*CTNNB1*	*FANCE*	*H3F3A*	*MAP2K1*	*MYC*	*PIK3R2*	*RAF1*	*SPOP*
AIP	*BRAF*	*CXCR4*	*FANCF*	*H3F3B*	*MAP2K2*	*MYCN*	*PIM1*	*RASA1*	*SRC*
AKT1	*BRCA1*	*CYLD*	*FANCG*	*HDAC1*	*MAP2K4*	*MYD88*	*PKN1*	*RB1*	*SSBP1*
AKT2	*BRCA2*	*CYP17A1*	*FANCI*	*HIST1H3B*	*MAP3K1*	*NBN*	*PMS1*	*RELA*	*STAG2*
AKT3	*BRD3*	*DDR2*	*FANCL*	*HIST1H3C*	*MAPK1*	*NF1*	*PMS2*	*RET*	*STAT3*
ALK	*BRD4*	*DICER1*	*FANCM*	*HNF1A*	*MAPK3*	*NF2*	*POLD1*	*RHOA*	*STK11*
AMER1	*BRIP1*	*DNMT3A*	*FAS*	*HOXB13*	*MAST1*	*NFE2L2*	*POLD2*	*RNF43*	*SUFU*
APC	*BTK*	*EGFR*	*FAT1*	*HRAS*	*MAST2*	*NFKBIA*	*POLD3*	*ROS1*	*TERT*
AR	*CALR*	*EGFR vIII*	*FBXW7*	*IDH1*	*MAX*	*NOTCH1*	*POLD4*	*RPA1*	*TET2*
ARAF	*CARD11*	*EGLN1*	*FGFR1*	*IDH2*	*MED12*	*NOTCH2*	*POLE*	*RPA2*	*TFE3*
ARHGAP26	*CASP8*	*ELF3*	*FGFR2*	*INSR*	*MEF2B*	*NPM1*	*POLQ*	*RPA3*	*TFEB*
ARHGAP35	*CBFB*	*EP300*	*FGFR3*	*IRF4*	*MEN1*	*NRAS*	*POT1*	*RPA4*	*THADA*
ARID1A	*CCND1*	*EPHA2*	*FGFR4*	*JAK1*	*MET*	*NRG1*	*PPARG*	*RSPO2*	*TMEM127*
ARID2	*CCND2*	*ERBB2*	*FGR*	*JAK2*	*MET Exon 14 Skipping*	*NSD1*	*PPP2R1A*	*RSPO3*	*TMPRSS2*
AR-V7	*CCND3*	*ERBB3*	*FH*	*JAK3*	*MGA*	*NTHL1*	*PPP2R2A*	*RUNX1*	*TNFAIP3*
ASXL1	*CD274*	*ERBB4*	*FLCN*	*KDM5C*	*MGMT*	*NTRK1*	*PRDM1*	*SDHA*	*TNFRSF14*
ATM	*CD79B*	*ERCC2*	*FLT1*	*KDM6A*	*MITF*	*NTRK2*	*PRKACA*	*SDHAF2*	*TP53*
ATR	*CDC73*	*ERG*	*FLT3*	*KDR*	*MLH1*	*NTRK3*	*PRKAR1A*	*SDHB*	*TRAF7*
ATRX	*CDH1*	*ESR1*	*FLT4*	*KEAP1*	*MLH3*	*NUMBL*	*PRKCA*	*SDHC*	*TSC1*
AXIN1	*CDK12*	*ETV1*	*FOXA1*	*KIF1B*	*MPL*	*NUTM1*	*PRKCB*	*SDHD*	*TSC2*
AXIN2	*CDK4*	*ETV4*	*FOXL2*	*KIT*	*MRE11*	*PALB2*	*PTCH1*	*SETD2*	*U2AF*
AXL	*CDK6*	*ETV5*	*FUBP1*	*KLF4*	*MSH2*	*PARP1*	*PTEN*	*SF3B1*	*VHL*
B2M	*CDKN1B*	*ETV6*	*FYN*	*KMT2A*	*MSH3*	*PBRM1*	*PTPN11*	*SMAD2*	*WRN*
BAP1	*CDKN2A*	*EWSR1*	*GALNT12*	*KMT2C*	*MSH6*	*PCNA*	*RABL3*	*SMAD4*	*WT1*
BARD1	*CHEK1*	*EXO1*	*GATA3*	*KMT2D*	*MSMB*	*PDGFRA*	*RAC1*	*SMARCA4*	*XPO1*
BCL2	*CHEK2*	*EZH2*	*GLI2*	*KRAS*	*MST1R*	*PDGFRB*	*RAD50*	*SMARCB1*	*XRCC1*
BCL9	*CIC*	*FANCA*	*GNA11*	*LCK*	*MTOR*	*PHOX2B*	*RAD51B*	*SMARCE1*	*XRCC2*
BCOR	*CREBBP*	*FANCB*	*GNA13*	*LYN*	*MUSK*	*PIK3CA*	*RAD51C*	*SMO*	*YES1*

To order or learn more, visit **www.CarisLifeSciences.com.**
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