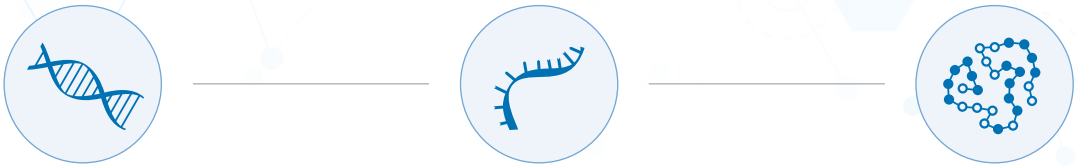
Comprehensive Tumor Profiling

CARIS LIFE SCIENCES

Caris Life Sciences' comprehensive molecular profiling approach to assess DNA, RNA and proteins reveals a molecular blueprint to help guide more precise and individualized treatment decisions.



DNA

Whole Exome Sequencing

SNVs, Indels, CNAs, Karyotyping, Viruses**

RNA

Whole Transcriptome Sequencing

*Gene Fusions, Variant Transcripts, Gene Expression**

Protein

Immunohistochemistry

Tumor-Relevant Protein Biomarkers

Technical Specifications

Sufficient tumor content (≥20% tumor nuclei) must be present to complete all analyses.

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	≥20% tumor nuclei. Accepted specimen types: FFPE block, unstained slides, core needle biopsy, fine needle aspirate, malignant fluid cell block, bone/bone metastasis. See *Tumor Profiling Requisition* for complete details.	
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	23,000+ genes	23,000+ genes
Average Depth of Coverage (DNA) **Average Read Count (RNA)**	1,500x for clinical genes	18 million reads
Positive Percent Agreement (PPA)	>97% for base substitutions at ≥ 5% mutant allele frequency; >97% for indels at ≥ 5% mutant allele frequency; >95% for copy number alterations (amplifications ≥ 6 copies)	>96%
Negative Percent Agreement (NPA)	>99%	>99%
Alterations	SNVs, Indels, CNAs, Karyotyping,* Viruses*	Fusions, Variant Transcripts, Gene Expression*
Viruses*	HPV 16 & 18 (Head & Neck, Anal, Genital, CUP)	
Genomic Signatures/Other	Genomic Loss of Heterozygosity (gLOH) Homologous Recombination Deficiency (HRD)* Microsatellite Instability (MSI) Tumor Mutational Burden (TMB) Human Leukocyte Antigen (HLA) Genotype*	
	Caris FOLFIRSTai™* Caris GPSai™*	

** Not available in all locations.*

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)
BRAF	DNA Mutation	vemurafenib, dabrafenib, cobimetinib, trametinib
		encorafenib + binimetinib (melanoma only)
		dabrafenib+trametinib
		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
CLDN18	IHC	zolbetuximab (gastric/GEJ only)
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, CNA	trastuzumab, lapatinib, neratinib (breast only), pertuzumab, T-DM1, fam-trastuzumab deruxtecan-nxki, tucatinib, margetuximab
	DNA Mutation	fam-trastuzumab deruxtecan-nxki, T-DM1 (NSCLC only)
ER/PR/ERBB2 (HER2)	IHC, CISH	sacituzumab govitecan
ESR1	DNA Mutation	elacestrant
FGFR2/3	DNA Mutation, RNA Fusion	erdafitinib (urothelial bladder only), pemigatinib, infigratinib (biliary tract cancers only), futibatinib (intrahepatic cholangiocarcinoma only)
FOLR1	IHC	mirvetuximab soravtansine (epithelial ovarian only)
gLOH (Genomic)	DNA Mutation	rucaparib (ovarian only)
HLA Genotype*	DNA Mutation	tebentafusp (uveal melanoma)
HRD*	DNA Mutation	niraparib, olaparib, rucaparib (epithelial ovarian 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, ripretinib, sunitinib (GIST only)
KRAS	DNA Mutation	resistance to cetuximab, panitumumab (CRC only)
		resistance to erlotinib/gefitinib (NSCLC only)
		sotorasib, adagrasib (G12C-mutated, NSCLC only)
		binimetinib, trametinib (low grade serous ovarian cancer only)
MEK1/2	DNA Mutation	resistance to BRAF and MEK inhibitor monotherapy
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)
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 & 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, CRC, small bowel adenocarcinoma 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) **HRD:** Homologous Recombination Deficiency
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.

Tumor Profiling Menu

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.

	WES	WTS	IHC/Other	AI Signatures
MI Profile™ Comprehensive Testing MI Tumor Seek Hybrid™ + IHCs and Other Tests by Tumor Type: Tissue-based WES and WTS analysis, plus additional tumor-type relevant biomarker testing (see below).	✔	✔	✔	✔
Next-Generation Sequencing Only MI Tumor Seek Hybrid™: Tissue-based WES and WTS analysis. Caris FOLFIRSTai™ reported for mCRC cases.	✔	✔	–	✔

AI-Powered Molecular Signatures

Caris GPSai™*
Cancer type similarity assessment that is intended to help identify the tumor of origin by comparing the molecular characteristics of the patient's tumor against other tumors in the Caris database.

Caris FOLFIRSTai™*
Chemotherapy response predictor that is intended to gauge a mCRC patient's likelihood of benefit from first-line FOLFOX+BV followed by FOLFIRI+BV, versus FOLFIRI+BV followed by FOLFOX+BV treatment.

Other Testing by Tumor Type

Tumor Type	Immunohistochemistry (IHC)	Other
Bladder	MMR, PD-L1 (22c3)	
Breast	AR, ER, Her2/Neu, PD-L1 (22c3), PR, PTEN	
Cancer of Unknown Primary – Female	AR, ER, Her2/Neu, MMR, PD-L1 (SP142)	
Cancer of Unknown Primary – Male	AR, HER2/Neu, MMR, PD-L1 (SP142)	
Cervical	ER, MMR, PD-L1 (22c3), PR	
Cholangiocarcinoma/ Hepatobiliary	Her2/Neu, MMR, PD-L1 (SP142)	
Colorectal and Small Intestinal	Her2/Neu, MMR, PD-L1 (SP142), PTEN	
Endometrial (all except uterine sarcoma)	ER, Her2/Neu, MMR, PD-L1 (SP142), PR, PTEN	
Esophageal Cancer	Her2/Neu, MMR, PD-L1 (22c3)	
Gastric/GEJ	CLDN18, Her2/Neu, MMR, PD-L1 (28-8)	*EBER* (Chromogenic *in situ* Hybridization)
GIST	MMR, PD-L1 (SP142), PTEN	
Glioma	PD-L1 (SP142)	*MGMT* Methylation (Pyrosequencing)
Head & Neck	MMR, p16, PD-L1 (22c3)	*EBER*, HPV (Chromogenic *in situ* Hybridization), HPV reflex to confirm p16 result
Kidney	MMR, PD-L1 (SP142)	
Lymphoma/Leukemia	–	

Tumor Type	Immunohistochemistry (IHC)	Other
Melanoma	MMR, PD-L1 (SP142)	
Merkel Cell	MMR, PD-L1 (SP142)	
Neuroendocrine	MMR, PD-L1 (SP142)	
Non-Small Cell Lung	ALK†, PD-L1 (22c3, 28-8, SP142, SP263)	
Ovarian	ER, FOLR1‡, MMR, PD-L1 (22c3), PR	
Pancreatic	MMR, PD-L1 (SP142)	
Prostate	AR, MMR, PD-L1 (SP142)	
Salivary Gland	AR, Her2/Neu, MMR, PD-L1 (SP142)	
Sarcoma	MMR, PD-L1 (SP142)	
Small Cell Lung	PD-L1 (22c3)	
Thyroid	MMR, PD-L1 (SP142)	
Uterine Sarcoma	ER, MMR, PD-L1 (SP142), PR, PTEN	
Vulvar Cancer (SCC)	MMR, PD-L1 (22c3)	
Other Tumors	MMR, PD-L1 (SP142)	

MMR = Mismatch Repair proteins: MLH1, MSH2, MSH6, PMS2
†ALK IHC only performed for NSCLC adenocarcinoma
‡FOLR1 IHC and HRD Status only performed for epithelial ovarian cancer.
**Not available in all locations.*

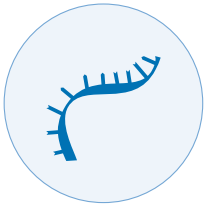
Caris Molecular Testing – Complete Gene Coverage

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 23,000+ genes.

Whole Exome Sequencing (WES) DNA

- 23,000+ genes
- 1,500x for clinical genes
- SNVs, Indels, CNAs & Karyotyping*
- 250,000 evenly-spaced genomic SNP
- Viruses*
- Genomic signatures:
  - Genomic Loss of Heterozygosity (gLOH)
  - Homologous Recombination Deficiency (HRD)*
  - Microsatellite Instability (MSI)
  - Tumor Mutational Burden (TMB)

  Other:
  - HLA Genotype*



Whole Transcriptome Sequencing (WTS) RNA

- 23,000+ genes
- 18 million read count
- Gene fusions, variant transcripts and gene expression*
- Novel translocation detection independent of intronic breakpoint

Gene List

Listed below are the genes most commonly associated with cancer. Full gene 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*

** Not available in all locations.*

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