

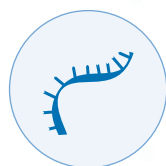
Comprehensive Tumor Profiling

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 <i>(see requisition for full details)</i>	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 <i>Tumor Profiling Requisition</i> 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	22,000+ genes	22,000+ genes
Average Depth of Coverage (DNA) Average Read Count (RNA)	800x for clinical genes	23 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%
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
BRAF	IHC	bicalutamide, leuprolide (salivary gland tumors only)
		vemurafenib, dabrafenib, cobimetinib, trametinib
	DNA Mutation	encorafenib + binimetinib (melanoma only)
		dabrafenib+trametinib
		atezolizumab + cobimetinib + vemurafenib (melanoma 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, mabocertinib (Exon 20 insertion; NSCLC only)
		erlotinib, gefitinib (NSCLC and CUP only)
ER	IHC	osimertinib, dacomitinib (NSCLC and CUP only)
		endocrine therapies
		everolimus (breast only)
ERBB2 (HER2)	IHC, CISH, CNA	palbociclib, ribociclib, abemaciclib (breast only)
	DNA Mutation	trastuzumab, lapatinib, neratinib (breast only), pertuzumab, T-DM1, fam-trastuzumab deruxtecan-nxki, tucatinib, margetuximab
ER/PR/ERBB2 (HER2)	IHC, CISH	fam-trastuzumab deruxtecan-nxki, T-DM1 (NSCLC only)
ESR1	DNA Mutation	sacituzumab govitecan (TNBC only)
		exemestane + everolimus, fulvestrant, palbociclib combination therapy (breast only)
FGFR2/3	DNA Mutation, RNA Fusion	resistance to aromatase inhibitors (breast only)
FOLR1	IHC	erdafitinib (urothelial bladder only), pemigatinib, infigratinib (biliary tract cancers only), futibatinib (intrahepatic cholangiocarcinoma only)
gLOH (Genomic)	DNA Mutation	mirvetuximab soravtansine (epithelial ovarian only)
HLA Genotype*	DNA Mutation	rucaparib (ovarian only)
HRD*	DNA Mutation	tebentafusp (uveal melanoma)
HRR	DNA Mutation, DNA Deletion	niraparib, olaparib, rucaparib (epithelial ovarian only)
IDH1	DNA Mutation	olaparib (prostate only)
		temozolomide (glioma only)
KIT	DNA Mutation	ivosidenib (biliary tract cancers only)
		imatinib
Ki-67	IHC	regorafenib, ripretinib, sunitinib (both GIST only)
		abemaciclib (early stage HR+ HER2- breast cancer only)
KRAS	DNA Mutation	resistance to cetuximab, panitumumab (CRC only)
		resistance to erlotinib/gefitinib (NSCLC only)
		resistance to trastuzumab, lapatinib, pertuzumab (CRC 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)
		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, 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.

MI Tumor Seek Hybrid™ (Next-Generation Sequencing across solid tumors)

Whole Exome Sequencing	Alterations	Genomic Signatures
	SNVs, Indels, CNAs, Karyotyping,* Viruses*	gLOH, HRD**, MSI, TMB, HLA*

Whole Transcriptome Sequencing	Alterations
	Fusions, Variant Transcripts, Gene Expression*

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 (SP142, 22c3)	
Breast	AR, ER, Her2/Neu, Ki-67 [^] , 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)	Her2 (Chromogenic <i>in situ</i> Hybridization)
Colorectal and Small Intestinal	Her2/Neu, MMR, PD-L1 (SP142), PTEN	
Endometrial	ER, MMR, PD-L1 (SP142), PR, PTEN	
Esophageal Cancer	Her2/Neu, MMR, PD-L1 (22c3)	
Gastric/GEJ	Her2/Neu, MMR, PD-L1 (28-8)	<i>EBER</i> , Her2 (Chromogenic <i>in situ</i> Hybridization)
GIST	MMR, PD-L1 (SP142), PTEN	
Glioma	PD-L1 (SP142)	<i>MGMT</i> Methylation (Pyrosequencing)
Head & Neck	MMR, p16, PD-L1 (22c3)	<i>EBER</i> , HPV (Chromogenic <i>in situ</i> 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 Serous	ER, Her2/Neu, MMR, PD-L1 (SP142), PR, PTEN	Her2 (Chromogenic <i>in situ</i> Hybridization)
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.

[^]Ki-67 IHC only for early stage breast cancer.

*Not available in all locations.

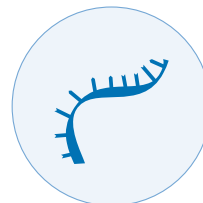
Caris Molecular Testing – Complete Gene Coverage

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 22,000+ genes.



Whole Exome Sequencing (WES) DNA

- 22,000+ genes
- 800x 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

- 22,000+ genes
- 23 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	BRC A1	CYLD	FANCG	HDAC1	MAP2K4	MYD88	PKN1	RB1	SSBP1
AKT2	BRC A2	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	HQXB13	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	RSP02	TMEM127
ARID2	CCND2	ERBB2	FGR	JAK2	MET Exon 14 Skipping	NSD1	PPP2R1A	RSP03	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	MIF	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	MSH4	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.

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