Technical Specifications

FoundationOne®Heme is a qualitative next-generation sequencing based laboratory developed test (LDT) for detection of substitutions, insertion and deletion alterations (indels), copy number alterations (CNAs), select gene rearrangements, and genomic signatures including microsatellite instability (MSI) and tumor mutational burden (TMB). FoundationOne Heme uses DNA and RNA isolated from formalin-fixed, paraffin-embedded (FFPE) tumor specimens, as well as from peripheral blood (PB), bone marrow aspirate (BMA) specimens and cytology smear specimens. FoundationOne Heme is intended to provide cancer genomic mutation profiling to be used by qualified health care professionals in accordance with professional guidelines in oncology for patients with hematologic neoplasms and solid tumors, including sarcomas. Genomic findings are not prescriptive or conclusive for labeled use of any specific therapeutic product.

Methods

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

PERFORMANCE CHARACTERISTICS			
Limit of Detection (LoD)	Base Substitutions	5% VAF	
	Insertions/Deletions	10% VAF	
	Copy-number Alterations (Amplifications or losses)	30% tumor purity	
	Gene Fusions and Rearrangements (DNA and RNA)	25 reads	
Limit of Blank (LoB)	No variants detected in tumor adjacent normal FFPE tissue		
Precision (Reproducibility and Repeatability)	Targeted Short Variants (Base substitutions and InDels)	100%	
	Targeted Gene Fusions and Rearrangements (DNA and RNA)	100%	
	Targeted Copy-number Alterations (Amplifications or loss)	100%	
Concordance (≥ LoD)	Targeted Variants (all)	PPA: 97.5%	NPA: 99.9%
	Base Substitutions	PPA: 99.1%	NPA: 99.9%
	Insertions/Deletions	PPA: 98.3%	NPA: 99.8%
	Copy Number Amplifications	PPA: 87.7%	NPA: 100%
	Copy Number Losses	PPA: 91.5%	NPA: 99.9%
	Gene Fusions and Rearrangements	PPA: 91.8%	NPA: 99.7%
	Tumor Mutational Burden (TMB)	OPA: 97.4%	
	Microsatellite Instability Status (MSI)	OPA: 100%	

- Note: Concordance data compares the NovaSeq configuration to the original HiSeq configuration. Accuracy study comparing HiSeq configuration to a reference CLIA-certified test demonstrated a PPA of 99% PPA and NPA of 98%. For details, please refer to the article, He, J. et al. Integrated genomic DNA/RNA profiling of hematologic malignancies in the clinical setting. Blood. (2016 June 16).

Reporting

- Test results are provided in an interpretive report, curated by biomedical informatics scientists, and approved by board-certified and licensed pathologists and hematopathologists with molecular genetic pathology expertise.
- Genomic findings are listed with clinically relevant targeted therapies, immunotherapies, and clinical trial options.
- Reported alterations may indicate response or lack of response to therapy (FDA-approved or in clinical trials) or may be unambiguous drivers of oncogenesis based on reported scientific literature.
- Reports include tumor mutational burden (TMB) status and microsatellite instability (MSI) status, biomarkers that may help predict response to checkpoint inhibitors.

FoundationOne Heme Gene List

DNA Gene List With Complete Exonic (Coding) Coverage (Base Substitutions, Indels, Copy number Alterations)[1]

ABL1	*BRCA2*	*CKS1B*	*FAM46C*	*GNA13*	*IRF8*	*MEF2C*
ACTB	*BRD4*	*CPS1*	*FANCA*	*GNAQ*	*IRS2*	*MEN1*
AKT1	*BRIP1 (BACH1)*	*CREBBP*	*FANCC*	*GNAS*	*JAK1*	*MET*
AKT2	*BRSK1*	*CRKL*	*FANCD2*	*GPR124*	*JAK2*	*MIB1*
AKT3	*BTG2*	*CRLF2*	*FANCE*	*GRIN2A*	*JAK3*	*MITF*
ALK	*BTK*	*CSF1R*	*FANCF*	*GSK3B*	*JARID2*	*MKI67*
AMER1 (FAM123B or WTX)	*BTLA*	*CSF3R*	*FANCG*	*GTSE1*	*JUN*	*MLH1*
APC	*C11orf30 (EMSY)*	*CTCF*	*FANCL*	*HDAC1*	*KAT6A (MYST3)*	*MPL*
APH1A	*CAD*	*CTNNA1*	*FAS (TNFRSF6)*	*HDAC4*	*KDM2B*	*MRE11A*
AR	*CALR*	*CTNNB1*	*FBXO11*	*HDAC7*	*KDM4C*	*MSH2*
ARAF	*CARD11*	*CUX1*	*FBXO31*	*HGF*	*KDM5A*	*MSH3*
ARFRP1	*CBFB*	*CXCR4*	*FBXW7*	*HIST1H1C*	*KDM5C*	*MSH6*
ARHGAP26 (GRAF)	*CBL*	*DAXX*	*FGF10*	*HIST1H1D*	*KDM6A*	*MTOR*
ARID1A	*CCND1*	*DDR2*	*FGF14*	*HIST1H1E*	*KDR*	*MUTYH*
ARID2	*CCND2*	*DDX3X*	*FGF19*	*HIST1H2AC*	*KEAP1*	*MYC*
ASMTL	*CCND3*	*DNM2*	*FGF23*	*HIST1H2AG*	*KIT*	*MYCL (MYCL1)*
ASXL1	*CCNE1*	*DNMT3A*	*FGF3*	*HIST1H2AL*	*KLHL6*	*MYCN*
ATM	*CCT6B*	*DOT1L*	*FGF4*	*HIST1H2AM*	*KMT2A (MLL)*	*MYD88*
ATR	*CD22*	*DTX1*	*FGF6*	*HIST1H2BC*	*KMT2C (MLL3)*	*MYO18A*
ATRX	*CD274 (PD-L1)*	*DUSP2*	*FGFR1*	*HIST1H2BJ*	*KMT2D (MLL2)*	*NCOR2*
AURKA	*CD36*	*DUSP9*	*FGFR2*	*HIST1H2BK*	*KRAS*	*NCSTN*
AURKB	*CD58*	*EBF1*	*FGFR3*	*HIST1H2BO*	*LEF1*	*NF1*
AXIN1	*CD70*	*ECT2L*	*FGFR4*	*HIST1H3B*	*LRP1B*	*NF2*
AXL	*CD79A*	*EED*	*FHIT*	*HNF1A*	*LRRK2*	*NFE2L2*
B2M	*CD79B*	*EGFR*	*FLCN*	*HRAS*	*MAF*	*NFKBIA*
BAP1	*CDC73*	*ELP2*	*FLT1*	*HSP90AA1*	*MAFB*	*NKX2-1*
BARD1	*CDH1*	*EP300*	*FLT3*	*ICK*	*MAGED1*	*NOD1*
BCL10	*CDK12*	*EPHA3*	*FLT4*	*ID3*	*MALT1*	*NOTCH1*
BCL11B	*CDK4*	*EPHA5*	*FLYWCH1*	*IDH1*	*MAP2K1 (MEK1)*	*NOTCH2*
BCL2	*CDK6*	*EPHA7*	*FOXL2*	*IDH2*	*MAP2K2 (MEK2)*	*NPM1*
BCL2L2	*CDK8*	*EPHB1*	*FOXO1*	*IGF1R*	*MAP2K4*	*NRAS*
BCL6	*CDKN1B*	*ERBB2*	*FOXO3*	*IKBKE*	*MAP3K1*	*NSD1*
BCL7A	*CDKN2A*	*ERBB3*	*FOXP1*	*IKZF1*	*MAP3K14*	*NT5C2*
BCOR	*CDKN2B*	*ERBB4*	*FRS2*	*IKZF2*	*MAP3K6*	*NTRK1*
BCORL1	*CDKN2C*	*ERG*	*GADD45B*	*IKZF3*	*MAP3K7*	*NTRK2*
BIRC3	*CEBPA*	*ESR1*	*GATA1*	*IL7R*	*MAPK1*	*NTRK3*
BLM	*CHD2*	*ETS1*	*GATA2*	*INHBA*	*MCL1*	*NUP93*
BRAF	*CHEK1*	*ETV6*	*GATA3*	*INPP4B*	*MDM2*	*NUP98*
BRCA1	*CHEK2*	*EXOSC6*	*GID4 (C17orf39)*	*INPP5D (SHIP)*	*MDM4*	*P2RY8*
	CIC	*EZH2*	*GNA11*	*IRF1*	*MED12*	*PAG1*
	CIITA	*FAF1*	*GNA12*	*IRF4*	*MEF2B*	*PAK3*

Current Gene List ⟶

FoundationOne Heme Gene List (Continued)

PALB2
PASK
PAX5
PBRM1
PC
PCBP1
PCLO
PDCD1 (PD-1)
PDCD11
PDCD1LG2 (PD-L2)
PDGFRA
PDGFRB
PDK1
PHF6
PIK3CA
PIK3CG
PIK3R1
PIK3R2
PIM1
PLCG2
POT1
PPP2R1A
PRDM1
PRKAR1A
PRKDC
PRSS8
PTCH1
PTEN
PTPN11
PTPN2
PTPN6 (SHP-1)
PTPRO
RAD21
RAD50
RAD51
RAF1
RARA
RASGEF1A
RB1
RELN
RET
RHOA
RICTOR
RNF43
ROS1
RPTOR
RUNX1
S1PR2
SDHA
SDHB
SDHC
SDHD
SERP2
SETBP1
SETD2
SF3B1
SGK1
SMAD2
SMAD4
SMARCA1
SMARCA4
SMARCB1
SMC1A
SMC3
SMO
SOCS1
SOCS2
SOCS3
SOX10
SOX2
SPEN
SPOP
SRC
SRSF2
STAG2
STAT3
STAT4
STAT5A
STAT5B
STAT6
STK11
SUFU
SUZ12
TAF1
TBL1XR1
TCF3 (E2A)
TCL1A (TCL1)
TET2
TGFBR2
TLL2
TMEM30A
TMSB4XP8 (TMSL3)
TNFAIP3
TNFRSF11A
TNFRSF14
TNFRSF17
TOP1
TP53
TP63
TRAF2
TRAF3
TRAF5
TSC1
TSC2
TSHR
TUSC3
TYK2
U2AF1
U2AF2
VHL
WDR90
WHSC1 (MMSET or NSD2)
WISP3
WT1
XBP1
XPO1
YY1AP1
ZMYM3
ZNF217
ZNF24 (ZSCAN3)
ZNF703
ZRSR2

Rearrangements with Select Intronic (Non-Coding) Coverage[2]

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

Genes with RNA Sequencing Coverage (Fusions)

Please note, some VUS* rearrangements between targeted genes and unknown fusion partners may not be reported.

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)
LASP1
LCP1
LMO1
LMO2
LPP
LYL1
MAF
MAFB
MALT1
MDS2
MECOM

Current Gene List ⟶

FoundationOne Heme Gene List (Continued)

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 (MMSET or NSD2)
TFE3
TFG
TFPT
TFRC
TLX1
TLX3
TMPRSS2
TNFRSF11A
TOP1
TP63
TPM3
TPM4
TRIM24
TRIP11
TTL
TYK2
USP6
WHSC1 (MMSET or NSD2)
WHSC1L1
YPEL5
ZBTB16
ZMYM2
ZNF384
ZNF521

• VUS: Variants of Unknown Significance

FoundationOne Heme is a laboratory developed test that was developed and its performance characteristics determined by Foundation Medicine. FoundationOne Heme has not been cleared or approved by the U.S. Food and Drug Administration. For more information on FoundationOne Heme, please visit foundationmedicine.com/heme.

References:

1. Current as of April 2024. Please visit foundationmedicine.com/heme for the most up to date gene list.
2. Select introns only. Detailed list available upon request.

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