FOUNDATIONONE™ Heme

Technical Information and Test Overview

Molecular diagnostics are routinely used to understand the molecular mechanism of individual patients' hematological 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 individualize treatment by matching a patient with the best therapy for their cancer.[1] This approach may be valuable in the treatment of hematologic malignancies, sarcomas and pediatric cancers, which have their own unique genomic profiles.

Methods

FoundationOne™ Heme is designed to analyze and interpret sequence information for somatically altered genes in human hematologic malignancies (leukemias, lymphomas, and myelomas), sarcomas, and pediatric 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 analyzes the complete coding DNA sequences of 405 genes, as well as selected introns of 31 genes involved in rearrangements. FoundationOne 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

Test results are provided in an interpretive report, both in hard copy and via the FoundationOne Interactive Cancer Explorer™.[2]

If a clinically relevant alteration is found in any one of the genes 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 Heme that has not yet been adequately characterized 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 Heme analytical methodology has identified the presence of the alteration in less than 10% of the assayed tumor DNA.

FoundationOne Heme Includes the Commonly Tested Genes for Hematologic Malignancies, Sarcomas and Pediatric Cancers

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

Current Gene List

FoundationOne Heme includes tests for genomic alterations in each of the genes listed. FoundationOne Heme is designed to interrogate the entire coding sequence of 405 genes, selected introns of 31 genes involved in rearrangements and utilizes RNA sequencing to interrogate 265 genes known to be somatically altered in human hematologic malignancies, sarcomas and pediatric 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
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

gene list continued on following page

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

FOUNDATIONONE™ Heme

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	

[1.]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. 9th ed. Kindle ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2011.

[2.]Please contact client.services@foundationmedicine.com to set up an Interactive Cancer Explorer account.

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