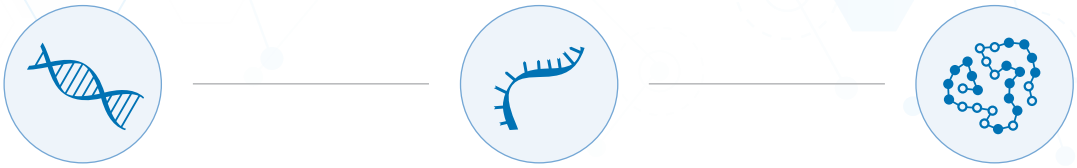
Comprehensive Tumor Profiling

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 *(see requsition 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	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.*

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, MMR, 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 *in situ* 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 (22c3)	*EBER*, Her2 (Chromogenic *in situ* Hybridization)
GIST	MMR, PD-L1 (SP142), PTEN	
Glioma	MMR, 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†, MMR, PD-L1 (22c3, 28-8, SP142, SP263)	
Ovarian	ER, 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	MMR, PD-L1 (22c3)	
Thyroid	MMR, PD-L1 (SP142)	
Uterine Serous	ER, Her2/Neu, MMR, PD-L1 (SP142), PR, PTEN	Her2 (Chromogenic *in situ* 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.

** Not available in all locations.*

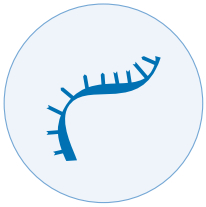
Caris Molecular Testing – Complete Gene Coverage

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	*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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