

Technical Specifications



FoundationOne®Heme is a comprehensive[†] genomic profiling assay for haematologic malignancies and sarcomas.



Methods¹

FoundationOne Heme:

- Uses hybrid-capture next-generation sequencing.
- Identifies the four classes of genomic alterations (base substitutions, insertions and deletions, copy number alterations, rearrangements, and reports microsatellite instability and tumour mutational burden).
- 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 haematopathologist or pathologist to ensure specimen viability and tumour 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 ≥ 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 ^a and MSI ^b	
Specimen Type	Peripheral whole blood, bone marrow aspirate, FFPE block or slides, or extracted nucleic acid (see Specimen Instructions for more details)	
Turnaround Time	3 Weeks ^c	

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

^b Hall MJ, et al. Multigene Panels to Evaluate Hereditary Cancer Risk: Reckless or Relevant? J Clin Oncol. 2016 Dec;34(34):418-4187."

^c 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 board-certified and licensed pathologists and haematopathologists.
- Genomic findings are listed with clinically relevant targeted therapies, immunotherapies, and clinical trials (if applicable).
- Reported alterations may indicate response or lack of response to validated targets for therapy (approved or in clinical trials), or may be drivers of oncogenesis based on reported scientific knowledge.
- Reports include tumor mutational burden (TMB) status and microsatellite instability (MSI) status.



Current Gene List[†]

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	ASMTL	ASXL1
ATM	ATR	ATRAX	AURKA	AURKB	AXIN1	AXL	B2M	BAP1
BARD1	BCL10	BCL11B	BCL2	BCL2L2	BCL6	BCL7A	BCOR	BCORL1
BIRC3	BLM	BRAF	BRCA1	BRCA2	BRD4	BRIP1 (BACH1)	BRSK1	BTG2
BTK	BTLA	C11orf30 (EMSY)	CAD	CALR	CARD11	CBFB	CBL	CCND1
CCND2	CCND3	CCNE1	CCT6B	CD22	CD274 (PD-L1)	CD36	CD58	CD70
CD79A	CD79B	CDC73	CDH1	CDK12	CDK4	CDK6	CDK8	CDKN1B
CDKN2A	CDKN2B	CDKN2C	CEBPA	CHD2	CHEK1	CHEK2	CIC	CIITA
CKS1B	CPS1	CREBBP	CRKL	CRLF2	CSF1R	CSF3R	CTCF	CTNNA1
CTNNB1	CUX1	CXCR4	DAXX	DDR2	DDX3X	DNM2	DNMT3A	DOT1L
DTX1	DUSP2	DUSP9	EBF1	ECT2L	EED	EGFR	ELP2	EP300
EPHA3	EPHA5	EPHA7	EPHB1	ERBB2	ERBB3	ERBB4	ERG	ESR1
ETS1	ETV6	EXOSC6	EZH2	FAF1	FAM46C	FANCA	FANCC	FANCD2
FANCE	FANCF	FANCG	FANCL	FAS (TNFRSF6)	FBXO11	FBXO31	FBXW7	FGF10
FGF14	FGF19	FGF23	FGF3	FGF4	FGF6	FGFR1	FGFR2	FGFR3
FGFR4	FHIT	FLCN	FLT1	FLT3	FLT4	FLYWCH1	FOXL2	FOXO1
FOXO3	FOXP1	FRS2	GADD45B	GATA1	GATA2	GATA3	GID4 (C17orf39)	GNA11
GNA12	GNA13	GNAQ	GNAS	GPR124	GRIN2A	GSK3B	GTSE1	HDAC1
HDAC4	HDAC7	HGF	HIST1H1C	HIST1H1D	HIST1H1E	HIST1H2AC	HIST1H2AG	HIST1H2AL
HIST1H2AM	HIST1H2BC	HIST1H2BJ	HIST1H2BK	HIST1H2BO	HIST1H3B	HNF1A	HRAS	HSP90AA1
ICK	ID3	IDH1	IDH2	IGF1R	IKBKE	IKZF1	IKZF2	IKZF3
IL7R	INHBA	INPP4B	INPP5D (SHIP)	IRF1	IRF4	IRF8	IRS2	JAK1
JAK2	JAK3	JARID2	JUN	KAT6A (MYST3)	KDM2B	KDM4C	KDM5A	KDM5C
KDM6A	KDR	KEAP1	KIT	KLHL6	KMT2A (MLL)	KMT2C (MLL3)	KMT2D (MLL2)	KRAS
LEF1	LRP1B	LRRK2	MAF	MAFB	MAGED1	MALT1	MAP2K1 (MEK1)	MAP2K2 (MEK2)
MAP2K4	MAP3K1	MAP3K14	MAP3K6	MAP3K7	MAPK1	MCL1	MDM2	MDM4
MED12	MEF2B	MEF2C	MEN1	MET	MIB1	MITF	MKI67	MLH1
MPL	MRE11A	MSH2	MSH3	MSH6	MTOR	MUTYH	MYC	MYCL (MYCL1)
MYCN	MYD88	MYO18A	NCOR2	NCSTN	NF1	NF2	NFE2L2	NFKBIA
NKX2-1	NOD1	NOTCH1	NOTCH2	NPM1	NRAS	NSD1	NT5C2	NTRK1
NTRK2	NTRK3	NUP93	NUP98	P2RY8	PAG1	PAK3	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	PRKARIA	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	WSP3	WT1	XBP1	XPO1	YY1AP1
ZMYM3	ZNF217	ZNF24 (ZSCAN3)	ZNF703	ZRSR2				

Genes With Select Intronic (Non-Coding) Coverage

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	TPRSS2	TRG					



Genes with RNA sequencing coverage

<i>ABII</i>	<i>ABL1</i>	<i>ABL2</i>	<i>ACSL6</i>	<i>AFF1</i>	<i>AFF4</i>	<i>ALK</i>	<i>ARHGAP26</i> ^(GRAF)	
<i>ARHGEF12</i>	<i>ARID1A</i>	<i>ARNT</i>	<i>ASXL1</i>	<i>ATF1</i>	<i>ATG5</i>	<i>ATIC</i>	<i>BCL10</i>	<i>BCL11A</i>
<i>BCL11B</i>	<i>BCL2</i>	<i>BCL3</i>	<i>BCL6</i>	<i>BCL7A</i>	<i>BCL9</i>	<i>BCOR</i>	<i>BCR</i>	<i>BIRC3</i>
<i>BRAF</i>	<i>BTG1</i>	<i>CAMTA1</i>	<i>CARS</i>	<i>CBFA2T3</i>	<i>CBFB</i>	<i>CBL</i>	<i>CCND1</i>	<i>CCND2</i>
<i>CCND3</i>	<i>CD274</i> ^(PD-L1)	<i>CDK6</i>	<i>CDX2</i>	<i>CHIC2</i>	<i>CHN1</i>	<i>CIC</i>	<i>CIITA</i>	<i>CLP1</i>
<i>CLTC</i>	<i>CLTCL1</i>	<i>CNTRL</i> ^(CEP110)	<i>COL1A1</i>	<i>CREB3L1</i>	<i>CREB3L2</i>	<i>CREBBP</i>	<i>CRLF2</i>	<i>CSF1</i>
<i>CTNNB1</i>	<i>DDIT3</i>	<i>DDX10</i>	<i>DDX6</i>	<i>DEK</i>	<i>DUSP22</i>	<i>EGFR</i>	<i>EIF4A2</i>	<i>ELF4</i>
<i>ELL</i>	<i>ELN</i>	<i>EML4</i>	<i>EP300</i>	<i>EPOR</i>	<i>EPS15</i>	<i>ERBB2</i>	<i>ERG</i>	<i>ETS1</i>
<i>ETV1</i>	<i>ETV4</i>	<i>ETV5</i>	<i>ETV6</i>	<i>EWSR1</i>	<i>FCGR2B</i>	<i>FCRL4</i>	<i>FEV</i>	<i>FGFR1</i>
<i>FGFR1OP</i>	<i>FGFR2</i>	<i>FGFR3</i>	<i>FLI1</i>	<i>FNBP1</i>	<i>FOXO1</i>	<i>FOXO3</i>	<i>FOXO4</i>	<i>FOXP1</i>
<i>FSTL3</i>	<i>FUS</i>	<i>GAS7</i>	<i>GLI1</i>	<i>GMPS</i>	<i>GPHN</i>	<i>HERPUD1</i>	<i>HEY1</i>	<i>HIP1</i>
<i>HIST1H4I</i>	<i>HLF</i>	<i>HMGA1</i>	<i>HMGA2</i>	<i>HOXA11</i>	<i>HOXA13</i>	<i>HOXA3</i>	<i>HOXA9</i>	<i>HOXC11</i>
<i>HOXC13</i>	<i>HOXD11</i>	<i>HOXD13</i>	<i>HSP90AA1</i>	<i>HSP90AB1</i>	<i>IGH</i>	<i>IGK</i>	<i>IGL</i>	<i>IKZF1</i>
<i>IL21R</i>	<i>IL3</i>	<i>IRF4</i>	<i>ITK</i>	<i>JAK1</i>	<i>JAK2</i>	<i>JAK3</i>	<i>JAZF1</i>	<i>KAT6A</i> ^(MYST3)
<i>KDSR</i>	<i>KIF5B</i>	<i>KMT2A</i> ^(MLL)	<i>LASP1</i>	<i>LCPI</i>	<i>LMO1</i>	<i>LMO2</i>	<i>LPP</i>	<i>LYL1</i>
<i>MAF</i>	<i>MAFB</i>	<i>MALT1</i>	<i>MDS2</i>	<i>MECOM</i>	<i>MKL1</i>	<i>MLF1</i>	<i>MLLT1</i> ^(ENL)	<i>MLLT10</i> ^(AF10)
<i>MLLT3</i>	<i>MLLT4</i> ^(AF6)	<i>MLLT6</i>	<i>MN1</i>	<i>MNX1</i>	<i>MSI2</i>	<i>MSN</i>	<i>MUC1</i>	<i>MYB</i>
<i>MYC</i>	<i>MYH11</i>	<i>MYH9</i>	<i>NACA</i>	<i>NBEAP1</i> ^(BCL8)	<i>NCOA2</i>	<i>NDRG1</i>	<i>NF1</i>	<i>NF2</i>
<i>NFKB2</i>	<i>NIN</i>	<i>NOTCH1</i>	<i>NPM1</i>	<i>NR4A3</i>	<i>NSD1</i>	<i>NTRK1</i>	<i>NTRK2</i>	<i>NTRK3</i>
<i>NUMA1</i>	<i>NUP214</i>	<i>NUP98</i>	<i>NUTM2A</i>	<i>OMD</i>	<i>P2RY8</i>	<i>PAFAH1B2</i>	<i>PAX3</i>	<i>PAX5</i>
<i>PAX7</i>	<i>PBX1</i>	<i>PCM1</i>	<i>PCSK7</i>	<i>PDCD1LG2</i> ^(PD-L2)	<i>PDE4DIP</i>	<i>PDGFB</i>	<i>PDGFRA</i>	<i>PDGFRB</i>
<i>PER1</i>	<i>PHF1</i>	<i>PICALM</i>	<i>PIM1</i>	<i>PLAG1</i>	<i>PML</i>	<i>POU2AF1</i>	<i>PPP1CB</i>	<i>PRDM1</i>
<i>PRDM16</i>	<i>PRRX1</i>	<i>PSIP1</i>	<i>PTCH1</i>	<i>PTK7</i>	<i>RABEP1</i>	<i>RAF1</i>	<i>RALGDS</i>	<i>RAP1GDS1</i>
<i>RARA</i>	<i>RBM15</i>	<i>RET</i>	<i>RHOH</i>	<i>RNF213</i>	<i>ROS1</i>	<i>RPL22</i>	<i>RPN1</i>	<i>RUNX1</i>
<i>RUNX1T1</i> ^(ETO)	<i>RUNX2</i>	<i>SEC31A</i>	<i>SEPT5</i>	<i>SEPT6</i>	<i>SEPT9</i>	<i>SET</i>	<i>SH3GL1</i>	<i>SLCIA2</i>
<i>SNX29</i> ^(RUNC2A)	<i>SRSF3</i>	<i>SS18</i>	<i>SSX1</i>	<i>SSX2</i>	<i>SSX4</i>	<i>STAT6</i>	<i>STL</i>	<i>SYK</i>
<i>TAF15</i>	<i>TAL1</i>	<i>TAL2</i>	<i>TBL1XR1</i>	<i>TCF3</i> ^(E2A)	<i>TCL1A</i> ^(TCL1)	<i>TEC</i>	<i>TET1</i>	<i>TFE3</i>
<i>TFG</i>	<i>TFPT</i>	<i>TFRC</i>	<i>TLX1</i>	<i>TLX3</i>	<i>TMPRSS2</i>	<i>TNFRSF11A</i>	<i>TOP1</i>	<i>TP63</i>
<i>TPM3</i>	<i>TPM4</i>	<i>TRIM24</i>	<i>TRIP11</i>	<i>TTL</i>	<i>TYK2</i>	<i>USP6</i>	<i>WHSC1</i> ^(MMSET or NSD2)	
<i>WHSC1L1</i>	<i>YPEL5</i>	<i>ZBTB16</i>	<i>ZMYM2</i>	<i>ZNF384</i>	<i>ZNF521</i>			

† Comprehensive Genomic Profiling with FoundationOne Heme involves:

- Next generation sequencing of the DNA of 406 cancer-related genes known to be clinically relevant to solid tumours
- Uniform coverage across the entire coding sequence of each gene plus select introns from 31 genes frequently rearranged in cancer
- Next generation sequencing of the RNA of 265 cancer-related genes known to be clinically relevant to solid tumours
- Use of hybrid-capture technology to identify base substitutions, insertions/deletions, copy number alterations and rearrangements

‡ Current as of November 2019. Please visit www.foundationmedicine.com for the most up-to-date gene list.

References

- 1 He, J. et al. (2016) Integrated genomic DNA/RNA profiling of hematologic malignancies in the clinical setting. *Blood*. 127(24):3004-14.

