

Technical Specifications

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



Methods¹

- 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 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 [†] and MSI [‡]	
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 [§]	

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

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

[§] 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 haematopathologists.
- 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 Foundation Medicine Secure Email and Foundation Medicine online portal.

Current Gene List²

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	ASXL1
ATM	ATR	ATRX	AURKA	AURKB	AXIN1	AXL	B2M
BARD1	BCL10	BCL11B	BCL2	BCL2L2	BCL6	BCL7A	BCOR
BIRC3	BLM	BRAF	BRCA1	BRCA2	BRD4	BRIP1 (BACH1)	BRSK1
BTK	BTLA	C11orf30 (EMSY)	CAD	CALR	CARD11	CBFB	CBL
CCND2	CCND3	CCNE1	CCT6B	CD22	CD274 (PD-L1)	CD36	CD58
CD79A	CD79B	CDC73	CDH1	CDK12	CDK4	CDK6	CDK8
CDKN2A	CDKN2B	CDKN2C	CEBPA	CHD2	CHEK1	CHEK2	CIC
CKS1B	CPS1	CREBBP	CRKL	CRLF2	CSF1R	CSF3R	CTCF
CTNNB1	CUX1	CXCR4	DAXX	DDR2	DDX3X	DNM2	DNMT3A
DTX1	DUSP2	DUSP9	EBF1	ECT2L	EED	EGFR	ELP2
EPHA3	EPHA5	EPHA7	EPHB1	ERBB2	ERBB3	ERBB4	ERG
ETS1	ETV6	EXOSC6	EZH2	FAF1	FAM46C	FANCA	FANCC
FANCE	FANCF	FANCG	FANCL	FAS (TNFRSF6)	FBXO11	FBXO31	FBXW7
GF14	FGF19	FGF23	FGF3	FGF4	FGF6	FGFR1	FGFR2
FGFR4	FHIT	FLCN	FLT1	FLT3	FLT4	FLYWCH1	FOXL2
FOXO3	FOXP1	FRS2	GADD45B	GATA1	GATA2	GATA3	GID4 (C17orf39)
GNA12	GNA13	GNAQ	GNAS	GPR124	GRIN2A	GSK3B	GTSE1
HDAC4	HDAC7	HGF	HIST1H1C	HIST1H1D	HIST1H1E	HIST1H2AC	HIST1H2AG
HIST1H2AM	HIST1H2BC	HIST1H2BJ	HIST1H2BK	HIST1H2BO	HIST1H3B	HNF1A	HRAS
ICK	ID3	IDH1	IDH2	IGF1R	IKBKE	IKZF1	IKZF2
IL7R	INHBA	INPP4B	INPP5D (SHIP)	IRF1	IRF4	IRF8	IRS2
JAK2	JAK3	JARID2	JUN	KAT6A (MYST3)	KDM2B	KDM4C	KDM5A
KDM6A	KDR	KEAP1	KIT	KLHL6	KMT2A (MLL)	KMT2C (MLL3)	KMT2D (MLL2)
LEF1	LRP1B	LRRK2	MAF	MAFB	MAGED1	MALT1	MAP2K1 (MEK1)
MAP2K4	MAP3K1	MAP3K14	MAP3K6	MAP3K7	MAPK1	MCL1	MDM2
MED12	MEF2B	MEF2C	MEN1	MET	MIB1	MITF	MKI67
MPL	MRE11A	MSH2	MSH3	MSH6	MTOR	MUTYH	MYC
MYCN	MYD88	MYO18A	NCOR2	NCSTN	NF1	NF2	NFE2L2
NKX2-1	NOD1	NOTCH1	NOTCH2	NPM1	NRAS	NT5C2	NTRK1
NTRK3	NUP93	NUP98	P2RY8	PAG1	PAK3	PALB2	PASK
PBRM1	PC	PCBP1	PCLO	PDCD1 (PD-1)	PDCD11	PDCD1LG2 (PD-L2)	PDGFRA
PDK1	PHF6	PIK3CA	PIK3CG	PIK3R1	PIK3R2	PIM1	PLCG2
PPP2R1A	PRDM1	PRKAR1A	PRKDC	PRSS8	PTCH1	PTEN	PTPN11
PTPN6 (SHP-1)	PTPRO	RAD21	RAD50 (SHP-1)	RAD51	RAF1	RARA	RASGEF1A
RELN	RET	RHOA	RICTOR	RNF43	ROS1	RPTOR	RUNX1
SDHA	SDHB	SDHC	SDHD	SERP2	SETBP1	SETD2	SF3B1
SMAD2	SMAD4	SMARCA1	SMARCA4	SMARCB1	SMC1A	SMC3	SMO
SOCS2	SOCS3	SOX10	SOX2	SPEN	SPOP	SRC	SRSF2
STAT3	STAT4	STAT5A	STAT5B	STAT6	STK11	SUFU	SUZ12
TBL1XR1	TCF3 (E2A)	TCL1A (TCL1)	TET2	TGFBR2	TLL2	TMEM30A	TMSB4XP8 (TMSL3)
TNFAIP3	TNFRSF11A	TNFRSF14	TNFRSF17	TOP1	TP53	TP63	TRAF2
TRAF5	TSC1	TSC2	TSHR	TUSC3	TYK2	U2AF1	U2AF2
WDR90	WHSC1 (MMSET or NSD2)		WISP3	WT1	XBPI	XPO1	YY1AP1
ZNF217	ZNF24 (ZSCAN3)	ZNF703	ZRSR2				

Select DNA Rearrangements³

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					



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	FOXPI
FSTL3	FUS	GAS7	GLI1	GMPS	GPHN	HERPUD1	HEY1	HIP1
HIST1H4I	HLF	HMGAI	HMGAI2	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	LCPI	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	SLCIA2
SNX29 (RUNC2A)	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	TOP1	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: "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 September 2018. Please visit www.foundationmedicine.com for the most up-to-date gene list.
- 3 Select Introns only. Detailed list available upon request.