



Intended Use

FoundationOne Liquid CDx is a next generation sequencing based in vitro diagnostic device that analyzes 324 genes. Substitutions and insertion and deletion alterations (indels) are reported in 311 genes, copy number alterations (CNAs) are reported in 310 genes, and gene rearrangements are reported in 324 genes. The test also detects tumor fraction and the genomic signatures blood tumor mutational burden (bTMB) and microsatellite instability high (MSI-H) status. FoundationOne Liquid CDx utilizes circulating cell-free DNA (cfDNA) isolated from plasma derived from the anti-coagulated peripheral whole blood of cancer patients. The test is intended to be used as a companion diagnostic to identify patients who may benefit from treatment with targeted therapies in accordance with the approved therapeutic product labeling. Additionally, FoundationOne Liquid CDx is intended to provide tumor mutation profiling to be used by qualified health care professionals in accordance with professional guidelines in oncology for patients with malignant neoplasms.

A negative result from a plasma specimen does not mean that the patient's tumor is negative for genomic findings. Patients who are negative for genomic findings should be reflexed to routine biopsy and their tumor mutation status confirmed using an FDA-approved tumor tissue test, if feasible.

FoundationOne Liquid CDx is a single-site assay performed at Foundation Medicine, Inc. in Cambridge, MA.



Summary of Analytical Sensitivity and Specificity

Results from our Limit of Detection (LoD) study are shown below, indicating the median variant allele frequency, tumor fraction or unstable loci at which the test has shown 95% probability of detection. Please refer to our product labeling for a list of the 75 genes baited for enhanced sensitivity and complete product specifications.

ALTERATION TYPE	BAIT SET REGION	MEDIAN LIMIT OF DETECTION (LOD)
Short Variants	Enhanced Sensitivity	0.40% VAF
	Standard Sensitivity	0.82% VAF
Rearrangements	Enhanced Sensitivity	0.37% VAF
	Standard Sensitivity	0.90% VAF
Copy Number Amplification	NA	21.7% TF
Copy Number Loss	NA	30.4% TF
MSI	NA	0.8% Unstable loci
bTMB (component indels)	NA	1.00% VAF
bTMB (component subs)	NA	1.00% VAF

VAF = variant allele frequency; TF = tumor fraction
The accuracy of %VAF / %TF have not been analytically validated

In our Limit of Blank study, which evaluated variant calling in healthy donors, 1,735 unique variants were included in the analysis for a total of 137,065 data points. A total of 18 false positives were observed across 4 unique short variants. The LoB was determined to be the ideal value of zero for short variants, rearrangements and CNAs. The false positive rate was shown to be 0% for rearrangements and CNAs and 0.013% (-1 in 8,000) for short variants (substitutions and indels).



FoundationOne Liquid CDx Gene List[†]

As a professional service, FoundationOne Liquid CDx interrogates 324 genes, including 309 genes with complete exonic (coding) coverage and 15 genes with only select non-coding coverage (indicated with an *); **75 genes (indicated in bold) are captured with increased sensitivity** and have complete exonic (coding) coverage unless otherwise noted. The test also detects tumor fraction and the genomic signatures blood mutational burden (bTMB) and microsatellite instability high (MSI-H) status.

ABL1 [Exons 4-9]	ALOX12B	ASXL1	BAP1	BCR* [Introns 8, 13, 14]	BRIP1	CASP8
ACVR1B	AMER1 (FAM123B)	ATM	BARD1	BRAF [Exons 11-18, Introns 7-10]	BTG1	CBFB
AKT1 [Exon 3]	APC	ATR	BCL2	BRCA1 [Introns 2, 7, 8, 12, 16, 19, 20]	BTG2	CBL
AKT2	AR	ATRAX	BCL2L1	BRCA2 [Intron 2]	BTK [Exons 2, 15]	CCND1
AKT3	ARAF [Exons 4, 5, 7, 11, 13, 15, 16]	AURKA	BCL2L2	BRD4	C11orf30 (EMSY)	CCND2
ALK [Exons 20-29 Introns 18,19]	ARFRP1	AURKB	BCL6		C17orf39 (GID4)	CCND3
	ARID1A	AXINI	BCOR		CALR	CCNE1
		AXL	BCORL1		CARD11	CD22

(FoundationOne Liquid CDx Gene List continued)

CD70	ERBB2	FOXL2	KLHL6	NF1	PPARG	SMAD2
CD74* [Introns 6-8]	ERBB3 [Exons 3, 6, 7, 8, 10, 12, 20, 21, 23, 24, 25]	FUBP1	KMT2A (MLL) [Introns 6, 8-11, Intron 7]	NF2	PPP2R1A	SMAD4
CD79A	ERBB4	GABRA6	KMT2D (MLL2)	NFE2L2	PPP2R2A	SMARCA4
CD79B	ERCC4	GATA3	KRAS	NFKBIA	PRDM1	SMARCB1
CD274 (PD-L1)	ERG	GATA4	LTN1	NKX2-1	PRKARIA	SMO
CDC73	ERRFI1	GATA6	LTK	NOTCH1	PRKCI	SNCAIP
CDH1	ESR1 [Exons 4-8]	GNAI1 [Exons 4, 5]	LYN	NOTCH2 [Intron 26]	PTCH1	SOCS1
CDK12	ETV4* [Intron 8]	GNAI3	MAF	NOTCH3	PTEN	SOX2
CDK4	ETV5* [Introns 6,7]	GNAQ [Exons 4, 5]	MAP2K1 (MEK1) [Exons 2, 3]	NPM1 [Exons 4-6, 8, 10]	PTPN11	SOX9
CDK6	ETV6* [Introns 5,6]	GNAS [Exons 1, 8]	MAP2K2 (MEK2) [Exons 2-4, 6, 7]	NRAS [Exons 2, 3]	PTPRO	SPEN
CDK8	EWSR1* [Introns 7-13]	GRM3	MAP2K4	NSD3 (WHSC1L1)	QKI	SPOP
CDKN1A	EZH2 [Exons 4, 16, 17, 18]	GSK3B	MAP3K1	NT5C2	RAC1	SRC
CDKN1B	EZR* [Introns 9-11]	H3F3A	MAP3K13	NTRK1 [Exons 14, 15, Introns 8-11]	RAD21	STAG2
CDKN2A	FAM46C	HDAC1	MAPK1	NTRK2 [Intron 12]	RAD51	STAT3
CDKN2B	FANCA	HGF	MCL1	NTRK3 [Exons 16, 17]	RAD51B	STK11
CDKN2C	FANCC	HNF1A	MDM2	NUTM1* [Intron 1]	RAD51C	SUFU
CEBPA	FANCG	HRAS [Exons 2, 3]	MDM4	P2RY8	RAD51D	SYK
CHEK1	FANCL	HSD3B1	MED12	PALB2	RAD52	TBX3
CHEK2	FAS	ID3	MEF2B	PARK2	RAD54L	TEK
CIC	FBXW7	IDH1 [Exon 4]	MEN1	PARP1	RAF1 [Exons 3, 4, 6, 7, 10, 14, 15, 17, Introns 4-8]	TERC* (ncRNA)
CREBBP	FGF10	IDH2 [Exon 4]	MERTK	PARP2	RARA [Intron 2]	TERT* (Promoter)
CRKL	FGF12	IGF1R	MET	PARP3	RB1	TET2
CSF1R	FGF14	IKBKE	MI1F	PAX5	RBM10	TGFBR2
CSF3R	FGF19	IKZF1	MKMK1	PBRM1	REL	TIPARP
CTCF	FGF23	INPP4B	MLH1	PDCC1 (PD-1)	RET [Introns 7, 8, Exons 11, 13-16, Introns 9-11]	TMPRSS2* [Introns 1-3]
CTNNA1	FGF3	IRF2	MPL [Exon 10]	PDCD1 (PD-L1)	RFA	REL
CTNNB1 [Exon 3]	FGF4	IRF4	MRE11A	PDCD1LG2 (PD-L2)	RNF43	TNFAIP3
CUL3	FGF6	IRS2	MSH2 [Intron 5]	PDGFRA [Exons 12, 18, Introns 7, 9, 11]	ROSI [Exons 31, 36-38, 40, Introns 31-35]	TNFRSF14
CUL4A	FGFR1 [Introns 1, 5, Intron 17]	JAK1	MSH3	PDGFRB [Exons 12-21, 23]	RPTOR	TP53
CXCR4	FGFR2 [Intron 1, Intron 17]	JAK2 [Exon 14]	MSH6	PDK1	RSPO2* [Intron 1]	TSC1
CYP17A1	FGFR3 [Exons 7, 9 (alternative designation exon 10), 14, 18, Intron 17]	JAK3 [Exons 5, 11, 12, 13, 15, 16]	MST1R	PIK3C2B	SDC4* [Intron 2]	TSC2
DAXX	FLCN	JUN	MTAP	PIK3C2G	SDHA	TYRO3
DDR1	FLT1	KDM5A	MTOR [Exons 19, 30, 39, 40, 43-45, 47, 48, 53, 56]	PIK3CA Exons 2, 3, 5-8, 10, 14, 19, 21 (Coding Exons 1, 2, 4-7, 9, 13, 18, 20)	SDHB	U2AF1
DDR2 [Exons 5, 17, 18]	FLT3 [Exons 14, 15, 20]	KDM5C	MUTYH	PIK3CB	SDHC	VEGFA
DIS3	FH	KDM6A	MYB* [Intron 14]	PIK3R1	SDHD	VHL
DNMT3A	FLN1	KDR	MYC [Intron 1]	PIM1	SETD2	WHSC1
DOT1L	FLN2	KEAP1	MYCL (MYCL1)	PMS1	SF3B1	WT1
EED	FLT3 [Exons 14, 15, 20]	KEL	MYCN	POLD1	SGK1	XPO1
EGFR [Introns 7, 15, 24-27]	FLN3	KIT [Exons 8, 9, 11, 12, 13, 17, Intron 16]	MYD88 [Exon 4]	POLE	SLC34A2* [Intron 4]	XRCC2
EP300	FLN4		NBN			ZNF217
EPHA3						ZNF703
EPHB1						
EPHB4						

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*Current as of August 2020. Please visit foundationmedicine.com for the most up-to-date gene list.

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