

## Comprehensive Tumour Profiling

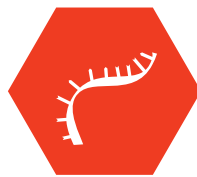
*A better foundation for Molecular Intelligence*

The Caris Molecular Intelligence® comprehensive tumour profiling approach to assess DNA, RNA and proteins reveals a molecular blueprint to guide more precise and individualised treatment decisions from among 50+ FDA-approved therapies.



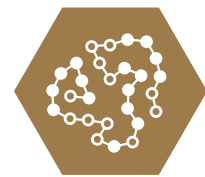
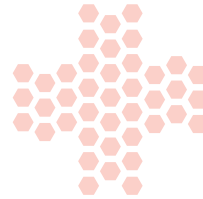
### DNA

Mutations, Indels &  
Copy Number Alterations



### RNA

Fusions & Variant Transcripts



### Protein

Immunohistochemistry

## Technical Specifications

Sufficient tumour must be present to complete all analysis. If you have any questions, please contact our AUS/NZ distributor Precision Oncology on +61 8 6245 2020.

| Technical Information   | IHC   | CISH   | FISH   |
|---|---|--|--|
| <b>Sample Requirements</b><br><i>(see requisition for full details)</i> | 1 unstained slide at 4µm thickness from FFPE block, with evaluable tumour present, per IHC test | 1 unstained slide at 4µm thickness from FFPE block, with at least 20-100 evaluable tumour cells present, per CISH test | 2 unstained slides at 4µm thickness from FFPE block, with at least 100 evaluable cells present and 10% tumour, per FISH test |
| <b>Sensitivity/Specificity</b>  | >95%  | >95%   | >95%   |

| Technical Information  | Next-Generation Sequencing   |  |
|--|--|--|
|  | Mutations and Copy Number Alterations (DNA)  | Fusions (RNA)  |
| <b>Sample Requirements</b>   | FFPE block or 10 unstained slides with a minimum of 20% malignant origin. Needle biopsy is also acceptable (4-6 cores).  | FFPE block or 2-5 unstained slides with a minimum of 20% malignant origin. Needle biopsy is also acceptable (4-6 cores). |
| <b>Tumour Enrichment (when necessary)</b>                                  | Microdissection to isolate and increase the number of cancer cells to improve test performance and increase the chance for successful testing from small tumour samples            |  |
| <b>PPV</b>   | >99%   | >98%   |
| <b>Sensitivity</b>   | > 95% for base substitutions at ≥ 5% mutant allele frequency;<br>> 95% for indels at ≥ 5% mutant allele frequency;<br>>90% for copy number alterations (amplifications ≥ 6 copies) | >97%   |
| <b>Average Depth of Coverage (DNA)</b><br><b>Average Depth/Count (RNA)</b> | >750X  | >30,000 Unique RNA Fragments   |
| <b>Number of Genes</b>   | 592 genes  | 53 genes   |
| <b>Genomic Signatures</b>  | Microsatellite Instability (MSI),<br>Tumour Mutational Burden (TMB)  | -  |

# Biomarker Analysis by Tumour Type

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

| MI Profile™                      |  |  |                          |                 |  |
|----------------------------------|--|--|--------------------------|-----------------|--|
| Tumour Type                      | Immunohistochemistry (IHC)                       | Next-Generation Sequencing (NGS)<br><i>(see reverse for gene list)</i> |                          |                 | Other  |
|                                  |  | DNA  | Genomic Signatures (DNA) | RNA             |  |
| Bladder                          | AR, ER, Her2/Neu, MMR, PD-L1, PR                 | Mutation, CNA Analysis   | MSI, TMB                 | Fusion Analysis |  |
| Breast                           | AR, ER, Her2/Neu, MMR, PD-L1, PR, PTEN, TRKA/B/C | Mutation, CNA Analysis   | MSI, TMB                 | Fusion Analysis | Her2, TOP2A ( <i>Chromogenic in situ Hybridization</i> ) |
| Cancer of Unknown Primary        | ALK, AR, ER, Her2/Neu, MMR, PD-L1, PR, TRKA/B/C  | Mutation, CNA Analysis   | MSI, TMB                 | Fusion Analysis |  |
| Cervical                         | AR, ER, Her2/Neu, MMR, PD-L1, PR, TRKA/B/C       | Mutation, CNA Analysis   | MSI, TMB                 | Fusion Analysis |  |
| Cholangiocarcinoma/Hepatobiliary | AR, ER, Her2/Neu, MMR, PD-L1, PR                 | Mutation, CNA Analysis   | MSI, TMB                 | Fusion Analysis | Her2 ( <i>Chromogenic in situ Hybridization</i> )        |
| Colorectal and Small Intestinal  | AR, ER, Her2/Neu, MMR, PD-L1, PR, TRKA/B/C       | Mutation, CNA Analysis   | MSI, TMB                 | Fusion Analysis |  |
| Endometrial                      | AR, ER, Her2/Neu, MMR, PD-L1, PR, TRKA/B/C       | Mutation, CNA Analysis   | MSI, TMB                 | Fusion Analysis |  |
| Esophageal SCC                   | AR, ER, Her2/Neu, MMR, PD-L1, PR, TRKA/B/C       | Mutation, CNA Analysis   | MSI, TMB                 | Fusion Analysis |  |
| Gastric                          | AR, ER, Her2/Neu, MMR, PD-L1, PR, TRKA/B/C       | Mutation, CNA Analysis   | MSI, TMB                 | Fusion Analysis | Her2 ( <i>Chromogenic in situ Hybridization</i> )        |
| GIST                             | AR, ER, Her2/Neu, MMR, PD-L1, PR, TRKA/B/C       | Mutation, CNA Analysis   | MSI, TMB                 | Fusion Analysis |  |
| Glioma                           | AR, ER, MMR, PD-L1, PR                           | Mutation, CNA Analysis   | MSI, TMB                 | Fusion Analysis | MGMT Methylation ( <i>Pyrosequencing</i> )               |
| Head & Neck                      | AR, ER, Her2/Neu, MMR, PD-L1, PR, TRKA/B/C       | Mutation, CNA Analysis   | MSI, TMB                 | Fusion Analysis |  |
| Kidney                           | AR, ER, Her2/Neu, MMR, PD-L1, PR, TRKA/B/C       | Mutation, CNA Analysis   | MSI, TMB                 | Fusion Analysis |  |
| Melanoma                         | AR, ER, MMR, PD-L1, PR, TRKA/B/C                 | Mutation, CNA Analysis   | MSI, TMB                 | Fusion Analysis |  |
| Merkel Cell                      | MMR, PD-L1, TRKA/B/C                             | Mutation, CNA Analysis   | MSI, TMB                 | Fusion Analysis |  |
| Neuroendocrine/Small Cell Lung   | AR, ER, MMR, PD-L1, PR, TRKA/B/C                 | Mutation, CNA Analysis   | MSI, TMB                 | Fusion Analysis |  |
| Non-Small Cell Lung              | ALK, AR, ER, Her2/Neu, MMR, PD-L1, PR            | Mutation, CNA Analysis   | MSI, TMB                 | Fusion Analysis |  |
| Ovarian                          | AR, ER, Her2/Neu, MMR, PD-L1, PR, TRKA/B/C       | Mutation, CNA Analysis   | MSI, TMB                 | Fusion Analysis |  |
| Pancreatic                       | AR, ER, Her2/Neu, MMR, PD-L1, PR, TRKA/B/C       | Mutation, CNA Analysis   | MSI, TMB                 | Fusion Analysis |  |
| Prostate                         | AR, ER, MMR, PD-L1, PR, TRKA/B/C                 | Mutation, CNA Analysis   | MSI, TMB                 | Fusion Analysis |  |
| Salivary Gland                   | AR, ER, Her2/Neu, MMR, PD-L1, PR, TRKA/B/C       | Mutation, CNA Analysis   | MSI, TMB                 | Fusion Analysis |  |
| Sarcoma                          | AR, ER, MMR, PD-L1, PR, TRKA/B/C                 | Mutation, CNA Analysis   | MSI, TMB                 | Fusion Analysis |  |
| Thyroid                          | AR, ER, Her2/Neu, MMR, PD-L1, PR                 | Mutation, CNA Analysis   | MSI, TMB                 | Fusion Analysis |  |
| Uterine Serous                   | AR, ER, Her2/Neu, MMR, PD-L1, PR, TRKA/B/C       | Mutation, CNA Analysis   | MSI, TMB                 | Fusion Analysis | Her2 ( <i>Chromogenic in situ Hybridization</i> )        |
| Other Tumours                    | AR, ER, Her2/Neu, MMR, PD-L1, PR, TRKA/B/C       | Mutation, CNA Analysis   | MSI, TMB                 | Fusion Analysis |  |

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

For PD-L1 IHC testing, Dako antibody 22c3 is run for all NSCLC, Cervical, Gastric and Gastroesophageal Junction (GEJ) cancers. 22c3 will be added to Bladder cancers with a CPS score, run side-by-side with SP142. Dako antibody 22c3 is available upon request for other tumour types. For TRK IHC positive results, reflex Fusion testing will be performed.

# Next-Generation Sequencing Gene List

## Next-Generation Sequencing – Genomic Signatures (DNA)

Microsatellite Instability (MSI)

Tumour Mutational Burden (TMB)

## Next-Generation Sequencing – Point Mutations and Indels (DNA)

|                 |          |        |          |               |        |              |         |         |          |
|-----------------|----------|--------|----------|---------------|--------|--------------|---------|---------|----------|
| ABI1            | BRD4     | CRLF2  | FOXO4    | HOXC11        | KLFL4  | MUC1         | PAK3    | RHOH    | TAL2     |
| ABL1            | BTG1     | DDB2   | FSTL3    | HOXC13        | KLK2   | MUTYH        | PATZ1   | RNF213  | TBL1XR1  |
| ACKR3           | BTK      | DDIT3  | GATA1    | HOXD11        | LASP1  | MYCL (MYCL1) | PAX8    | RPL10   | TCEA1    |
| AKT1            | C15orf65 | DNM2   | GATA2    | HOXD13        | LMO1   | NBN          | PDE4DIP | SEPT5   | TCL1A    |
| AMER1 (FAM123B) | CBLC     | DNMT3A | GNA11    | HRAS          | LMO2   | NDRG1        | PHF6    | SEPT6   | TERT     |
| AR              | CD79B    | EIF4A2 | GPC3     | IKBKE         | MAFB   | NKX2-1       | PHOX2B  | SFPQ    | TFE3     |
| ARAF            | CDH1     | ELF4   | HEY1     | INHBA         | MAX    | NONO         | PIK3CG  | SLC45A3 | TFPT     |
| ATP2B3          | CDK12    | ELN    | HIST1H3B | IRS2          | MECOM  | NOTCH1       | PLAG1   | SMARCA4 | THRAP3   |
| ATRX            | CDKN2B   | ERCC1  | HIST1H4I | JUN           | MED12  | NRAS         | PMS1    | SOCS1   | TLX3     |
| BCL11B          | CDKN2C   | ETV4   | HLF      | KAT6A (MYST3) | MKL1   | NUMA1        | POU5F1  | SOX2    | TMPPRSS2 |
| BCL2            | CEBPA    | FAM46C | HMG2P46  | KAT6B         | MLLT11 | NUTM2B       | PPP2R1A | SPOP    | UBR5     |
| BCL2L2          | CHCHD7   | FANCF  | HNF1A    | KCNJ5         | MN1    | OLIG2        | PRF1    | SRC     | VHL      |
| BCOR            | CNOT3    | FEV    | HOXA11   | KDM5C         | MPL    | OMD          | PRKDC   | SSX1    | WAS      |
| BCORL1          | COL1A1   | FOXL2  | HOXA13   | KDM6A         | MSN    | P2RY8        | RAD21   | STAG2   | ZBTB16   |
| BRD3            | COX6C    | FOXO3  | HOXA9    | KDSR          | MTC1P1 | PAFAH1B2     | RECQL4  | TAL1    | ZRSR2    |

## Next-Generation Sequencing – Point Mutations, Indels and Copy Number Alterations

|          |              |                  |         |                 |               |                 |          |         |          |
|----------|--------------|------------------|---------|-----------------|---------------|-----------------|----------|---------|----------|
| ABL2     | BRCA1        | CREB1            | ESR1    | FUS             | KLHL6         | MYC             | PER1     | RUNX1   | TFEB     |
| ACSL3    | BRCA2        | CREB3L1          | ETV1    | GAS7            | KMT2A (MLL)   | MYCN            | PICALM   | RUNX1T1 | TFG      |
| ACSL6    | BRIP1        | CREB3L2          | ETV5    | GATA3           | KMT2C (MLL3)  | MYD88           | PIK3CA   | SBDS    | TFRC     |
| ADGRA2   | BUB1B        | CREBBP           | ETV6    | GID4 (C17orf39) | KMT2D (MLL2)  | MYH11           | PIK3R1   | SDC4    | TGFB2    |
| AFDN     | CACNA1D      | CRKL             | EWSR1   | GMP5            | KNL1          | MYH9            | PIK3R2   | SDHAF2  | TLX1     |
| AFF1     | CALR         | CRTC1            | EXT1    | GNA13           | KRAS          | NACA            | PIM1     | SDHB    | TNFAIP3  |
| AFF3     | CAMTA1       | CRTC3            | EXT2    | GNAQ            | KTN1          | NCKIP5D         | PML      | SDHC    | TNFRSF14 |
| AFF4     | CANT1        | CSF1R            | EZH2    | GNA5            | LCK           | NCOA1           | PMS2     | SDHD    | TNFRSF17 |
| AKAP9    | CARD11       | CSF3R            | EZR     | GOLGA5          | LCP1          | NCOA2           | POLE     | SEPT9   | TOP1     |
| AKT2     | CARS         | CTCF             | FANCA   | GOPC            | LGR5          | NCOA4           | POT1     | SET     | TP53     |
| AKT3     | CASP8        | CTLA4            | FANCC   | GPHN            | LHFPL6        | NF1             | POU2AF1  | SETBP1  | TPM3     |
| ALDH2    | CBFA2T3      | CTNNA1           | FANCD2  | GRIN2A          | LIFR          | NF2             | PPARG    | SETD2   | TPM4     |
| ALK      | CBFB         | CTNNA1           | FANCE   | GSK3B           | LPP           | NFE2L2          | PRCC     | SF3B1   | TPR      |
| APC      | CBL          | CYLD             | FANCG   | H3F3A           | LRIG3         | NFIB            | PRDM1    | SH2B3   | TRAF7    |
| ARFRP1   | CBLB         | CYP2D6           | FANCL   | H3F3B           | LRP1B         | NFKB2           | PRDM16   | SH3GL1  | TRIM26   |
| ARHGAP26 | CCDC6        | DAXX             | FAS     | HERPUD1         | LYL1          | NFKBIA          | PRKAR1A  | SLC34A2 | TRIM27   |
| ARHGEF12 | CCNB1IP1     | DDR2             | FBXO11  | HGF             | MAF           | NIN             | PRRX1    | SMAD2   | TRIM33   |
| ARID1A   | CCND1        | DDX10            | FBXW7   | HIP1            | MALT1         | NOTCH2          | PSIP1    | SMAD4   | TRIP11   |
| ARID2    | CCND2        | DDX5             | FCRL4   | HMG1            | MAML2         | NPM1            | PTCH1    | SMARCB1 | TRRAP    |
| ARNT     | CCND3        | DDX6             | FGF10   | HMG2            | MAP2K1 (MEK1) | NSD1            | PTEN     | SMARCE1 | TSC1     |
| ASPSR1   | CCNE1        | DEK              | FGF14   | HNRNP2B1        | MAP2K2 (MEK2) | NSD2            | PTPN11   | SMO     | TSC2     |
| ASXL1    | CD274 (PDL1) | DICER1           | FGF19   | HOOK3           | MAP2K4        | NSD3            | PTPRC    | SNX29   | TSHR     |
| ATF1     | CD74         | DOT1L            | FGF23   | HSP90AA1        | MAP3K1        | NTSC2           | RABEP1   | SOX10   | TTL      |
| ATIC     | CD79A        | EBF1             | FGF3    | HSP90AB1        | MCL1          | NTRK1           | RAC1     | SPECC1  | U2AF1    |
| ATM      | CDC73        | ECT2L            | FGF4    | IDH1            | MDM2          | NTRK2           | RAD50    | SPEN    | USP6     |
| ATP1A1   | CDH11        | EGFR             | FGF6    | IDH2            | MDM4          | NTRK3           | RAD51    | SRGAP3  | VEGFA    |
| ATR      | CDK4         | ELK4             | FGFR1   | IGF1R           | MDS2          | NUP214          | RAD51B   | SRSF2   | VEGFB    |
| AURKA    | CDK6         | ELL              | FGFR1OP | IKZF1           | MEF2B         | NUP93           | RAF1     | SRSF3   | VTI1A    |
| AURKB    | CDK8         | EML4             | FGFR2   | IL2             | MEN1          | NUP98           | RALGDS   | SS18    | WDCP     |
| AXIN1    | CDKN1B       | EMSY             | FGFR3   | IL21R           | MET           | NUTM1           | RANBP17  | SS18L1  | WIF1     |
| AXL      | CDKN2A       | EP300            | FGFR4   | IL6ST           | MITF          | PALB2           | RAP1GDS1 | STAT3   | WISP3    |
| BAP1     | CDX2         | EPHA3            | FH      | IL7R            | MLF1          | PAX3            | RARA     | STAT4   | WRN      |
| BARD1    | CHEK1        | EPHA5            | FHIT    | IRF4            | MLH1          | PAX5            | RB1      | STAT5B  | WT1      |
| BCL10    | CHEK2        | EPHB1            | FIP1L1  | ITK             | MLLT1         | PAX7            | RBM15    | STIL    | WWTR1    |
| BCL11A   | CHIC2        | EPS15            | FLCN    | JAK1            | MLLT10        | PBRM1           | REL      | STK11   | XPA      |
| BCL2L11  | CHN1         | ERBB2 (HER2/NEU) | FLI1    | JAK2            | MLLT3         | PBX1            | RET      | SUFU    | XPC      |
| BCL3     | CIC          | ERBB3 (HER3)     | FLT1    | JAK3            | MLLT6         | PCM1            | RICTOR   | SUZ12   | XPO1     |
| BCL6     | CIITA        | ERBB4 (HER4)     | FLT3    | JAZF1           | MXN1          | PCSK7           | RM12     | SYK     | YWHAE    |
| BCL7A    | CLP1         | ERC1             | FLT4    | KDM5A           | MRE11         | PDCD1 (PD1)     | RNF43    | TAF15   | ZMYM2    |
| BCL9     | CLTC         | ERCC2            | FNBP1   | KDR (VEGFR2)    | MSH2          | PDCD1LG2 (PDL2) | ROS1     | TCF12   | ZNF217   |
| BCR      | CLTCL1       | ERCC3            | FOXA1   | KEAP1           | MSH6          | PDGFB           | RPL22    | TCF3    | ZNF331   |
| BIRC3    | CNBP         | ERCC4            | FOXO1   | KIAA1549        | MSI2          | PDGFRA          | RPL5     | TCF7L2  | ZNF384   |
| BLM      | CNTRL        | ERCC5            | FOXP1   | KIF5B           | MTOR          | PDGFRB          | RPN1     | TET1    | ZNF521   |
| BMPR1A   | COPB1        | ERG              | FUBP1   | KIT             | MYB           | PDK1            | RPTOR    | TET2    | ZNF703   |
| BRAF     |              |                  |         |                 |               |                 |          |         |          |

## Next-Generation Sequencing – Gene Fusions (RNA)

## Variant Transcripts (RNA)

|          |       |       |        |        |        |       |          |                      |
|----------|-------|-------|--------|--------|--------|-------|----------|----------------------|
| AKT3     | EGFR  | ESR1  | MAST1  | NOTCH2 | PDGFRA | RAF1  | TFE3     |                      |
| ALK      | EWSR1 | ETV1  | MAST2  | NRG1   | PDGFRB | RELA  | TFEB     |                      |
| ARHGAP26 | FGR   | ETV4  | MET    | NTRK1  | PIK3CA | RET   | THADA    | EGFR vIII            |
| AXL      | FGFR1 | ETV5  | MSMB   | NTRK2  | PKN1   | ROSO  | TMPPRSS2 |                      |
| BRAF     | FGFR2 | ETV6  | MUSK   | NTRK3  | PPARG  | RSPO2 |          |                      |
| BRD3     | FGFR3 | INSR  | MYB    | NUMBL  | PRKCA  | RSPO3 |          | MET Exon 14 Skipping |
| BRD4     | ERG   | MAML2 | NOTCH1 | NUTM1  | PRKCB  | TERT  |          |                      |

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