



# Technical Specifications



FoundationOneHeme is a comprehensive genomic profiling assay for hematologic malignancies and sarcomas.



## Methods<sup>1</sup>

- Uses hybrid-capture next-generation sequencing.
- Identifies the four classes of genomic alterations (base substitutions, insertions and deletions, copy number alterations, and rearrangements).
- Sequences DNA of the entire coding region of 406 genes and selected introns of 31 genes involved in rearrangements.
- Sequences RNA of 265 genes commonly rearranged in cancer to better identify known and novel gene fusions.
- Sequences to a median depth of ~500X unique coverage for DNA and RNA to an average of ~6.9 million unique pairs.
- All specimen are reviewed by a hematopathologist or pathologist to ensure specimen viability and tumor content.

### PERFORMANCE SPECIFICATIONS

|                          |  |       |
|--------------------------|--|-------|
| Sensitivity              | Base Substitutions at $\geq 5\%$ Minor Allele Frequency  | > 99% |
|                          | Insertions/Deletions (1-40 base pairs) at $\geq 10\%$ Minor Allele Frequency   | 98%   |
|                          | Focal Copy Number Alterations (homozygous deletions or amplifications $\geq 8$ copies)   | > 95% |
|                          | Known Gene Fusions   | > 95% |
| Specificity (PPV)        | Positive Predictive Value (PPV) for Base Substitutions, Insertions/Deletions and Focal Copy Number Alterations                             | > 99% |
|                          | Positive Predictive Value (PPV) for Known Gene Fusions   | > 95% |
| Reproducibility          | Concordance between replicates inter-batch   | 97%   |
|                          | Concordance between replicates intra-batch   | 97%   |
| Immunotherapy Biomarkers | TMB <sup>†</sup> and MSI <sup>‡</sup>  |       |
| Specimen Type            | Peripheral whole blood, bone marrow aspirate, FFPE block or slides, or extracted nucleic acid (see Specimen Instructions for more details) |       |
| Turnaround Time          | 2 Weeks <sup>§</sup>   |       |

<sup>†</sup> Chalmers ZR, et al. "Analysis of 100,000 human cancer genomes reveals the landscape of tumor mutational burden". Genome Med. 2017;9(1):34.

<sup>‡</sup> Hall MJ, et al. Multigene Panels to Evaluate Hereditary Cancer Risk: Reckless or Relevant? J Clin Oncol. 2016 Dec;34(34):4186-4187."

<sup>§</sup> Based on typical turnaround time from receipt of sample



## Reporting

- Test results are provided in an interpretive report, curated by biomedical informatics scientists, and approved by on-site board-certified and licensed pathologists and hematopathologists.
- Genomic findings are listed with clinically relevant targeted therapies, immunotherapies, and clinical trials.
- 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.
- Reports include tumor mutational burden (TMB) status and microsatellite instability (MSI) status, biomarkers that may help predict response to checkpoint inhibitors.
- Test results are available via our online portal at [www.foundationmedicine.com](http://www.foundationmedicine.com)\* or by fax.

\*Visit [foundationmedicine.com](http://foundationmedicine.com) to create an online account.

## Current Gene List<sup>2</sup>

Entire coding sequence (base substitutions, indels, copy number alterations)

|               |                       |                 |               |                 |               |                        |                 |
|---------------|-----------------------|-----------------|---------------|-----------------|---------------|------------------------|-----------------|
| ABL1          | ACTB                  | AKT1            | AKT2          | AKT3            | ALK           | AMER1 (FAM123B or WTX) | APC             |
| APH1A         | AR                    | ARAF            | ARFRP1        | ARHGAP26 (GRAF) | ARID1A        | ARID2                  | ASMLT           |
| ATM           | ATR                   | ATRX            | AURKA         | AURKB           | AXIN1         | AXL                    | ASXL1           |
| BARD1         | BCL10                 | BCL11B          | BCL2          | BCL2L2          | BCL6          | BCL7A                  | B2M             |
| BIRC3         | BLM                   | BRAF            | BRCA1         | BRCA2           | BRD4          | BRIP1 (BACH1)          | BCOR            |
| BTK           | BTLA                  | C11orf30 (EMSY) | CAD           | CALR            | CARD11        | CBFB                   | BCORL1          |
| CCND2         | CCND3                 | CCNE1           | CCT6B         | CD22            | CD274 (PD-L1) | CD36                   | BTG2            |
| CD79A         | CD79B                 | CDC73           | CDH1          | CDK12           | CDK4          | CDK6                   | CBL             |
| CDKN2A        | CDKN2B                | CDKN2C          | CEBPA         | CHD2            | CHEK1         | CHEK2                  | CCND1           |
| CKS1B         | CPS1                  | CREBBP          | CRKL          | CRLF2           | CSF1R         | CSF3R                  | CD58            |
| CTNNB1        | CUX1                  | CXCR4           | DAXX          | DDR2            | DDX3X         | DNM2                   | CDK8            |
| DTX1          | DUSP2                 | DUSP9           | EBF1          | ECT2L           | EED           | EGFR                   | CDKN1B          |
| EPHA3         | EPHA5                 | EPHA7           | EPHB1         | ERBB2           | ERBB3         | ERBB4                  | CIC             |
| ETS1          | ETV6                  | EXOSC6          | EZH2          | FAF1            | FAM46C        | FANCA                  | CTCF            |
| FANCE         | FANCF                 | FANCG           | FANCL         | FAS (TNFRSF6)   | FBXO11        | FBXO31                 | CTNNA1          |
| FGF14         | FGF19                 | FGF23           | FGF3          | FGF4            | FGF6          | FGFR1                  | CITTA           |
| FGFR4         | FHIT                  | FLCN            | FLT1          | FLT3            | FLT4          | FLYWCH1                | CTCF            |
| FOXO3         | FOXP1                 | FRS2            | GADD45B       | GATA1           | GATA2         | GATA3                  | DNMT3A          |
| GNA12         | GNA13                 | GNAQ            | GNAS          | GPR124          | GRIN2A        | GSK3B                  | DOT1L           |
| HDAC4         | HDAC7                 | HGF             | HIST1H1C      | HIST1H1D        | HIST1H1E      | HIST1H2AC              | EP300           |
| HIST1H2AM     | HIST1H2BC             | HIST1H2BJ       | HIST1H2BK     | HIST1H2BO       | HIST1H3B      | HNF1A                  | ERG             |
| ICK           | ID3                   | IDH1            | IDH2          | IGF1R           | IKBKE         | IKZF1                  | ERBB3           |
| IL7R          | INHBA                 | INPP4B          | INPP5D (SHIP) | IRF1            | IRF4          | IRS2                   | ESR1            |
| JAK2          | JAK3                  | JARID2          | JUN           | KAT6A (MYST3)   | KDM2B         | KDM4C                  | FANCC           |
| KDM6A         | KDR                   | KEAP1           | KIT           | KLHL6           | KMT2A (MLL)   | KMT2C (MLL3)           | FANCD2          |
| LEF1          | LRP1B                 | LRRK2           | MAF           | MAFB            | MAGED1        | MALT1                  | FBXW7           |
| MAP2K4        | MAP3K1                | MAP3K14         | MAP3K6        | MAP3K7          | MAPK1         | MCL1                   | FGF10           |
| MED12         | MEF2B                 | MEF2C           | MEN1          | MET             | MIB1          | MITF                   | FGFR2           |
| MPL           | MRE11A                | MSH2            | MSH3          | MSH6            | MTOR          | MUTYH                  | FGFR3           |
| MYCN          | MYD88                 | MYO18A          | NCOR2         | NCSTN           | NF1           | NF2                    | FOXO1           |
| NKX2-1        | NOD1                  | NOTCH1          | NOTCH2        | NPM1            | NRAS          | NT5C2                  | GID4 (C17orf39) |
| NTRK3         | NUP93                 | NUP98           | P2RY8         | PAG1            | PAK3          | PALB2                  | GNAI1           |
| PBRM1         | PC                    | PCBP1           | PCLO          | PDCD1 (PD-1)    | PDCD11        | PDCD1LG2 (PD-L2)       | HDAC1           |
| PDK1          | PHF6                  | PIK3CA          | PIK3CG        | PIK3R1          | PIK3R2        | PIM1                   | HIST1H2AL       |
| PPP2R1A       | PRDM1                 | PRKARIA         | PRKDC         | PRSS8           | PTCH1         | PTEN                   | HSP90AA1        |
| PTPN6 (SHP-1) | PTPRO                 | RAD21           | RAD50         | RAD51           | RAF1          | RARA                   | ICKZF1          |
| RELN          | RET                   | RHOA            | RICTOR        | RNF43           | ROS1          | RPTOR                  | IKZF2           |
| SDHA          | SDHB                  | SDHC            | SDHD          | SERP2           | SETBP1        | SETD2                  | IRS2            |
| SMAD2         | SMAD4                 | SMARCA1         | SMARCA4       | SMARCB1         | SMC1A         | SMC3                   | JAK1            |
| SOCS2         | SOCS3                 | SOX10           | SOX2          | SPEN            | SPOP          | SRC                    | KDM5A           |
| STAT3         | STAT4                 | STAT5A          | STAT5B        | STAT6           | STK11         | SUFU                   | KDM5C           |
| TBL1XR1       | TCF3 (E2A)            | TCL1A (TCL1)    | TET2          | TGFBR2          | TLL2          | TMEM30A                | KRAS            |
| TNFAIP3       | TNFRSF11A             | TNFRSF14        | TNFRSF17      | TOPI            | TP53          | TP63                   | KMT2D (MLL2)    |
| TRAF5         | TSC1                  | TSC2            | TSHR          | TUSC3           | TYK2          | U2AF1                  | KMT2L (MLL3)    |
| WDR90         | WHSC1 (MMSET or NSD2) | WISP3           | WTI           | WT1             | XBPI          | XPO1                   | KRAS            |
| ZNF217        | ZNF24 (ZSCAN3)        | ZNF703          | ZRSR2         |                 |               |                        | MAP2K2 (MEK2)   |

### Select DNA Rearrangements<sup>3</sup>

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

## Select RNA Gene Fusions

|                 |               |                |          |                  |              |           |                       |               |
|-----------------|---------------|----------------|----------|------------------|--------------|-----------|-----------------------|---------------|
| ABI1            | ABL1          | ABL2           | ACSL6    | AFF1             | AFF4         | ALK       | ARHGAP26 (GRAF)       |               |
| ARHGEF12        | ARID1A        | ARNT           | ASXL1    | ATF1             | ATG5         | ATIC      | BCL10                 | BCL11A        |
| BCL11B          | BCL2          | BCL3           | BCL6     | BCL7A            | BCL9         | BCOR      | BCR                   | BIRC3         |
| BRAF            | BTG1          | CAMTA1         | CARS     | CBFA2T3          | CBFB         | CBL       | CCND1                 | CCND2         |
| CCND3           | CD274 (PD-L1) | CDK6           | CDX2     | CHIC2            | CHN1         | CIC       | CIITA                 | CLP1          |
| CLTC            | CLTCL1        | CNTRL (CEP110) | COL1A1   | CREB3L1          | CREB3L2      | CREBBP    | CRLF2                 | CSF1          |
| CTNNB1          | DDIT3         | DDX10          | DDX6     | DEK              | DUSP22       | EGFR      | EIF4A2                | ELF4          |
| ELL             | ELN           | EML4           | EP300    | EPOR             | EPS15        | ERBB2     | ERG                   | ETS1          |
| ETV1            | ETV4          | ETV5           | ETV6     | EWSR1            | FCGR2B       | FCRL4     | FEV                   | FGFR1         |
| FGFR1OP         | FGFR2         | FGFR3          | FLI1     | FNBP1            | FOXO1        | FOXO3     | FOXO4                 | FOXP1         |
| FSTL3           | FUS           | GAS7           | GLI1     | GMPS             | GPHN         | HERPUD1   | HEY1                  | HIP1          |
| HIST1H4I        | HLF           | HMGA1          | HMGA2    | HOXA11           | HOXA13       | HOXA3     | HOXA9                 | HOXC11        |
| HOXC13          | HOXD11        | HOXD13         | HSP90AA1 | HSP90AB1         | IGH          | IGK       | IGL                   | IKZF1         |
| IL21R           | IL3           | IRF4           | ITK      | JAK1             | JAK2         | JAK3      | JAZF1                 | KAT6A (MYST3) |
| KDSR            | KIF5B         | KMT2A (MLL)    | LASPI    | LCP1             | LMO1         | LMO2      | LPP                   | LYL1          |
| MAF             | MAFB          | MALT1          | MDS2     | MECOM            | MKL1         | MLF1      | MLLT1 (ENL)           | MLLT10 (AF10) |
| MLLT3           | MLLT4 (AF6)   | MLLT6          | MN1      | MNX1             | MSI2         | MSN       | MUC1                  | MYB           |
| MYC             | MYH11         | MYH9           | NACA     | NBEAP1 (BCL8)    | NCOA2        | NDRG1     | NF1                   | NF2           |
| NFKB2           | NIN           | NOTCH1         | NPM1     | NR4A3            | NSD1         | NTRK1     | NTRK2                 | NTRK3         |
| NUMA1           | NUP214        | NUP98          | NUTM2A   | OMD              | P2RY8        | PAFAH1B2  | PAX3                  | PAX5          |
| PAX7            | PBX1          | PCM1           | PCSK7    | PDCD1LG2 (PD-L2) | PDE4DIP      | PDGFB     | PDGFRA                | PDGFRB        |
| PER1            | PHF1          | PICALM         | PIM1     | PLAG1            | PML          | POU2AF1   | PPP1CB                | PRDM1         |
| PRDM16          | PRRX1         | PSIP1          | PTCH1    | PTK7             | RABEP1       | RAF1      | RALGDS                | RAP1GDS1      |
| RARA            | RBM15         | RET            | RHOH     | RNF213           | ROS1         | RPL22     | RPN1                  | RUNX1         |
| RUNX1T1 (ETO)   | RUNX2         | SEC31A         | SEPT5    | SEPT6            | SEPT9        | SET       | SH3GL1                | SLC1A2        |
| SNX29 (RUNDC2A) | SRSF3         | SS18           | SSX1     | SSX2             | SSX4         | STAT6     | STL                   | SYK           |
| TAF15           | TAL1          | TAL2           | TBL1XR1  | TCF3 (E2A)       | TCL1A (TCL1) | TEC       | TET1                  | TFE3          |
| TFG             | TFPT          | TFRC           | TLX1     | TLX3             | TMPRSS2      | TNFRSF11A | TOPI                  | TP63          |
| TPM3            | TPM4          | TRIM24         | TRIP11   | TTL              | TYK2         | USP6      | WHSC1 (MMSET or NSD2) |               |
| WHSC1L1         | YPEL5         | ZBTB16         | ZMYM2    | ZNF384           | ZNF521       |           |                       |               |

To learn more about our scientific and analytical validation see our publication in Blood<sup>1</sup>: "Integrated genomic DNA/RNA profiling of hematologic malignancies in the clinical setting."

### References

1. He, J. et al. (2016) Integrated genomic DNA/RNA profiling of hematologic malignancies in the clinical setting. Blood, 127(24):3004-14.
2. Current as of November 2017. Please visit [www.foundationmedicine.com](http://www.foundationmedicine.com) for the most up-to-date gene list.
3. Select Introns only. Detailed list available upon request.