

ABOUT THE TEST FoundationOne®CDx is a next-generation sequencing (NGS) based assay that identifies genomic findings within hundreds of cancer-related genes.

PATIENT	DISEASE Unknown primary carcinoma (NOS)	PHYSICIAN	ORDERING PHYSICIAN Yeh, Yi-Chen	SPECIMEN	SPECIMEN SITE Parotid Gland
	NAME Lin, Hsiu Tzu		MEDICAL FACILITY Taipei Veterans General Hospital		SPECIMEN ID S111-46058A (PF22136)
	DATE OF BIRTH 18 October 1967		ADDITIONAL RECIPIENT None		SPECIMEN TYPE Slide Deck
	SEX Female		MEDICAL FACILITY ID 205872		DATE OF COLLECTION 09 November 2022
	MEDICAL RECORD # 31956180		PATHOLOGIST Not Provided		SPECIMEN RECEIVED 01 December 2022

Biomarker Findings

Microsatellite status - MS-Stable

Tumor Mutational Burden - 1 Muts/Mb

Genomic Findings

For a complete list of the genes assayed, please refer to the Appendix.

KEL R248W

MLL2 rearrangement exon 9

TNFAIP3 V377M - subclonal[†]

[†] See About the Test in appendix for details.

Report Highlights

- There are no highlights associated with this patient's genomic findings.

For more information on potential biological and clinical significance, see the Biomarker and Genomic Findings sections.

BIOMARKER FINDINGS

Microsatellite status - MS-Stable

Tumor Mutational Burden - 1 Muts/Mb

THERAPY AND CLINICAL TRIAL IMPLICATIONS

No therapies or clinical trials. See Biomarker Findings section

No therapies or clinical trials. See Biomarker Findings section

No therapies or clinical trials are associated with the Genomic Findings for this sample.

If you have questions or comments about this result, please contact your local

Customer Service team

(<https://www.rochefoundationmedicine.com/home/contact-us.html>)

GENOMIC FINDINGS WITH NO REPORTABLE THERAPEUTIC OR CLINICAL TRIAL OPTIONS

For more information regarding biological and clinical significance, including prognostic, diagnostic, germline, and potential chemosensitivity implications, see the Genomic Findings section.

KEL - R248W	p. 4	TNFAIP3 - V377M - subclonal	p. 5
MLL2 - rearrangement exon 9	p. 4		

NOTE Genomic alterations detected may be associated with activity of certain approved therapies; however, the agents listed in this report may have varied clinical evidence in the patient's tumor type. Therapies and the clinical trials listed in this report may not be complete and exhaustive. Neither the therapeutic agents nor the trials identified are ranked in order of potential or predicted efficacy for this patient, nor are they ranked in order of level of evidence for this patient's tumor type. This report should be regarded and used as a supplementary source of information and not as the single basis for the making of a therapy decision. All treatment decisions remain the full and final responsibility of the treating physician and physicians should refer to approved prescribing information for all therapies.

Therapies contained in this report may have been approved by the US FDA.

Disclaimer: Foundation Medicine Inc. only provides PDF report as an official issuance of the test result. Any other transformed format is not an "official / formal solution" and not guarantee the accuracy of this conversion. It is suggested the hospital to verify the outputs and validate the suitability of use.

ORDERED TEST # ORD-1514808-01

BIOMARKER FINDINGS

BIOMARKER

Microsatellite status

RESULT

MS-Stable

POTENTIAL TREATMENT STRATEGIES

— Targeted Therapies —

On the basis of clinical evidence, MSS tumors are significantly less likely than MSI-H tumors to respond to anti-PD-1 immune checkpoint inhibitors¹⁻³, including approved therapies nivolumab and pembrolizumab⁴. In a retrospective analysis of 361 patients with solid tumors treated with pembrolizumab, 3% were MSI-H and experienced a significantly higher ORR compared with non-MSI-H cases (70% vs. 12%, $p=0.001$)⁵.

FREQUENCY & PROGNOSIS

MSI-high (MSI-H) has been observed at high frequency in endometrial cancers (14-33%)⁶⁻¹³, colorectal cancers (CRCs; 10-15%)^{3,14-17}, and gastric cancers (12-35%)¹⁸⁻²¹ and at lower frequencies in many other tumor types, including esophageal²², small bowel²³⁻²⁷, hepatobiliary²⁸⁻³⁴, prostate³⁵⁻³⁷, and urinary tract carcinomas³⁸⁻⁴⁰. In one study, MSI-H status was associated with a positive prognostic effect in patients with gastric cancer treated with surgery alone and a negative predictive effect in patients treated with chemotherapy⁴¹. Data regarding the role of MSI-H on prognosis and survival in endometrial cancer are conflicting^{6,9-10,12,42-44}. However, studies specifically analyzing early stage endometrial cancer have reported a correlation between MSI-H and decreased survival^{8,11,13,43}, thereby suggesting that MSI-H predicts for poor prognosis in this subset of endometrial tumors.

FINDING SUMMARY

Microsatellite instability (MSI) is a condition of genetic hypermutability that generates excessive amounts of short insertion/deletion mutations in the genome; it generally occurs at microsatellite DNA sequences and is caused by a deficiency in DNA mismatch repair (MMR) in the tumor¹⁶. Defective MMR and consequent MSI occur as a result of genetic or epigenetic inactivation of one of the MMR pathway proteins, primarily MLH1, MSH2, MSH6, or PMS2^{16,45-46}. This sample is microsatellite-stable (MSS), equivalent to the clinical definition of an MSS tumor: one with mutations in none of the tested microsatellite markers^{15,47-48}. MSS status indicates MMR proficiency and typically correlates with intact expression of all MMR family proteins^{15-16,46,48}.

Disclaimer: Foundation Medicine Inc. only provides PDF report as an official issuance of the test result. Any other transformed format is not an "official / formal solution" and not guarantee the accuracy of this conversion. It is suggested the hospital to verify the outputs and validate the suitability of use.

© 2022 Foundation Medicine, Inc. All rights reserved.

Electronically signed by Erik Williams, M.D. | 09 December 2022
Julia Elvin, M.D., Ph.D., Laboratory Director CLIA: 22D2027531
Nimesh R. Patel, M.D., Laboratory Director CLIA: 34D2044309
Foundation Medicine, Inc. | www.rochefoundationmedicine.com

Sample Preparation: 150 Second St., 1st Floor, Cambridge, MA 02141 · CLIA: 22D2027531
Sample Analysis: 150 Second St., 1st Floor, Cambridge, MA 02141 · CLIA: 22D2027531
Post-Sequencing Analysis: 150 Second St., 1st Floor, Cambridge, MA 02141 · CLIA: 22D2027531

ORDERED TEST # ORD-1514808-01

BIOMARKER FINDINGS

BIOMARKER

Tumor Mutational Burden

RESULT

1 Muts/Mb

POTENTIAL TREATMENT STRATEGIES

— Targeted Therapies —

On the basis of clinical evidence in solid tumors, increased TMB may be associated with greater sensitivity to immunotherapeutic agents, including anti-PD-L1⁴⁹⁻⁵¹, anti-PD-1 therapies⁴⁹⁻⁵², and combination nivolumab and ipilimumab⁵³⁻⁵⁸. In multiple pan-tumor studies, increased tissue tumor mutational burden (TMB) was associated with sensitivity to immune checkpoint inhibitors^{49-52,59-63}. In the KEYNOTE 158 trial of pembrolizumab monotherapy for patients with solid tumors, significant improvement in ORR was observed for patients with TMB ≥ 10 Muts/Mb (as measured by this assay) compared with those with TMB < 10 Muts/Mb in a large cohort that included multiple tumor types⁵⁹; similar findings were observed in the KEYNOTE 028 and 012 trials⁵². At the same TMB cutpoint, retrospective analysis of patients with solid tumors treated with any checkpoint inhibitor identified that tissue TMB scores ≥ 10 Muts/Mb were associated with prolonged time to treatment failure compared with

scores < 10 muts/Mb (HR=0.68)⁶³. For patients with solid tumors treated with nivolumab plus ipilimumab in the CheckMate 848 trial, improved responses were observed in patients with a tissue TMB ≥ 10 Muts/Mb independent of blood TMB at any cutpoint in matched samples⁶⁴. However, support for higher TMB thresholds and efficacy was observed in the prospective Phase 2 MyPathway trial of atezolizumab for patients with pan-solid tumors, where improved ORR and DCR was seen in patients with TMB ≥ 16 Muts/Mb than those with TMB ≥ 10 and < 16 Muts/Mb⁶². Similarly, analyses across several solid tumor types reported that patients with higher TMB (defined as $\geq 16-20$ Muts/Mb) achieved greater clinical benefit from PD-1 or PD-L1-targeting monotherapy compared with patients with higher TMB treated with chemotherapy⁶⁵ or those with lower TMB treated with PD-1 or PD-L1-targeting agents⁵⁰.

FREQUENCY & PROGNOSIS

Carcinomas that have been reported to harbor the highest frequencies of elevated TMB include colorectal (CRC) (8-25%)^{17,66}, endometrial (7-24%)⁶⁷, intestinal type gastric (20%)⁶⁸, and non-small cell lung carcinoma (NSCLC; 8-13%)⁶⁹⁻⁷⁰. In patients with NSCLC, increased TMB is associated with higher tumor grade and poor prognosis⁷¹, as well as with a decreased frequency of known driver mutations in EGFR, ALK, ROS1, or MET (1% of high-TMB samples each), but not BRAF (10.3%) or KRAS (9.4%)⁶⁹. Although some studies have reported a lack of association between smoking and

increased TMB in NSCLC⁷¹⁻⁷², several other large studies did find a strong link⁷³⁻⁷⁶. In CRC, elevated TMB is associated with a higher frequency of BRAF V600E driver mutations^{17,66} and with microsatellite instability (MSI)⁶⁶, which in turn has been reported to correlate with better prognosis^{14,77-83}. Although increased TMB is associated with increased tumor grade in endometrioid endometrial carcinoma^{67,84-86} and bladder cancer⁸⁷, it is also linked with improved prognosis in patients with these tumor types⁶⁷.

FINDING SUMMARY

Tumor mutation burden (TMB, also known as mutation load) is a measure of the number of somatic protein-coding base substitution and insertion/deletion mutations occurring in a tumor specimen. TMB is affected by a variety of causes, including exposure to mutagens such as ultraviolet light in melanoma⁸⁸⁻⁸⁹ and cigarette smoke in lung cancer⁹⁰⁻⁹¹, treatment with temozolomide-based chemotherapy in glioma⁹²⁻⁹³, mutations in the proofreading domains of DNA polymerases encoded by the POLE and POLD1 genes^{17,67,94-96}, and microsatellite instability (MSI)^{17,67,96}. This sample harbors a TMB level associated with lower rates of clinical benefit from treatment with PD-1- or PD-L1-targeting immune checkpoint inhibitors compared with patients with tumors harboring higher TMB levels, based on several studies in multiple solid tumor types^{50-51,59}.

Disclaimer: Foundation Medicine Inc. only provides PDF report as an official issuance of the test result. Any other transformed format is not an "official / formal solution" and not guarantee the accuracy of this conversion. It is suggested the hospital to verify the outputs and validate the suitability of use.

© 2022 Foundation Medicine, Inc. All rights reserved.

Electronically signed by Erik Williams, M.D. | 09 December 2022
Julia Elvin, M.D., Ph.D., Laboratory Director CLIA: 22D2027531
Nimesh R. Patel, M.D., Laboratory Director CLIA: 34D2044309
Foundation Medicine, Inc. | www.rochefoundationmedicine.com

Sample Preparation: 150 Second St., 1st Floor, Cambridge, MA 02141 · CLIA: 22D2027531
Sample Analysis: 150 Second St., 1st Floor, Cambridge, MA 02141 · CLIA: 22D2027531
Post-Sequencing Analysis: 150 Second St., 1st Floor, Cambridge, MA 02141 · CLIA: 22D2027531

ORDERED TEST # ORD-1514808-01

GENOMIC FINDINGS

GENE

KEL

ALTERATION
R248W

TRANSCRIPT ID
NM_000420.2

CODING SEQUENCE EFFECT
742C>T

VARIANT CHROMOSOMAL POSITION
chr7:142651453

VARIANT ALLELE FREQUENCY (% VAF)
49.3%

POTENTIAL TREATMENT STRATEGIES

— Targeted Therapies —

There are no therapies available to target genomic alterations in KEL.

FREQUENCY & PROGNOSIS

KEL mutations have been reported up to 3.0% in tumors of the lung, endometrium, stomach, large intestine, soft tissue, and liver, with a higher incidence of 8.0% in various skin tumors (COSMIC, 2022)⁹⁷. However, the mechanism by which KEL mutations may contribute to tumorigenesis is not known.

FINDING SUMMARY

KEL encodes a transmembrane glycoprotein with similarities to zinc-dependent metalloproteases; this glycoprotein is highly polymorphic and forms the Kell blood group antigen⁹⁸.

GENE

MLL2

ALTERATION
rearrangement exon 9

POTENTIAL TREATMENT STRATEGIES

— Targeted Therapies —

There are no targeted therapies available to address genomic alterations in MLL2.

FREQUENCY & PROGNOSIS

MLL2 alterations are observed in a number of solid tumor contexts (COSMIC, 2022)⁹⁷, and are especially prevalent in lung squamous cell carcinoma (SCC)⁹⁹ and small cell lung carcinoma (SCLC)¹⁰⁰. MLL2 mutation was found to be an independent prognostic factor of poor PFS and OS in non-small cell lung cancer, but not in SCLC¹⁰¹. One study reported that MLL2 truncating mutations were more common in recurrent ovary granulosa cell tumors (GCT) compared with primary GCTs (24% [10/42] vs. 3.0% [1/32])¹⁰². In a study of esophageal SCC, high MLL2 expression positively correlated with tumor stage, differentiation, and size, and negatively correlated

with OS¹⁰³.

FINDING SUMMARY

MLL2 encodes an H3K4-specific histone methyltransferase that is involved in the transcriptional response to progesterone signaling¹⁰⁴. Germline de novo mutations of MLL2 are responsible for the majority of cases of Kabuki syndrome, a complex and phenotypically distinctive developmental disorder¹⁰⁵. A significant number of inactivating MLL2 alterations have been observed in multiple tumor types, suggesting a tumor suppressor role¹⁰⁶.

Disclaimer: Foundation Medicine Inc. only provides PDF report as an official issuance of the test result. Any other transformed format is not an "official / formal solution" and not guarantee the accuracy of this conversion. It is suggested the hospital to verify the outputs and validate the suitability of use.

© 2022 Foundation Medicine, Inc. All rights reserved.

Electronically signed by Erik Williams, M.D. | 09 December 2022
Julia Elvin, M.D., Ph.D., Laboratory Director CLIA: 22D2027531
Nimesh R. Patel, M.D., Laboratory Director CLIA: 34D2044309
Foundation Medicine, Inc. | www.rochefoundationmedicine.com

Sample Preparation: 150 Second St., 1st Floor, Cambridge, MA 02141 · CLIA: 22D2027531
Sample Analysis: 150 Second St., 1st Floor, Cambridge, MA 02141 · CLIA: 22D2027531
Post-Sequencing Analysis: 150 Second St., 1st Floor, Cambridge, MA 02141 · CLIA: 22D2027531

ORDERED TEST # ORD-1514808-01

GENOMIC FINDINGS
GENE

TNFAIP3

ALTERATION

V377M - subclonal

TRANSCRIPT ID

NM_006290.2

CODING SEQUENCE EFFECT

1129G>A

VARIANT CHROMOSOMAL POSITION

chr6:138199711

VARIANT ALLELE FREQUENCY (% VAF)

0.78%

POTENTIAL TREATMENT STRATEGIES
— Targeted Therapies —

There are no therapies that address the loss of TNFAIP3. A2o has multiple functions and is subject to a wide range of genomic lesions, thereby making it challenging to develop a unified therapeutic approach. Potential avenues targeting dysregulation of ubiquitination pathways include

anti-CD20 therapies, such as rituximab, and proteasome inhibitors, such as bortezomib¹⁰⁷. RNAi-mediated downregulation of TNFAIP3 has been reported to sensitize multiple myeloma cells to bortezomib¹⁰⁸.

FREQUENCY & PROGNOSIS

In the COSMIC dataset, TNFAIP3 mutations have been reported in 3.5% of prostate, 3.1% of endometrial, 2.8% of skin, 2.7% of gastric, and 2.4% of large intestine cancers (Jan 2022)⁹⁷. Overexpression of TNFAIP3 has been associated with aggressive high-grade ER-/PR-negative breast tumors¹⁰⁹, resistance to TNF-alpha and TRAIL-induced apoptosis in glioblastoma¹¹⁰⁻¹¹¹ and to chemotherapy in acute lymphoblastic leukemia¹¹², and poor prognosis in adrenocortical carcinoma¹¹³. Loss of heterozygosity in the genomic region including TNFAIP3 has been found in 16.8% (25/149) of colorectal adenocarcinomas, and significantly decreased TNFAIP3 mRNA expression has been observed in colorectal cancer (CRC) tumors compared with adjacent non-neoplastic mucosa¹¹⁴. Reduced A2o expression has been

suggested as a marker of poor prognosis in CRC¹¹⁵.

FINDING SUMMARY

TNFAIP3 encodes tumor necrosis factor alpha-induced protein 3, also known as A2o, a regulator of NF-kB signaling and apoptosis¹¹⁶ that has both ubiquitin ligase and deubiquitinase activities¹¹⁷⁻¹¹⁸ and whose loss or inactivation may be tumorigenic¹¹⁹. TNFAIP3 is frequently deleted or mutated in lymphoma, where it functions as a tumor suppressor¹¹⁹, but its expression and function are context dependent in solid tumors^{116,120-123}, leukemia^{112,124-125}, and multiple myeloma¹²⁶⁻¹²⁷. TNFAIP3 mutations that disrupt the A2op37 chain (amino acids 371-790), which mediates ubiquitin ligase activity and interaction with the cIAP1/TRAF2 complex^{117,128}, are predicted to be inactivating. In T-cells, cleavage of A2o codon R439 by MALT1 has been shown to upregulate NFkB signaling; R439A has been shown to block MALT1-mediated NF-kB activation¹²⁹; however, the function of R439 mutations outside of the context of T-cell lymphoma has not been reported.

Disclaimer: Foundation Medicine Inc. only provides PDF report as an official issuance of the test result. Any other transformed format is not an "official / formal solution" and not guarantee the accuracy of this conversion. It is suggested the hospital to verify the outputs and validate the suitability of use.

© 2022 Foundation Medicine, Inc. All rights reserved.

Electronically signed by Erik Williams, M.D. | 09 December 2022
 Julia Elvin, M.D., Ph.D., Laboratory Director CLIA: 22D2027531
 Nimesh R. Patel, M.D., Laboratory Director CLIA: 34D2044309
 Foundation Medicine, Inc. | www.rochefoundationmedicine.com

Sample Preparation: 150 Second St., 1st Floor, Cambridge, MA 02141 • CLIA: 22D2027531
 Sample Analysis: 150 Second St., 1st Floor, Cambridge, MA 02141 • CLIA: 22D2027531
 Post-Sequencing Analysis: 150 Second St., 1st Floor, Cambridge, MA 02141 • CLIA: 22D2027531

ORDERED TEST # ORD-1514808-01

APPENDIX
Variants of Unknown Significance

NOTE One or more variants of unknown significance (VUS) were detected in this patient's tumor. These variants may not have been adequately characterized in the scientific literature at the time this report was issued, and/or the genomic context of these alterations makes their significance unclear. We choose to include them here in the event that they become clinically meaningful in the future.

CHEK1
G401D

DAXX
E457del

FANCC
A325T

FGFR3
L164V

MLL2
L4575I and T4110I

MSH3
P63_P64insAAPPAP

NOTCH3
R75Q

PALB2
P758R

Disclaimer: Foundation Medicine Inc. only provides PDF report as an official issuance of the test result. Any other transformed format is not an "official / formal solution" and not guarantee the accuracy of this conversion. It is suggested the hospital to verify the outputs and validate the suitability of use.

© 2022 Foundation Medicine, Inc. All rights reserved.

Electronically signed by Erik Williams, M.D. | 09 December 2022
Julia Elvin, M.D., Ph.D., Laboratory Director CLIA: 22D2027531
Nimesh R. Patel, M.D., Laboratory Director CLIA: 34D2044309
Foundation Medicine, Inc. | www.rochefoundationmedicine.com

Sample Preparation: 150 Second St., 1st Floor, Cambridge, MA 02141 · CLIA: 22D2027531
Sample Analysis: 150 Second St., 1st Floor, Cambridge, MA 02141 · CLIA: 22D2027531
Post-Sequencing Analysis: 150 Second St., 1st Floor, Cambridge, MA 02141 · CLIA: 22D2027531

ORDERED TEST # ORD-1514808-01

APPENDIX

Genes Assayed in FoundationOne®CDx

FoundationOne CDx is designed to include genes known to be somatically altered in human solid tumors that are validated targets for therapy, either approved or in clinical trials, and/or that are unambiguous drivers of oncogenesis based on current knowledge. The current assay interrogates 324 genes as well as introns of 36 genes involved in rearrangements. The assay will be updated periodically to reflect new knowledge about cancer biology.

DNA GENE LIST: ENTIRE CODING SEQUENCE FOR THE DETECTION OF BASE SUBSTITUTIONS, INSERTION/DELETIONS, AND COPY NUMBER ALTERATIONS

ABL1	ACVR1B	AKT1	AKT2	AKT3	ALK	ALOX12B	AMER1 (FAM123B or WTX)	
APC	AR	ARAF	ARFRP1	ARID1A	ASXL1	ATM	ATR	ATRX
AURKA	AURKB	AXIN1	AXL	BAP1	BARD1	BCL2	BCL2L1	BCL2L2
BCL6	BCOR	BCORL1	BRAF	BRCA1	BRCA2	BRD4	BRIP1	BTG1
BTG2	BTK	CALR	CARD11	CASP8	CBFB	CBL	CCND1	CCND2
CCND3	CCNE1	CD22	CD274 (PD-L1)	CD70	CD79A	CD79B	CDC73	CDH1
CDK12	CDK4	CDK6	CDK8	CDKN1A	CDKN1B	CDKN2A	CDKN2B	CDKN2C
CEBPA	CHEK1	CHEK2	CIC	CREBBP	CRKL	CSF1R	CSF3R	CTCF
CTNNA1	CTNNB1	CUL3	CUL4A	CXCR4	CYP17A1	DAXX	DDR1	DDR2
DIS3	DNMT3A	DOT1L	EED	EGFR	EMSY (C11orf30)	EP300	EPHA3	EPHB1
EPHB4	ERBB2	ERBB3	ERBB4	ERCC4	ERG	ERF1	ESR1	EZH2
FANCA	FANCC	FANCG	FANCL	FAS	FBXW7	FGF10	FGF12	FGF14
FGF19	FGF23	FGF3	FGF4	FGF6	FGFR1	FGFR2	FGFR3	FGFR4
FH	FLCN	FLT1	FLT3	FOXL2	FUBP1	GABRA6	GATA3	GATA4
GATA6	GID4 (C17orf39)	GNA11	GNA13	GNAQ	GNAS	GRM3	GSK3B	H3-3A (H3F3A)
HDAC1	HGF	HNFA1	HRAS	HSD3B1	ID3	IDH1	IDH2	IGF1R
IKBKE	IKZF1	INPP4B	IRF2	IRF4	IRS2	JAK1	JAK2	JAK3
JUN	KDM5A	KDM5C	KDM6A	KDR	KEAP1	KEL	KIT	KLHL6
KMT2A (MLL)	KMT2D (MLL2)	KRAS	LTK	LYN	MAF	MAP2K1 (MEK1)	MAP2K2 (MEK2)	MAP2K4
MAP3K1	MAP3K13	MAPK1	MCL1	MDM2	MDM4	MED12	MEF2B	MEN1
MERTK	MET	MITF	MKNK1	MLH1	MPL	MRE11 (MRE11A)	MSH2	MSH3
MSH6	MST1R	MTAP	MTOR	MUTYH	MYC	MYCL (MYCL1)	MYCN	MYD88
NBN	NF1	NF2	NFE2L2	NFKBIA	NKX2-1	NOTCH1	NOTCH2	NOTCH3
NPM1	NRAS	NSD2 (WHSC1 or MMSET)	NSD3 (WHSC1L1)	NT5C2	NTRK1	NTRK2	NTRK3	NTRK3
P2RY8	PALB2	PARP1	PARP2	PARP3	PAX5	PBRM1	PDCD1 (PD-1)	PDCD1LG2 (PD-L2)
PDGFRA	PDGFRB	PDK1	PIK3C2B	PIK3C2G	PIK3CA	PIK3CB	PIK3R1	PIM1
PMS2	POLD1	POLE	PPARG	PPP2R1A	PPP2R2A	PRDM1	PRKAR1A	PRKCI
PRKN (PARK2)	PTCH1	PTEN	PTPN11	PTPRO	QKI	RAC1	RAD21	RAD51
RAD51B	RAD51C	RAD51D	RAD52	RAD54L	RAF1	RARA	RB1	RBM10
REL	RET	RICTOR	RNF43	ROS1	RPTOR	SDHA	SDHB	SDHC
SDHD	SETD2	SF3B1	SGK1	SMAD2	SMAD4	SMARCA4	SMARCB1	SMO
SNCAIP	SOC1	SOX2	SOX9	SPEN	SPOP	SRC	STAG2	STAT3
STK11	SUFU	SYK	TBX3	TEK	TENT5C (FAM46C)	TET2	TET2	TGFB2
TIPARP	TNFAIP3	TNFRSF14	TP53	TSC1	TSC2	TYRO3	U2AF1	VEGFA
VHL	WT1	XPO1	XRCC2	ZNF217	ZNF703			

DNA GENE LIST: FOR THE DETECTION OF SELECT REARRANGEMENTS

ALK	BCL2	BCR	BRAF	BRCA1	BRCA2	CD74	EGFR	ETV4
ETV5	ETV6	EWSR1	EZR	FGFR1	FGFR2	FGFR3	KIT	KMT2A (MLL)
MSH2	MYB	MYC	NOTCH2	NTRK1	NTRK2	NUTM1	PDGFRA	RAF1
RARA	RET	ROS1	RSP02	SDC4	SLC34A2	TERC*	TERT**	TPRSS2

*TERC is an NCRNA

**Promoter region of TERT is interrogated

ADDITIONAL ASSAYS: FOR THE DETECTION OF SELECT CANCER BIOMARKERS

Homologous Recombination status
Loss of Heterozygosity (LOH) score
Microsatellite (MS) status
Tumor Mutational Burden (TMB)

Disclaimer: Foundation Medicine Inc. only provides PDF report as an official issuance of the test result. Any other transformed format is not an "official / formal solution" and not guarantee the accuracy of this conversion. It is suggested the hospital to verify the outputs and validate the suitability of use.


© 2022 Foundation Medicine, Inc. All rights reserved.

Electronically signed by Erik Williams, M.D. | 09 December 2022
Julia Elvin, M.D., Ph.D., Laboratory Director CLIA: 22D2027531
Nimesh R. Patel, M.D., Laboratory Director CLIA: 34D2044309
Foundation Medicine, Inc. | www.rochefoundationmedicine.com

Sample Preparation: 150 Second St., 1st Floor, Cambridge, MA 02141 • CLIA: 22D2027531
Sample Analysis: 150 Second St., 1st Floor, Cambridge, MA 02141 • CLIA: 22D2027531
Post-Sequencing Analysis: 150 Second St., 1st Floor, Cambridge, MA 02141 • CLIA: 22D2027531

ORDERED TEST # ORD-1514808-01

APPENDIX
About FoundationOne®CDx

FoundationOne CDx fulfills the requirements of the European Directive 98/79 EC for in vitro diagnostic medical devices and is registered as a CE-IVD product by Foundation Medicine's EU Authorized Representative, Qarad b.v.b.a, Ciplstraat 3, 2440 Geel, Belgium. 

ABOUT FOUNDATIONONE CDx

FoundationOne CDx was developed and its performance characteristics determined by Foundation Medicine, Inc. (Foundation Medicine). FoundationOne CDx may be used for clinical purposes and should not be regarded as purely investigational or for research only. Foundation Medicine's clinical reference laboratories are qualified to perform high-complexity clinical testing.

Please refer to technical information for performance specification details:
www.rochefoundationmedicine.com/f1cdxtech.

INTENDED USE

FoundationOne®CDx (F1CDx) is a next generation sequencing based in vitro diagnostic device for detection of substitutions, insertion and deletion alterations (indels), and copy number alterations (CNAs) in 324 genes and select gene rearrangements, as well as genomic signatures including microsatellite instability (MSI), tumor mutational burden (TMB), and for selected forms of ovarian cancer, loss of heterozygosity (LOH) score, using DNA isolated from formalin-fixed, paraffin-embedded (FFPE) tumor tissue specimens. The test is intended as a companion diagnostic to identify patients who may benefit from treatment with therapies in accordance with approved therapeutic product labeling. Additionally, F1CDx 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 solid malignant neoplasms.

TEST PRINCIPLE

FoundationOne CDx will be performed exclusively as a laboratory service using DNA extracted from formalin-fixed, paraffin-embedded (FFPE) tumor samples. The proposed assay will employ a single DNA extraction method from routine FFPE biopsy or surgical resection specimens, 50-1000 ng of which will undergo whole-genome shotgun library construction and hybridization-based capture of all coding exons from 309 cancer-related genes, one promoter region, one non-coding (ncRNA), and select intronic regions from 34 commonly rearranged genes, 21 of which also include the coding exons. The assay therefore includes

detection of alterations in a total of 324 genes.

Using an Illumina® HiSeq platform, hybrid capture-selected libraries will be sequenced to high uniform depth (targeting >500X median coverage with >99% of exons at coverage >100X). Sequence data will be processed using a customized analysis pipeline designed to accurately detect all classes of genomic alterations, including base substitutions, indels, focal copy number amplifications, homozygous gene deletions, and selected genomic rearrangements (e.g., gene fusions). Additionally, genomic signatures including loss of heterozygosity (LOH), microsatellite instability (MSI) and tumor mutational burden (TMB) will be reported.

THE REPORT

Incorporates analyses of peer-reviewed studies and other publicly available information identified by Foundation Medicine; these analyses and information may include associations between a molecular alteration (or lack of alteration) and one or more drugs with potential clinical benefit (or potential lack of clinical benefit), including drug candidates that are being studied in clinical research. The F1CDx report may be used as an aid to inform molecular eligibility for clinical trials. Note: A finding of biomarker alteration does not necessarily indicate pharmacologic effectiveness (or lack thereof) of any drug or treatment regimen; a finding of no biomarker alteration does not necessarily indicate lack of pharmacologic effectiveness (or effectiveness) of any drug or treatment regimen.

Diagnostic Significance

FoundationOne CDx identifies alterations to select cancer-associated genes or portions of genes (biomarkers). In some cases, the Report also highlights selected negative test results regarding biomarkers of clinical significance.

Qualified Alteration Calls (Equivocal and Subclonal)

An alteration denoted as "amplification – equivocal" implies that the FoundationOne CDx assay data provide some, but not unambiguous, evidence that the copy number of a gene exceeds the threshold for identifying copy number amplification. The threshold used in FoundationOne CDx for identifying a copy number amplification is four (4) for *ERBB2* and six (6) for all other genes. Conversely, an alteration denoted as "loss – equivocal" implies that the FoundationOne CDx assay data provide some, but not unambiguous, evidence for homozygous deletion of the gene in question. An alteration denoted as "subclonal" is one that the FoundationOne CDx analytical

methodology has identified as being present in <10% of the assayed tumor DNA.

Ranking of Therapies and Clinical Trials
Ranking of Therapies in Summary Table

Therapies are ranked based on the following criteria: Therapies with clinical benefit (ranked alphabetically within each evidence category), followed by therapies associated with resistance (when applicable).

Ranking of Clinical Trials

Pediatric trial qualification → Geographical proximity → Later trial phase.

NATIONAL COMPREHENSIVE CANCER NETWORK® (NCCN®) CATEGORIZATION

Biomarker and genomic findings detected may be associated with certain entries within the NCCN Drugs & Biologics Compendium® (NCCN Compendium®) (www.nccn.org). The NCCN Categories of Evidence and Consensus indicated reflect the highest possible category for a given therapy in association with each biomarker or genomic finding. Please note, however, that the accuracy and applicability of these NCCN categories within a report may be impacted by the patient's clinical history, additional biomarker information, age, and/or co-occurring alterations. For additional information on the NCCN categories, please refer to the NCCN Compendium®. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). © National Comprehensive Cancer Network, Inc. 2022. All rights reserved. To view the most recent and complete version of the guidelines, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

Limitations

1. In the fraction-based MSI algorithm, a tumor specimen will be categorized as MSI-H, MSS, or MS-Equivocal according to the fraction of microsatellite loci determined to be altered or unstable (i.e., the fraction unstable loci score). In the F1CDx assay, MSI is evaluated based on a genome-wide analysis across >2000 microsatellite loci. For a given microsatellite locus, non-somatic alleles are discarded, and the microsatellite is categorized as unstable if remaining alleles differ from the reference genome. The final fraction unstable loci score is calculated as the number of unstable microsatellite loci divided by the number of evaluable microsatellite loci. The MSI-H and MSS cut-off thresholds were determined by

Disclaimer: Foundation Medicine Inc. only provides PDF report as an official issuance of the test result. Any other transformed format is not an "official / formal solution" and not guarantee the accuracy of this conversion. It is suggested the hospital to verify the outputs and validate the suitability of use.

© 2022 Foundation Medicine, Inc. All rights reserved.

Electronically signed by Erik Williams, M.D. | 09 December 2022
 Julia Elvin, M.D., Ph.D., Laboratory Director CLIA: 22D2027531
 Nimesh R. Patel, M.D., Laboratory Director CLIA: 34D2044309
 Foundation Medicine, Inc. | www.rochefoundationmedicine.com

Sample Preparation: 150 Second St., 1st Floor, Cambridge, MA 02141 · CLIA: 22D2027531
 Sample Analysis: 150 Second St., 1st Floor, Cambridge, MA 02141 · CLIA: 22D2027531
 Post-Sequencing Analysis: 150 Second St., 1st Floor, Cambridge, MA 02141 · CLIA: 22D2027531

ORDERED TEST # ORD-1514808-01

APPENDIX

About FoundationOne®CDx

- analytical concordance to a PCR comparator assay using a pan-tumor FFPE tissue sample set. Patients with results categorized as "MS-Stable" with median exon coverage <300X, "MS-Equivocal," or "Cannot Be Determined" should receive confirmatory testing using a validated orthogonal (alternative) method.
- TMB by F1CDx is determined by counting all synonymous and non-synonymous variants present at 5% allele frequency or greater (after filtering) and the total number is reported as mutations per megabase (mut/Mb) unit. Observed TMB is dependent on characteristics of the specific tumor focus tested for a patient (e.g., primary vs. metastatic, tumor content) and the testing platform used for the detection; therefore, observed TMB results may vary between different specimens for the same patient and between detection methodologies employed on the same sample. The TMB calculation may differ from TMB calculations used by other assays depending on variables such as the amount of genome interrogated, percentage of tumor, assay limit of detection (LoD), filtering of alterations included in the score, and the read depth and other bioinformatic test specifications. Refer to the SSED for a detailed description of these variables in FMI's TMB calculation https://www.accessdata.fda.gov/cdrh_docs/pdf17/P170019B.pdf. The clinical validity of TMB defined by this panel has been established for TMB as a qualitative output for a cut-off of 10 mutations per megabase but has not been established for TMB as a quantitative score.
 - Homologous Recombination status may be reported for epithelial ovarian, peritoneal, or Fallopian tube carcinomas (Coleman et al., 2017; 28916367). Samples with deleterious *BRCA1/2* alteration and/or Loss of Heterozygosity (LOH) score $\geq 16\%$ will be reported as "HRD Positive" and samples with absence of these findings will be reported as "HRD Not Detected," agnostic of potential secondary *BRCA1/2* reversion alterations. Certain potentially deleterious missense or small in-frame deletions in *BRCA1/2* may not be classified as deleterious and, in the absence of an elevated LOH profile, samples with such mutations may be classified as "HRD Not Detected." A result of "HRD Not Detected" does not rule out the presence of a *BRCA1/2* alteration or an elevated LOH profile outside the assay performance characteristic limitations.
 - The LOH score is determined by analyzing SNPs spaced at 1Mb intervals across the genome on the FoundationOne CDx test and

extrapolating an LOH profile, excluding arm- and chromosome-wide LOH segments. Detection of LOH has been verified only for ovarian cancer patients, and the LOH score result may be reported for epithelial ovarian, peritoneal, or Fallopian tube carcinomas. The LOH score will be reported as "Cannot Be Determined" if the sample is not of sufficient quality to confidently determine LOH. Performance of the LOH classification has not been established for samples below 35% tumor content. There may be potential interference of ethanol with LOH detection. The interfering effects of xylene, hemoglobin, and triglycerides on the LOH score have not been demonstrated.

- Alterations reported may include somatic (not inherited) or germline (inherited) alterations; however, the test does not distinguish between germline and somatic alterations. The test does not provide information about susceptibility.
- Biopsy may pose a risk to the patient when archival tissue is not available for use with the assay. The patient's physician should determine whether the patient is a candidate for biopsy.
- Reflex testing to an alternative FDA approved companion diagnostic should be performed for patients who have an *ERBB2* amplification result detected with copy number equal to 4 (baseline ploidy of tumor +2) for confirmatory testing. While this result is considered negative by FoundationOne®CDx (F1CDx), in a clinical concordance study with an FDA approved FISH test, 70% (7 out of 10 samples) were positive, and 30% (3 out of 10 samples) were negative by the FISH test with an average ratio of 2.3. The frequency of *ERBB2* copy number 4 in breast cancer is estimated to be approximately 2%. Multiple references listed in <https://www.mycancergenome.org/content/disease/breast-cancer/ERBB2/238/> report the frequency of HER2 overexpression as 20% in breast cancer. Based on the F1CDx HER2 CDx concordance study, approximately 10% of HER2 amplified samples had copy number 4. Thus, total frequency is conservatively estimated to be approximately 2%.

REPORT HIGHLIGHTS

The Report Highlights includes select genomic and therapeutic information with potential impact on patient care and treatment that is specific to the genomics and tumor type of the sample analyzed. This section may highlight information including targeted therapies with potential sensitivity or resistance; evidence-matched clinical trials; and variants with potential diagnostic, prognostic, nontargeted treatment, germline, or clonal

hematopoiesis implications. Information included in the Report Highlights is expected to evolve with advances in scientific and clinical research. Findings included in the Report Highlights should be considered in the context of all other information in this report and other relevant patient information. Decisions on patient care and treatment are the responsibility of the treating physician.

VARIANT ALLELE FREQUENCY

Variant Allele Frequency (VAF) represents the fraction of sequencing reads in which the variant is observed. This attribute is not taken into account for therapy inclusion, clinical trial matching, or interpretive content. Caution is recommended in interpreting VAF to indicate the potential germline or somatic origin of an alteration, recognizing that tumor fraction and tumor ploidy of samples may vary.

Precision of VAF for base substitutions and indels

BASE SUBSTITUTIONS	%CV*
Repeatability	5.11 - 10.40
Reproducibility	5.95 - 12.31
INDELS	%CV*
Repeatability	6.29 - 10.00
Reproducibility	7.33 - 11.71

*Interquartile Range = 1st Quartile to 3rd Quartile

VARIANTS TO CONSIDER FOR FOLLOW-UP GERMLINE TESTING

The variants indicated for consideration of follow-up germline testing are 1) limited to reportable short variants with a protein effect listed in the ClinVar genomic database (Landrum et al., 2018; 29165669) as Pathogenic, Pathogenic/Likely Pathogenic, or Likely Pathogenic (by an expert panel or multiple submitters), 2) associated with hereditary cancer-predisposing disorder(s), 3) detected at an allele frequency of >10%, and 4) in select genes reported by the ESMO Precision Medicine Working Group (Mandelker et al., 2019; 31050713) to have a greater than 10% probability of germline origin if identified during tumor sequencing. The selected genes are *ATM*, *BAP1*, *BRCA1*, *BRCA2*, *BRIP1*, *CHEK2*, *FH*, *FLCN*, *MLH1*, *MSH2*, *MSH6*, *MUTYH*, *PALB2*, *PMS2*, *POLE*, *RAD51C*, *RAD51D*, *RET*, *SDHA*, *SDHB*, *SDHC*, *SDHD*, *TSC2*, and *VHL*, and are not inclusive of all cancer susceptibility genes. The content in this report should not substitute for genetic counseling or follow-up germline testing, which is needed to distinguish whether a finding in this patient's

Disclaimer: Foundation Medicine Inc. only provides PDF report as an official issuance of the test result. Any other transformed format is not an "official / formal solution" and not guarantee the accuracy of this conversion. It is suggested the hospital to verify the outputs and validate the suitability of use.

© 2022 Foundation Medicine, Inc. All rights reserved.

Electronically signed by Erik Williams, M.D. | 09 December 2022
Julia Elvin, M.D., Ph.D., Laboratory Director CLIA: 22D2027531
Nimesh R. Patel, M.D., Laboratory Director CLIA: 34D2044309
Foundation Medicine, Inc. | www.rochefoundationmedicine.com

Sample Preparation: 150 Second St., 1st Floor, Cambridge, MA 02141 · CLIA: 22D2027531
Sample Analysis: 150 Second St., 1st Floor, Cambridge, MA 02141 · CLIA: 22D2027531
Post-Sequencing Analysis: 150 Second St., 1st Floor, Cambridge, MA 02141 · CLIA: 22D2027531

ORDERED TEST # ORD-1514808-01

APPENDIX

About FoundationOne®CDx

tumor sequencing is germline or somatic.
Interpretation should be based on clinical context.

VARIANTS THAT MAY REPRESENT CLONAL HEMATOPOIESIS

Variants that may represent clonal hematopoiesis (CH) are limited to select reportable short variants in defined genes identified in solid tumors only. Variant selection was determined based on gene tumor-suppressor or oncogene status, known role in solid tumors versus hematological malignancies, and literature prevalence. The defined genes are *ASXL1*, *CBL*, *DNMT3A*, *IDH2*, *JAK2*, *KMT2D (MLL2)*, *MPL*, *MYD88*, *SF3B1*, *TET2*, and *U2AF1* and are not inclusive of all CH genes. The content in this report should not substitute for dedicated hematological workup. Comprehensive genomic profiling of solid tumors detects nontumor alterations that are due to CH. Patient-matched peripheral blood mononuclear cell sequencing is required to conclusively determine if this alteration is present in tumor or is secondary to CH. Interpretation should be based on clinical context.

LEVEL OF EVIDENCE NOT PROVIDED

Drugs with potential clinical benefit (or potential lack of clinical benefit) are not evaluated for source or level of published evidence.

NO GUARANTEE OF CLINICAL BENEFIT

This Report makes no promises or guarantees that a particular drug will be effective in the treatment of disease in any patient. This Report also makes no promises or guarantees that a drug with potential lack of clinical benefit will in fact provide no clinical benefit.

NO GUARANTEE OF REIMBURSEMENT

Foundation Medicine makes no promises or guarantees that a healthcare provider, insurer or other third party payor, whether private or governmental, will reimburse a patient for the cost of FoundationOne CDx.

TREATMENT DECISIONS ARE RESPONSIBILITY OF PHYSICIAN

Drugs referenced in this Report may not be suitable for a particular patient. The selection of any, all or none of the drugs associated with potential clinical benefit (or potential lack of clinical benefit) resides entirely within the discretion of the treating physician. Indeed, the information in this Report must be considered in conjunction with all other relevant information regarding a particular patient, before the patient's treating physician recommends a course of treatment. Decisions on patient care and treatment must be based on the independent medical judgment of the treating physician, taking

into consideration all applicable information concerning the patient's condition, such as patient and family history, physical examinations, information from other diagnostic tests, and patient preferences, in accordance with the standard of care in a given community. A treating physician's decisions should not be based on a single test, such as this Test, or the information contained in this Report. Certain sample or variant characteristics may result in reduced sensitivity. FoundationOne CDx is performed using DNA derived from tumor, and as such germline events may not be reported.

SELECT ABBREVIATIONS

ABBREVIATION	DEFINITION
CR	Complete response
DCR	Disease control rate
DNMT	DNA methyltransferase
HR	Hazard ratio
ITD	Internal tandem duplication
MMR	Mismatch repair
mut/Mb	Mutations per megabase
NOS	Not otherwise specified
ORR	Objective response rate
OS	Overall survival
PD	Progressive disease
PFS	Progression-free survival
PR	Partial response
SD	Stable disease
TKI	Tyrosine kinase inhibitor

REFERENCE SEQUENCE INFORMATION

Sequence data is mapped to the human genome, Genome Reference Consortium Human Build 37 (GRCh37), also known as hg19.

MR Suite Version (RG) 7.4.0

Disclaimer: Foundation Medicine Inc. only provides PDF report as an official issuance of the test result. Any other transformed format is not an "official / formal solution" and not guarantee the accuracy of the data. The median exon coverage for this sample is 796x. The suitability of use.

ORDERED TEST # ORD-1514808-01

APPENDIX
References

1. Gatalica Z, et al. Cancer Epidemiol. Biomarkers Prev. (2014) PMID: 25392179
2. Kroemer G, et al. Oncoimmunology (2015) PMID: 26140250
3. Lal N, et al. Oncoimmunology (2015) PMID: 25949894
4. Le DT, et al. N. Engl. J. Med. (2015) PMID: 26028255
5. Ayers et al., 2016; ASCO-SITC Abstract P60
6. Zigelboim I, et al. J. Clin. Oncol. (2007) PMID: 17513808
7. Hampel H, et al. Cancer Res. (2006) PMID: 16885385
8. Stelloo E, et al. Clin. Cancer Res. (2016) PMID: 27006490
9. Kanopienė D, et al. Medicina (Kaunas) (2014) PMID: 25458958
10. Black D, et al. J. Clin. Oncol. (2006) PMID: 16549821
11. Nout RA, et al. Gynecol. Oncol. (2012) PMID: 22609107
12. Steinbakk A, et al. Cell Oncol (Dordr) (2011) PMID: 21547578
13. Bilbao C, et al. Int. J. Radiat. Oncol. Biol. Phys. (2010) PMID: 20005452
14. Guastadisegni C, et al. Eur. J. Cancer (2010) PMID: 20627535
15. Pawlik TM, et al. Dis. Markers (2004) PMID: 15528785
16. Kocarnik JM, et al. Gastroenterol Rep (Oxf) (2015) PMID: 26337942
17. Nature (2012) PMID: 22810696
18. Hiyama T, et al. J. Gastroenterol. Hepatol. (2004) PMID: 15209621
19. Wu MS, et al. Cancer Res. (1998) PMID: 9537253
20. dos Santos NR, et al. Gastroenterology (1996) PMID: 8536886
21. Fang WL, et al. Biomed Res Int (2013) PMID: 23555086
22. Farris AB, et al. Am. J. Surg. Pathol. (2011) PMID: 21422910
23. Agaram NP, et al. Am. J. Clin. Pathol. (2010) PMID: 20395525
24. Ruemmele P, et al. Am. J. Surg. Pathol. (2009) PMID: 19252434
25. Planck M, et al. Cancer (2003) PMID: 12627520
26. Hibi K, et al. Jpn. J. Cancer Res. (1995) PMID: 7775257
27. Muneyuki T, et al. Dig. Dis. Sci. (2000) PMID: 11117578
28. Zhang SH, et al. World J. Gastroenterol. (2005) PMID: 15918185
29. Chiappini F, et al. Carcinogenesis (2004) PMID: 14656944
30. Suto T, et al. J Surg Oncol (2001) PMID: 11223838
31. Momoi H, et al. J. Hepatol. (2001) PMID: 11580146
32. Liengswangwong U, et al. Int. J. Cancer (2003) PMID: 14506736
33. Moy AP, et al. Virchows Arch. (2015) PMID: 25680569
34. Yoshida T, et al. J. Gastroenterol. (2000) PMID: 11063221
35. Pritchard CC, et al. Nat Commun (2014) PMID: 25255306
36. Azzouzi AR, et al. BJU Int. (2007) PMID: 17233803
37. Burger M, et al. J. Mol. Med. (2006) PMID: 16924473
38. Bai S, et al. Am. J. Clin. Pathol. (2013) PMID: 23690119
39. Giedl J, et al. Am. J. Clin. Pathol. (2014) PMID: 25319978
40. Yamamoto Y, et al. Clin. Cancer Res. (2006) PMID: 16675567
41. Smyth et al., 2015; ASCO Gastrointestinal Cancers Symposium Abstract 62
42. Bilbao-Sieyro C, et al. Oncotarget (2014) PMID: 25026289
43. Mackay HJ, et al. Eur. J. Cancer (2010) PMID: 20304627
44. Arabi H, et al. Gynecol. Oncol. (2009) PMID: 19275958
45. You JF, et al. Br. J. Cancer (2010) PMID: 21081928
46. Bairwa NK, et al. Methods Mol. Biol. (2014) PMID: 24623249
47. Boland CR, et al. Cancer Res. (1998) PMID: 9823339
48. Boland CR, et al. Gastroenterology (2010) PMID: 20420947
49. Samstein RM, et al. Nat. Genet. (2019) PMID: 30643254
50. Goodman AM, et al. Mol. Cancer Ther. (2017) PMID: 28835386
51. Goodman AM, et al. Cancer Immunol Res (2019) PMID: 31405947
52. Cristescu R, et al. Science (2018) PMID: 30309915
53. Ready N, et al. J. Clin. Oncol. (2019) PMID: 30785829
54. Hellmann MD, et al. N. Engl. J. Med. (2018) PMID: 29658845
55. Hellmann MD, et al. Cancer Cell (2018) PMID: 29657128
56. Hellmann MD, et al. Cancer Cell (2018) PMID: 29731394
57. Rozeman EA, et al. Nat Med (2021) PMID: 33558721
58. Sharma P, et al. Cancer Cell (2020) PMID: 32916128
59. Marabelle A, et al. Lancet Oncol. (2020) PMID: 32919526
60. Ott PA, et al. J. Clin. Oncol. (2019) PMID: 30557521
61. Cristescu R, et al. J Immunother Cancer (2022) PMID: 35101941
62. Friedman CF, et al. Cancer Discov (2022) PMID: 34876409
63. Sturgill EG, et al. Oncologist (2022) PMID: 35274716
64. Schenker et al., 2022; AACR Abstract 7845
65. Legrand et al., 2018; ASCO Abstract 12000
66. Stadler ZK, et al. J. Clin. Oncol. (2016) PMID: 27022117
67. Cancer Genome Atlas Research Network, et al. Nature (2013) PMID: 23636398
68. Frampton et al., 2016; ASCO Abstract 11558
69. Spigel et al., 2016; ASCO Abstract 9017
70. Jiang et al., 2016; ASCO Abstract e23128
71. Xiao D, et al. Oncotarget (2016) PMID: 27009843
72. Shim HS, et al. J Thorac Oncol (2015) PMID: 26200269
73. Govindan R, et al. Cell (2012) PMID: 22980976
74. Ding L, et al. Nature (2008) PMID: 18948947
75. Imielinski M, et al. Cell (2012) PMID: 22980975
76. Kim Y, et al. J. Clin. Oncol. (2014) PMID: 24323028
77. Samowitz WS, et al. Cancer Epidemiol. Biomarkers Prev. (2001) PMID: 11535541
78. Elsaleh H, et al. Clin Colorectal Cancer (2001) PMID: 12445368
79. Brueckl WM, et al. Anticancer Res. () PMID: 12820457
80. Guidoboni M, et al. Am. J. Pathol. (2001) PMID: 11438476
81. Gryfe R, et al. N. Engl. J. Med. (2000) PMID: 10631274
82. Sinicrope FA, et al. Gastroenterology (2006) PMID: 16952542
83. Laghi L, et al. Dig Dis (2012) PMID: 22722556
84. Mehnert JM, et al. J. Clin. Invest. (2016) PMID: 27159395
85. Hussein YR, et al. Mod. Pathol. (2015) PMID: 25394778
86. Church DN, et al. Hum. Mol. Genet. (2013) PMID: 23528559
87. Cazier JB, et al. Nat Commun (2014) PMID: 24777035
88. Pfeifer GP, et al. Mutat. Res. (2005) PMID: 15748635
89. Hill VK, et al. Annu Rev Genomics Hum Genet (2013) PMID: 23875803
90. Pfeifer GP, et al. Oncogene (2002) PMID: 12379884
91. Rizvi NA, et al. Science (2015) PMID: 25765070
92. Johnson BE, et al. Science (2014) PMID: 24336570
93. Choi S, et al. Neuro-oncology (2018) PMID: 29452419
94. Briggs S, et al. J. Pathol. (2013) PMID: 23447401
95. Heitzer E, et al. Curr. Opin. Genet. Dev. (2014) PMID: 24583393
96. Roberts SA, et al. Nat. Rev. Cancer (2014) PMID: 25568919
97. Tate JG, et al. Nucleic Acids Res. (2019) PMID: 30371878
98. Clapéron A, et al. J. Biol. Chem. (2005) PMID: 15769748
99. Nature (2012) PMID: 22960745
100. Augert A, et al. J Thorac Oncol (2017) PMID: 28007623
101. Ardeshtir-Larijani F, et al. Clin Lung Cancer (2018) PMID: 29627316
102. Hillman RT, et al. Nat Commun (2018) PMID: 29950560
103. Abudurehman A, et al. J. Cancer Res. Clin. Oncol. (2018) PMID: 29532228
104. Vicent GP, et al. Genes Dev. (2011) PMID: 21447625
105. Hannibal MC, et al. Am. J. Med. Genet. A (2011) PMID: 21671394
106. Fagan RJ, et al. Cancer Lett. (2019) PMID: 31128216
107. Hymowitz SG, et al. Nat. Rev. Cancer (2010) PMID: 20383180
108. Zhu YX, et al. Blood (2011) PMID: 21289309
109. Vendrell JA, et al. Oncogene (2007) PMID: 17297453
110. Hjelmeland AB, et al. PLoS Biol. (2010) PMID: 20186265
111. Bellail AC, et al. Cancer Discov (2012) PMID: 22585859
112. Chen S, et al. Leuk. Res. (2015) PMID: 26159495
113. Hantel C, et al. Mol. Cell. Endocrinol. (2016) PMID: 26768118
114. Ungerback J, et al. Carcinogenesis (2012) PMID: 22843550
115. Bavi P, et al. Clin Epigenetics (2011) PMID: 22704353
116. Harhaj EW, et al. Cell Res. (2011) PMID: 21119682
117. Wertz IE, et al. Nature (2004) PMID: 15258597
118. Wertz IE, et al. Nature (2015) PMID: 26649818
119. Honma K, et al. Blood (2009) PMID: 19608751
120. Wang X, et al. Oncotarget (2016) PMID: 26909601
121. Couch G, et al. Cancer Prev Res (Phila) (2016) PMID: 27072986
122. Wang Y, et al. PLoS ONE (2015) PMID: 26485275
123. Salim H, et al. Genes Chromosomes Cancer (2013) PMID: 23929716
124. Saitoh Y, et al. Leukemia (2016) PMID: 26437781
125. Johansson P, et al. Int. J. Cancer (2016) PMID: 26199174
126. Broyl A, et al. Blood (2010) PMID: 20574050
127. Troppan K, et al. PLoS ONE (2015) PMID: 25856582
128. Yamaguchi N, et al. Sci Rep (2013) PMID: 24008839
129. Coornaert B, et al. Nat. Immunol. (2008) PMID: 18223652

Disclaimer: Foundation Medicine Inc. only provides PDF report as an official issuance of the test result. Any other transformed format is not an "official / formal solution" and not guarantee the accuracy of this conversion. It is suggested the hospital to verify the outputs and validate the suitability of use.