

### DNA Gene List: Entire Coding Sequence (Base Substitutions, Indels, Copy Number Alterations)

|                 |              |               |                 |               |              |                 |         |                       |
|-----------------|--------------|---------------|-----------------|---------------|--------------|-----------------|---------|-----------------------|
| APH1A           | CCND3        | DUSP2         | FHIT            | ID3           | MAP3K1       | NUP93           | RET     | TCF3 (E2A)            |
| AR              | CCNE1        | DUSP9         | FLCN            | IDH1          | MAP3K14      | NUP98           | RHOA    | TCL1A (TCL1)          |
| ARAF            | CCT6B        | EBF1          | FLT1            | IDH2          | MAP3K6       | P2RY8           | RICTOR  | TET2                  |
| ARFRP1          | CD22         | ECT2L         | FLT3            | IGF1R         | MAP3K7       | PAG1            | RNF43   | TGFBR2                |
| ARHGAP26 (GRAF) | CD274 (PDL1) | EED           | FLT4            | IKBKE         | MAPK1        | PAK3            | ROS1    | TLL2                  |
| ARID1A          | CD36         | EGFR          | FLYWCH1         | IKZF1         | MCL1         | PALB2           | RPTOR   | TMEM30A               |
| ARID2           | CD58         | ELP2          | FOXL2           | IKZF2         | MDM2         | PASK            | RUNX1   | TMSB4XP8 (TMSL3)      |
| ASMTL           | CD70         | EP300         | FOXO1           | IKZF3         | MDM4         | PAX5            | S1PR2   | TNFAIP3               |
| ASXL1           | CD79A        | EPHA3         | FOXO3           | IL7R          | MED12        | PBRM1           | SDHA    | TNFRSF11A             |
| ATM             | CD79B        | EPHA5         | FOXP1           | INHBA         | MEF2B        | PC              | SDHB    | TNFRSF14              |
| ATR             | CDC73        | EPHA7         | FRS2            | INPP4B        | MEF2C        | PCBP1           | SDHC    | TNFRSF17              |
| ATRX            | CDH1         | EPHB1         | GADD45B         | INPP5D (SHIP) | MEN1         | PCLO            | SDHD    | TOP1                  |
| AURKA           | CDK12        | ERBB2         | GATA1           | IRF1          | MET          | PDCD1           | SERP2   | TP53                  |
| AURKB           | CDK4         | ERBB3         | GATA2           | IRF4          | MIB1         | PDCD11          | SETBP1  | TP63                  |
| AXIN1           | CDK6         | ERBB4         | GATA3           | IRF8          | MITF         | PDCD1LG2 (PDL2) | SETD2   | TRAF2                 |
| AXL             | CDK8         | ERG           | GID4 (C17orf39) | IRS2          | MKI67        | PDGFRA          | SF3B1   | TRAF3                 |
| B2M             | CDKN1B       | ESR1          | GNA11           | JAK1          | MLH1         | PDGFRB          | SGK1    | TRAF5                 |
| BAP1            | CDKN2A       | ETS1          | GNA12           | JAK2          | MPL          | PDK1            | SMAD2   | TSC1                  |
| BARD1           | CDKN2B       | ETV6          | GNA13           | JAK3          | MRE11A       | PHF6            | SMAD4   | TSC2                  |
| BCL10           | CDKN2C       | EXOSC6        | GNAQ            | JARID2        | MSH2         | PIK3CA          | SMARCA1 | TSHR                  |
| BCL11B          | CEBPA        | EZH2          | GNAS            | JUN           | MSH3         | PIK3CG          | SMARCA4 | TUSC3                 |
| BCL2            | CHD2         | FAF1          | GPR124          | KAT6A (MYST3) | MSH6         | PIK3R1          | SMARCB1 | TYK2                  |
| BCL2L2          | CHEK1        | FAM46C        | GRIN2A          | KDM2B         | MTOR         | PIK3R2          | SMC1A   | U2AF1                 |
| BCL6            | CHEK2        | FANCA         | GSK3B           | KDM4C         | MUTYH        | PIM1            | SMC3    | U2AF2                 |
| BCL7A           | CIC          | FANCC         | GTSE1           | KDM5A         | MYC          | PLCG2           | SMO     | VHL                   |
| BCOR            | CIITA        | FANCD2        | HDAC1           | KDM5C         | MYCL (MYCL1) | POT1            | SOCS1   | WDR90                 |
| BCORL1          | CKS1B        | FANCE         | HDAC4           | KDM6A         | MYCN         | PPP2R1A         | SOCS2   | WHSC1 (MMSET or NSD2) |
| BIRC3           | CPS1         | FANCF         | HDAC7           | KDR           | MYD88        | PRDM1           | SOCS3   | WISP3                 |
| BLM             | CREBBP       | FANCG         | HGF             | KEAP1         | MYO18A       | PRKAR1A         | SOX10   | WT1                   |
| BRAF            | CRKL         | FANCL         | HIST1H1C        | KIT           | NCOR2        | PRKDC           | SOX2    | XBP1                  |
| BRCA1           | CRLF2        | FAS (TNFRSF6) | HIST1H1D        | KLHL6         | NCSTN        | PRSS8           | SPEN    | XPO1                  |
| BRCA2           | CSF1R        | FBXO11        | HIST1H1E        | KMT2A (MLL)   | NF1          | PTCH1           | SPOP    | YY1AP1                |
| BRD4            | CSF3R        | FBXO31        | HIST1H2AC       | KMT2C (MLL3)  | NF2          | PTEN            | SRC     | ZMYM3                 |
| BRIP1           | CTCF         | FBXW7         | HIST1H2AG       | KMT2D (MLL2)  | NFE2L2       | PTPN11          | SRSF2   | ZNF217                |
| BRSK1           | CTNNA1       | FGF10         | HIST1H2AL       | KRAS          | NFKBIA       | PTPN2           | STAG2   | ZNF24 (ZSCAN3)        |
| BTG2            | CTNNB1       | FGF14         | HIST1H2AM       | LEF1          | NKX2-1       | PTPN6 (SHP-1)   | STAT3   | ZNF703                |
| BTK             | CUX1         | FGF19         | HIST1H2BC       | LRP1B         | NOD1         | PTPRO           | STAT4   | ZRSR2                 |

### Select DNA Rearrangements

|      |       |      |       |      |             |        |      |         |
|------|-------|------|-------|------|-------------|--------|------|---------|
| ALK  | BRAF  | EPOR | ETV6  | IGK  | JAK2        | NTRK1  | RAF1 | ROS1    |
| BCL2 | CCND1 | ETV1 | EWSR1 | IGL  | KMT2A (MLL) | PDGFRA | RARA | TMPRSS2 |
| BCL6 | CRLF2 | ETV4 | FGFR2 | JAK1 | MYC         | PDGFRB | RET  | TRG     |
| BCR  | EGFR  | ETV5 | IGH   |      |             |        |      |         |

### Select Gene Fusions

|                 |                |         |          |               |               |                 |                  |                       |
|-----------------|----------------|---------|----------|---------------|---------------|-----------------|------------------|-----------------------|
| ABI1            | CBFA2T3        | EIF4A2  | FUS      | JAK1          | MUC1          | PBX1            | RNF213           | TET1                  |
| ABL1            | CBFB           | ELF4    | GAS7     | JAK2          | MYB           | PCM1            | ROS1             | TFE3                  |
| ABL2            | CBL            | ELL     | GLI1     | JAK3          | MYC           | PCSK7           | RPL22            | TFG                   |
| ACSL6           | CCND1          | ELN     | GMPS     | JAZF1         | MYH11         | PDCD1LG2 (PDL2) | RPN1             | TFPT                  |
| AFF1            | CCND2          | EML4    | GPHN     | KAT6A (MYST3) | MYH9          | PDE4DIP         | RUNX1            | TFRC                  |
| AFF4            | CCND3          | EP300   | HERPUD1  | KDSR          | NACA          | PDGFB           | RUNX1T1 (ETO)    | TLX1                  |
| ALK             | CD274 (PDL1)   | EPOR    | HEY1     | KIF5B         | NBEAP1 (BCL8) | PDGFRA          | RUNX2            | TLX3                  |
| ARHGAP26 (GRAF) | CDK6           | EPS15   | HIP1     | KMT2A (MLL)   | NCOA2         | PDGFRB          | SEC31A           | TMPRSS2               |
| ARHGEF12        | CDX2           | ERBB2   | HIST1H4I | LASP1         | NDRG1         | PER1            | SEPT5            | TNFRSF11A             |
| ARID1A          | CHIC2          | ERG     | HLF      | LCP1          | NF1           | PHF1            | SEPT6            | TOP1                  |
| ARNT            | CHN1           | ETS1    | HMGA1    | LMO1          | NF2           | PICALM          | SEPT9            | TP63                  |
| ASXL1           | CIC            | ETV1    | HMGA2    | LMO2          | NFKB2         | PIM1            | SET              | TPM3                  |
| ATF1            | CIITA          | ETV4    | HOXA11   | LPP           | NIN           | PLAG1           | SH3GL1           | TPM4                  |
| ATG5            | CLP1           | ETV5    | HOXA13   | LYL1          | NOTCH1        | PML             | SLC1A2           | TRIM24                |
| ATIC            | CLTC           | ETV6    | HOXA3    | MAF           | NPM1          | POU2AF1         | SNX29 (RUND-C2A) | TRIP11                |
| BCL10           | CLTCL1         | EWSR1   | HOXA9    | MAFB          | NR4A3         | PPP1CB          | SRSF3            | TTL                   |
| BCL11A          | CNTRL (CEP110) | FCGR2B  | HOXC11   | MALT1         | NSD1          | PRDM1           | SS18             | TYK2                  |
| BCL11B          | COL1A1         | FCRL4   | HOXC13   | MDS2          | NTRK1         | PRDM16          | SSX1             | USP6                  |
| BCL2            | CREB3L1        | FEV     | HOXD11   | MECOM         | NTRK2         | PRRX1           | SSX2             | WHSC1 (MMSET or NSD2) |
| BCL3            | CREB3L2        | FGFR1   | HOXD13   | MKL1          | NTRK3         | PSIP1           | SSX4             | WHSC1L1               |
| BCL6            | CREBBP         | FGFR1OP | HSP90AA1 | MLF1          | NUMA1         | PTCH1           | STAT6            | YPEL5                 |
| BCL7A           | CRLF2          | FGFR2   | HSP90AB1 | MLLT1 (ENL)   | NUP214        | PTK7            | STL              | ZBTB16                |
| BCL9            | CSF1           | FGFR3   | IGH      | MLLT10 (AF10) | NUP98         | RABEP1          | SYK              | ZMYM2                 |
| BCOR            | CTNNB1         | FLI1    | IGK      | MLLT3         | NUTM2A        | RAF1            | TAF15            | ZNF384                |
| BCR             | DDIT3          | FNBP1   | IGL      | MLLT4 (AF6)   | OMD           | RALGDS          | TAL1             | ZNF521                |
| BIRC3           | DDX10          | FOXO1   | IKZF1    | MLLT6         | P2RY8         | RAP1GDS1        | TAL2             |                       |
| BRAF            | DDX6           | FOXO3   | IL21R    | MN1           | PAFAH1B2      | RARA            | TBL1XR1          |                       |
| BTG1            | DEK            | FOXO4   | IL3      | MNX1          | PAX3          | RBM15           | TCF3 (E2A)       |                       |
| CAMTA1          | DUSP22         | FOXP1   | IRF4     | MSI2          | PAX5          | RET             | TCL1A (TCL1)     |                       |
| CARS            | EGFR           | FSTL3   | ITK      | MSN           | PAX7          | RHOH            | TEC              |                       |

Molecular diagnostics are routinely used to understand the molecular mechanism of individual patients' haematological malignancies to diagnose disease and determine the patient's prognosis.

We now understand that cancer is a genomic disease, with molecular alterations fueling its progression. The explosion of genomic research over recent years has dramatically improved our knowledge of the disease, and it has led to the development of targeted therapies which enable physicians to individualise treatment by matching a patient with the best therapy for their cancer.<sup>1</sup> This approach may be valuable in the treatment of haematologic malignancies, sarcomas and paediatric cancers, which have their own unique genomic profiles.

## Methods

FoundationOne<sup>®</sup> Heme is designed to analyse and interpret sequence information for somatically altered genes in human haematologic malignancies (leukaemias, lymphomas, and myelomas), many sarcomas, and paediatric cancers. Genes included in this assay encode known or likely targets of therapies, either approved or in clinical trials, or are otherwise known drivers of oncogenesis. This assay analyses the complete coding DNA sequences of 405 genes, as well as selected introns of 31 genes involved in rearrangements. FoundationOne<sup>®</sup> Heme also interrogates the RNA sequence (cDNA) of 265 commonly rearranged genes to better identify gene fusions. The assay will be updated periodically to address new findings in the field of cancer biology.

## Reporting

If a clinically relevant alteration is found in any one of the genes, on the current gene list, the report will identify the gene and alteration and will provide an interpretation that is specific to the patient's cancer.

The gene or genes listed on the front page of the report are found to have one or more clinically relevant alterations. All other genes are not found to have any clinically relevant alterations. The complete list of genes that are tested appears below and can be found in the appendix of each report.

## Variants of Unknown Significance (VUS)

Often an alteration is detected in one of the genes included in FoundationOne<sup>®</sup> Heme that has not yet been adequately characterised in published scientific literature. We include these variants in the report so that they may be acted upon in the future should clinical evidence emerge.

## Equivocal

Equivocal designation signifies when there is some, but not unambiguous, evidence of amplification or homozygous loss of a gene.

## Subclonal

Subclonal designation signifies that the FoundationOne<sup>®</sup> Heme analytical methodology has identified the presence of the alteration in less than 10% of the assayed tumour DNA.

## FoundationOne<sup>®</sup> Heme Includes the Commonly Tested Genes for Haematologic Malignancies, Sarcomas and Paediatric Cancers

FoundationOne<sup>®</sup> Heme is a single comprehensive assay that can reveal all classes of actionable genomic alterations in cancer-driving genes, including fusions that are rarely tested for in haematologic malignancies, sarcomas or paediatric cancers. The FoundationOne<sup>®</sup> Heme report often reveals alterations that may lead to additional treatment options for physicians and their patients to consider.

<sup>1</sup> Samuels Y, Bardelli A, López-Otín C. The cancer genome. In: DeVita VT, Lawrence TS, Rosenberg SA, eds. DeVita, Hellman, and Rosenberg's Cancer Principles & Practice of Oncology: Primer of the Molecular Biology of Cancer. 9<sup>th</sup> ed. Kindle ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2011.

## Current Gene List

FoundationOne<sup>®</sup> Heme includes tests for genomic alterations in each of the genes listed. FoundationOne<sup>®</sup> Heme is designed to interrogate the entire coding sequence of 405 genes, selected introns of 31 genes involved in rearrangements and utilises RNA sequencing to interrogate 265 genes known to be somatically altered in human

haematologic malignancies, sarcomas and paediatric cancers based on recent scientific and clinical literature. Reported alterations may indicate response or lack of response to validated targets for therapy (approved or in clinical trials), or may be unambiguous drivers of oncogenesis based on reported scientific knowledge.

### DNA Gene List: Entire Coding Sequence (Base Substitutions, Indels, Copy Number Alterations)

|                        |                 |        |       |           |        |        |          |         |
|------------------------|-----------------|--------|-------|-----------|--------|--------|----------|---------|
| ABL1                   | BTLA            | CXCR4  | FGF23 | HIST1H2BJ | LRRK2  | NOTCH1 | RAD21    | STAT5A  |
| ACTB                   | C11orf30 (EMSY) | DAXX   | FGF3  | HIST1H2BK | MAF    | NOTCH2 | RAD50    | STAT5B  |
| AKT1                   | CAD             | DDR2   | FGF4  | HIST1H2BO | MAFB   | NPM1   | RAD51    | STAT6   |
| AKT2                   | CARD11          | DDX3X  | FGF6  | HIST1H3B  | MAGED1 | NRAS   | RAF1     | STK11   |
| AKT3                   | CBFB            | DNM2   | FGFR1 | HNF1A     | MALT1  | NT5C2  | RARA     | SUFU    |
| ALK                    | CBL             | DNMT3A | FGFR2 | HRAS      | MAP2K1 | NTRK1  | RASGEF1A | SUZ12   |
| AMER1 (FAM123B or WTX) | CCND1           | DOT1L  | FGFR3 | HSP90AA1  | MAP2K2 | NTRK2  | RB1      | TAF1    |
| APC                    | CCND2           | DTX1   | FGFR4 | ICK       | MAP2K4 | NTRK3  | RELN     | TBL1XR1 |

gene list continued on following page