

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 Skin melanoma
NAME Chen, Wen-Tao
DATE OF BIRTH 02 July 1953
SEX Male
MEDICAL RECORD # 26940830

PHYSICIAN
ORDERING PHYSICIAN Yeh, Yi-Chen
MEDICAL FACILITY Taipei Veterans General Hospital
ADDITIONAL RECIPIENT None
MEDICAL FACILITY ID 205872
PATHOLOGIST Not Provided

SPECIMEN
SPECIMEN SITE Rectum
SPECIMEN ID S112-79051 (PF23030)
SPECIMEN TYPE Slide Deck
DATE OF COLLECTION 14 February 2023
SPECIMEN RECEIVED 21 March 2023

Biomarker Findings

Microsatellite status - MS-Stable
Tumor Mutational Burden - 0 Muts/Mb

Genomic Findings

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

MYC amplification - equivocal[†]
JUN amplification - equivocal[†]

3 Disease relevant genes with no reportable alterations: *BRAF, KIT, NRAS*

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

Report Highlights

- Evidence-matched clinical trial options based on this patient's genomic findings: (p. [4](#))

BIOMARKER FINDINGS

Microsatellite status - MS-Stable

Tumor Mutational Burden - 0 Muts/Mb

GENOMIC FINDINGS

MYC - amplification - equivocal

9 Trials see p. [4](#)

THERAPY AND CLINICAL TRIAL IMPLICATIONS

No therapies or clinical trials. See Biomarker Findings section

No therapies or clinical trials. See Biomarker Findings section

**THERAPIES WITH CLINICAL RELEVANCE
(IN PATIENT'S TUMOR TYPE)**

none

**THERAPIES WITH CLINICAL RELEVANCE
(IN OTHER TUMOR TYPE)**

none

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.

JUN - amplification - equivocal p. [3](#)

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.

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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 has been detected in 16-32% of cutaneous melanomas in several small datasets, with the majority exhibiting MSI-low⁶. A higher frequency of MSI (low and high) has been reported in metastatic tumors (20-77%) compared to primary tumors (2-30%)⁷. No association between MSI status and clinicopathological features of patients with melanoma was reported in one study⁸.

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 tumor⁹. 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 PMS2⁹⁻¹¹. This sample is microsatellite-stable (MSS), equivalent to the clinical definition of an MSS tumor: one with mutations in none of the tested microsatellite markers¹²⁻¹⁴. MSS status indicates MMR proficiency and typically correlates with intact expression of all MMR family proteins^{9,11,13-14}.

BIOMARKER

Tumor Mutational Burden

RESULT

0 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-L1¹⁵⁻¹⁷, anti-PD-1 therapies¹⁵⁻¹⁸, and combination nivolumab and ipilimumab¹⁹⁻²⁴. In multiple studies of immune checkpoint inhibitors in melanoma, higher TMB has corresponded with clinical benefit from treatment with anti-PD-1 or anti-PD-L1 treatments^{18,25-26}. Increased TMB has been associated with longer PFS and OS for patients with melanoma treated with nivolumab, with studies reporting increased benefit for patients with a mutational load above 162 missense mutations per tumor (~equivalency >8 Muts/Mb

as measured by this assay)²⁷. Increased TMB (~equivalency >10.8 Muts/Mb as measured by this assay) has also been associated with longer PFS and OS for patients with melanoma treated with combination nivolumab and ipilimumab²⁷. Improved PFS and OS of patients with melanoma treated with ipilimumab has been observed across all TMB levels²⁸.

FREQUENCY & PROGNOSIS

A large-scale genomic analysis found that various melanoma subtypes harbored median TMBs between 6.3 and 14.4 Muts/Mb, and 25% to 40% of cases had elevated TMBs of greater than 20 Muts/Mb²⁹. Malignant melanoma has been reported to have a high prevalence of somatic mutations compared with other tumor types³⁰, with desmoplastic melanoma ranking among the highest of melanoma subtypes (median TMB of 62 Muts/Mb)³¹. Higher mutational load has been reported in NF1-mutant melanoma samples compared with BRAF-mutant, NRAS-mutant, or BRAF/NRAS/NF1 wild-type samples²⁵. In 1 study, elevated TMB correlated with PD-L1 positive status and increased OS in tissue specimens from patients with Stage 3 melanoma³². In another study, elevated

tissue TMB (>20 Muts/Mb) was associated with longer PFS and OS in patients treated with anti-PD-1 or anti-PD-L1 immunotherapy as compared with patients with lower TMB²⁵. Increased TMB has also been associated with histologic stage and cumulative sun exposure³³.

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 melanoma³⁴⁻³⁵ and cigarette smoke in lung cancer³⁶⁻³⁷, treatment with temozolomide-based chemotherapy in glioma³⁸⁻³⁹, mutations in the proofreading domains of DNA polymerases encoded by the POLE and POLD1 genes⁴⁰⁻⁴⁴, and microsatellite instability (MSI)^{40,43-44}. This sample harbors a TMB below levels that would be predicted to be associated with sensitivity to PD-1 or PD-L1-targeting immune checkpoint inhibitors, alone or in combination with other agents^{15-16,18,25,45-48}.

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GENOMIC FINDINGS

GENE

MYC

ALTERATION

amplification - equivocal

inhibitor alisertib and paclitaxel as second-line therapy for patients with MYC-overexpressed small cell lung cancer, but not for patients without MYC overexpression⁷⁶. A PR was reported for a patient with MYC-amplified invasive ductal breast carcinoma treated with an unspecified Aurora kinase inhibitor and taxol⁷⁷.

MYC amplification has also been shown to correlate with loss of BAP1, with concomitant MYC amplification and BAP1 loss reported in 27% of uveal melanoma cases in 1 study^{83,88}. Copy number gain of the genomic region that includes MYC has been observed in malignant melanoma cases and was suggested to be associated with a more aggressive clinical course and reduced OS⁸⁹⁻⁹⁰. High MYC protein expression is associated with improved survival for patients with uveal melanoma, which is in contrast to findings in cutaneous melanoma⁹¹⁻⁹².

POTENTIAL TREATMENT STRATEGIES

— Targeted Therapies —

Limited clinical data indicates that MYC activation may predict sensitivity to the pan-MYC inhibitor OMO-103; a Phase 1 study for patients with solid tumors reported 7 SDs (n=18), including 8% tumor reduction in a patient with pancreas adenocarcinoma⁴⁹. Preclinical data indicate MYC overexpression may predict sensitivity to investigational agents targeting CDK1⁵⁰⁻⁵¹, CDK2⁵², Aurora kinase A⁵³⁻⁶⁰, Aurora kinase B⁶¹⁻⁶⁴, glutaminase⁶⁵⁻⁶⁸, or BET bromodomain-containing proteins⁶⁹⁻⁷², as well as agents targeting both HDAC and PI3K⁷³⁻⁷⁵. Exploratory biomarker analysis in a Phase 2 study reported a PFS benefit associated with a combination of the Aurora A kinase

— Nontargeted Approaches —

MYC amplification has also been suggested to predict response to chemotherapy in patients with breast cancer in some studies⁷⁸⁻⁷⁹. Preclinical evidence suggests that colon cancer cells with MYC amplification may be more sensitive to 5-fluorouracil and paclitaxel⁸⁰⁻⁸¹.

FREQUENCY & PROGNOSIS

MYC amplification has been reported in 6.4% of skin melanomas analyzed in 1 study⁸². Copy number gains (amplification, intermediate increase, or simple gain) of MYC have been found in 11-70% of uveal melanomas and in 63% of hepatic metastatic lesions of primary uveal melanoma⁸³⁻⁸⁸.

FINDING SUMMARY

MYC (c-MYC) encodes a transcription factor that regulates many genes related to cell cycle regulation and cell growth. It is an oncogene and may be activated in as many as 20% of cancers⁹³. MYC dysregulation (amplification, overexpression, translocation) has been identified in a number of different cancer types⁹⁴. MYC amplification has been significantly linked with increased mRNA and protein levels and results in the dysregulation of a large number of target genes^{93,95-96}.

GENE

JUN

ALTERATION

amplification - equivocal

reported in 7% of sarcomas and at lower frequencies in other solid tumors (cBioPortal, 2023)⁹⁷⁻⁹⁸. Studies have reported JUN amplification in 18-24% of dedifferentiated liposarcoma (DDLPS) samples but not in well-differentiated liposarcomas (WDLPS)⁹⁹⁻¹⁰⁰, and it is implicated in the progression of liposarcoma from WDLPS to DDLPS¹⁰⁰⁻¹⁰². High levels of c-JUN expression have been reported in 47% (7/15) of high-grade central osteosarcomas¹⁰³, 45-53% of ovarian epithelial cancer tissues¹⁰⁴⁻¹⁰⁵, and 60% (30/50) of tongue cancer cases¹⁰⁶. Constitutive expression of c-JUN protein was reported in 91% (39/43) of renal cell carcinoma (RCC) primary tumors¹⁰⁷; high phosphorylated c-JUN levels in hepatocellular carcinoma (HCC) were associated with poor OS

and decreased response to sorafenib¹⁰⁸⁻¹⁰⁹.

Expression of c-JUN has been positively correlated with tumor grade and epithelial-mesenchymal transition in breast and endometrial tumors¹¹⁰⁻¹¹¹.

FINDING SUMMARY

JUN encodes oncogenic transcription factor c-JUN, which belongs to the family of activator protein 1 (AP-1) transcription factors. It is involved in development, proliferation, cell survival, and tumorigenesis¹¹²⁻¹¹⁵. Amplification of JUN has been correlated with increased protein expression^{101-102,116}.

POTENTIAL TREATMENT STRATEGIES

— Targeted Therapies —

There are no approved therapies or clinical trials to address JUN alterations.

FREQUENCY & PROGNOSIS

In large-scale datasets, JUN amplification has been

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CLINICAL TRIALS

NOTE Clinical trials are ordered by gene and prioritized by: age range inclusion criteria for pediatric patients, proximity to ordering medical facility, later trial phase, and verification of trial information within the last two months. While every effort is made to ensure the accuracy of the information contained below, the information available in the public domain is continually

updated and should be investigated by the physician or research staff. This is not a comprehensive list of all available clinical trials. Foundation Medicine displays a subset of trial options and ranks them in this order of descending priority: Qualification for pediatric trial → Geographical proximity → Later trial phase. Clinical trials listed here may have additional enrollment criteria that

may require medical screening to determine final eligibility. For additional information about listed clinical trials or to conduct a search for additional trials, please see clinicaltrials.gov. Or, visit <https://www.foundationmedicine.com/genomic-testing#support-services>.

GENE
MYC
ALTERATION
amplification - equivocal

RATIONALE
MYC overexpression may predict sensitivity to inhibition of CDKs, especially CDK1 and CDK2, of Aurora kinases, including Aurora kinase A and B,

and of BET domain proteins, which are reported to downregulate MYC expression and MYC-dependent transcriptional programs.

NCT05253053
PHASE 1/2

Study to Evaluate the Efficacy and Safety of TT-00420 as Monotherapy and Combination Therapy in Patients With Advanced Solid Tumors

TARGETS
Aurora kinase A, Aurora kinase B, PD-L1

LOCATIONS: Jinan (China), Beijing (China)

NCT04983810
PHASE 1/2

A Study to Investigate Fadracliclib (CYC065), in Subjects With Advanced Solid Tumors and Lymphoma

TARGETS
CDK2, CDK9

LOCATIONS: Seoul (Korea, Republic of), Barcelona (Spain), California, Texas

NCT05327010
PHASE 2

Testing the Combination of the Anti-cancer Drugs ZEN003694 (ZEN-3694) and Talazoparib in Patients With Advanced Solid Tumors, The ComBET Trial

TARGETS
PARP, BRD4, BRDT, BRD2, BRD3

LOCATIONS: Illinois, Texas, North Carolina, Georgia

NCT05053971
PHASE 1/2

Testing A New Anti-cancer Drug Combination, Entinostat and ZEN003694, for Advanced and Refractory Solid Tumors and Lymphomas

TARGETS
BRD3, BRD4, BRD2, BRDT, HDAC

LOCATIONS: Oklahoma, Connecticut, Florida

NCT04555837
PHASE 1/2

Alisertib and Pembrolizumab for the Treatment of Patients With Rb-deficient Head and Neck Squamous Cell Cancer

TARGETS
Aurora kinase A, PD-1

LOCATIONS: Texas

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CLINICAL TRIALS

NCT05252390

PHASE 1/2

NUV-868 as Monotherapy and in Combination With Olaparib or Enzalutamide in Adult Patients With Advanced Solid Tumors

TARGETS
BRD4, PARP, AR

LOCATIONS: Montana, California, Arizona, Michigan, Texas, Tennessee, Maryland, Virginia, North Carolina

NCT04742959

PHASE 1/2

Crossover Relative Bioavailability and Dose Escalation Study of TT-00420 Tablet in Patients With Advanced Solid Tumors

TARGETS
Aurora kinase A, Aurora kinase B

LOCATIONS: California, Illinois, Ohio, Texas, New Jersey

NCT01434316

PHASE 1

Veliparib and Dinaciclib in Treating Patients With Advanced Solid Tumors

TARGETS
PARP, CDK1, CDK9, CDK5, CDK2

LOCATIONS: Massachusetts

NCT04840589

PHASE 1

Testing the Combination of ZEN003694 and Nivolumab With or Without Ipilimumab in Solid Tumors

TARGETS
PD-1, CTLA-4, BRD4, BRDT, BRD2, BRD3

LOCATIONS: Ohio, Pennsylvania, New York, Maryland

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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.

ABL1
amplification

ALK
NM_004304.4: c.487G>T
(p.V163L)
chr2:30143039

CCND3
amplification

CDKN1A
amplification

CDKN2C
amplification

DAXX
amplification

DDR1
NM_001954.4: c.658G>A
(p.V220M)
chr6:30859249 and
amplification

FANCC
NM_000136.2: c.973G>A
(p.A325T)
chr9:97887391 and
amplification

GNAQ
amplification

GNAS
NM_016592.2: c.517G>C
(p.A173P)
chr20:57415678

HDAC1
NM_004964.2: c.1381G>A
(p.E461K)
chr1:32798310

IRF4
amplification

MKNK1
amplification

MUTYH
amplification

NBN
amplification

NOTCH1
amplification

NSD3 (WHSC1L1)
NM_023034.1: c.1373C>T
(p.A458V)
chr8:38187104

NTRK2
amplification

PIM1
amplification

PTCH1
amplification

RAD21
amplification

RAD54L
amplification

SYK
amplification

TBX3
NM_016569.3: c.1685C>T
(p.A562V)
chr12:115112055

TSC1
amplification

VEGFA
amplification

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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	ERRF1	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	HNFI1A	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)

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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

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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. 2023. 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

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- 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 ≥ 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

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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) 7.7.0

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The median exon coverage for this sample is 841x

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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. Kubeček O, et al. Melanoma Res. (2016) PMID: 27623135
7. Kubeček O, et al. Med. Hypotheses (2016) PMID: 27372860
8. Peris K, et al. J. Invest. Dermatol. (1995) PMID: 7561170
9. Kocarnik JM, et al. Gastroenterol Rep (Oxf) (2015) PMID: 26337942
10. You JF, et al. Br. J. Cancer (2010) PMID: 21081928
11. Bairwa NK, et al. Methods Mol. Biol. (2014) PMID: 24623249
12. Boland CR, et al. Cancer Res. (1998) PMID: 9823339
13. Pawlik TM, et al. Dis. Markers (2004) PMID: 15528785
14. Boland CR, et al. Gastroenterology (2010) PMID: 20420947
15. Samstein RM, et al. Nat. Genet. (2019) PMID: 30643254
16. Goodman AM, et al. Mol. Cancer Ther. (2017) PMID: 28835386
17. Goodman AM, et al. Cancer Immunol Res (2019) PMID: 31405947
18. Cristescu R, et al. Science (2018) PMID: 30309915
19. Ready N, et al. J. Clin. Oncol. (2019) PMID: 30785829
20. Hellmann MD, et al. N. Engl. J. Med. (2018) PMID: 29658845
21. Hellmann MD, et al. Cancer Cell (2018) PMID: 29657128
22. Hellmann MD, et al. Cancer Cell (2018) PMID: 29731394
23. Rozeman EA, et al. Nat Med (2021) PMID: 33558721
24. Sharma P, et al. Cancer Cell (2020) PMID: 32916128
25. Johnson DB, et al. Cancer Immunol Res (2016) PMID: 27671167
26. Ning B, et al. Front Pharmacol (2022) PMID: 35355708
27. Hodi et al., 2019; AACR abstract CT037
28. Liu L, et al. Clin. Cancer Res. (2019) PMID: 31515453
29. Chalmers ZR, et al. Genome Med (2017) PMID: 28420421
30. Alexandrov LB, et al. Nature (2013) PMID: 23945592
31. Shain AH, et al. Nat. Genet. (2015) PMID: 26343386
32. Madore J, et al. Clin. Cancer Res. (2016) PMID: 26960397
33. Shain AH, et al. N. Engl. J. Med. (2015) PMID: 26559571
34. Pfeifer GP, et al. Mutat. Res. (2005) PMID: 15748635
35. Hill VK, et al. Annu Rev Genomics Hum Genet (2013) PMID: 23875803
36. Pfeifer GP, et al. Oncogene (2002) PMID: 12379884
37. Rizvi NA, et al. Science (2015) PMID: 25765070
38. Johnson BE, et al. Science (2014) PMID: 24336570
39. Choi S, et al. Neuro-oncology (2018) PMID: 29452419
40. Cancer Genome Atlas Research Network, et al. Nature (2013) PMID: 23636398
41. Briggs S, et al. J. Pathol. (2013) PMID: 23447401
42. Heitzer E, et al. Curr. Opin. Genet. Dev. (2014) PMID: 24583393
43. Nature (2012) PMID: 22810696
44. Roberts SA, et al. Nat. Rev. Cancer (2014) PMID: 25568919
45. Eroglu Z, et al. Nature (2018) PMID: 29320474
46. Shin DS, et al. Cancer Discov (2017) PMID: 27903500
47. Riaz N, et al. Cell (2017) PMID: 29033130
48. Lancet Oncol. (2020) PMID: 32919529
49. Garraza et al., 2022; ENA Abstract 7
50. Horiuchi D, et al. J. Exp. Med. (2012) PMID: 22430491
51. Goga A, et al. Nat. Med. (2007) PMID: 17589519
52. Molenaar JJ, et al. Proc. Natl. Acad. Sci. U.S.A. (2009) PMID: 19525400
53. Dammert MA, et al. Nat Commun (2019) PMID: 31375684
54. Mollaoglu G, et al. Cancer Cell (2017) PMID: 28089889
55. Cardnell RJ, et al. Oncotarget (2017) PMID: 29088717
56. Wang L, et al. Mol Oncol (2017) PMID: 28417568
57. Takahashi Y, et al. Ann. Oncol. (2015) PMID: 25632068
58. Li Y, et al. Thyroid (2018) PMID: 30226440
59. Mahadevan D, et al. PLoS ONE (2014) PMID: 24893165
60. Park SI, et al. Target Oncol (2019) PMID: 31429028
61. Helfrich BA, et al. Mol. Cancer Ther. (2016) PMID: 27496133
62. Hook KE, et al. Mol. Cancer Ther. (2012) PMID: 22222631
63. Yang D, et al. Proc. Natl. Acad. Sci. U.S.A. (2010) PMID: 20643922
64. He J, et al. Anticancer Drugs (2019) PMID: 30540594
65. Shroff EH, et al. Proc. Natl. Acad. Sci. U.S.A. (2015) PMID: 25964345
66. Effenberger M, et al. Oncotarget (2017) PMID: 29156762
67. Qu X, et al. Biochem. Biophys. Res. Commun. (2018) PMID: 30103944
68. Xiang Y, et al. J. Clin. Invest. (2015) PMID: 25915584
69. Delmore JE, et al. Cell (2011) PMID: 21889194
70. Bandopadhyay P, et al. Clin. Cancer Res. (2014) PMID: 24297863
71. Lovén J, et al. Cell (2013) PMID: 23582323
72. Otto C, et al. Neoplasia (2019) PMID: 31734632
73. Dong LH, et al. J Hematol Oncol (2013) PMID: 23866964
74. Pei Y, et al. Cancer Cell (2016) PMID: 26977882
75. Fu XH, et al. Acta Pharmacol. Sin. (2019) PMID: 30224636
76. Owonikoko TK, et al. J Thorac Oncol (2020) PMID: 31655296
77. Ganesan P, et al. Mol. Cancer Ther. (2014) PMID: 25253784
78. Pereira CB, et al. PLoS ONE (2013) PMID: 23555992
79. Yasojima H, et al. Eur. J. Cancer (2011) PMID: 21741827
80. Arango D, et al. Cancer Res. (2001) PMID: 11406570
81. Bottone MG, et al. Exp. Cell Res. (2003) PMID: 14516787
82. Van Allen EM, et al. Science (2015) PMID: 26359337
83. Parrella P, et al. Invest. Ophthalmol. Vis. Sci. (2001) PMID: 11431428
84. Pigment Cell Melanoma Res (2012) PMID: 22268848
85. Höglund M, et al. Int. J. Cancer (2004) PMID: 14618616
86. Damato B, et al. Clin. Cancer Res. (2010) PMID: 20975103
87. Singh AD, et al. Arch. Pathol. Lab. Med. (2009) PMID: 19653714
88. Damato B, et al. Ophthalmology (2007) PMID: 17719643
89. Pouryazdanparast P, et al. Am. J. Surg. Pathol. (2012) PMID: 22020039
90. Pouryazdanparast P, et al. Mod. Pathol. (2012) PMID: 22555175
91. Chana JS, et al. Melanoma Res. (1998) PMID: 9610866
92. Chana JS, et al. Br J Ophthalmol (1999) PMID: 10209447
93. Dang CV, et al. Semin. Cancer Biol. (2006) PMID: 16904903
94. Nesbit CE, et al. Oncogene (1999) PMID: 10378696
95. Blacato J, et al. Br. J. Cancer (2004) PMID: 15083194
96. Fromont G, et al. Hum. Pathol. (2013) PMID: 23574779
97. Cerami E, et al. Cancer Discov (2012) PMID: 22588877
98. Gao J, et al. Sci Signal (2013) PMID: 23550210
99. Barretina J, et al. Nat. Genet. (2010) PMID: 20601955
100. Tap WD, et al. Genes Chromosomes Cancer (2011) PMID: 21117066
101. Mariani O, et al. Cancer Cell (2007) PMID: 17418412
102. Snyder EL, et al. J. Pathol. (2009) PMID: 19449367
103. Franchi A, et al. Virchows Arch. (1998) PMID: 9672192
104. Yokoyama Y, et al. J. Obstet. Gynaecol. Res. (1999) PMID: 10680335
105. Yokoyama Y, et al. Gynecol. Oncol. (1998) PMID: 9570981
106. Gupta S, et al. Sci Rep (2015) PMID: 26581505
107. Koo AS, et al. J. Urol. (1992) PMID: 1404666
108. Hagiwara S, et al. Br. J. Cancer (2012) PMID: 22596232
109. Chen W, et al. Sci Rep (2016) PMID: 26964667
110. Bircan S, et al. Pathol. Oncol. Res. (2005) PMID: 15800680
111. Ouelaa-Benslama R, et al. Int. J. Oncol. (2012) PMID: 22552300
112. Meng Q, et al. Protein Cell (2011) PMID: 22180088
113. Angel P, et al. Biochim. Biophys. Acta (1991) PMID: 1751545
114. Shaulian E, et al. Nat. Cell Biol. (2002) PMID: 11988758
115. Trierweiler C, et al. Cell Death Differ. (2016) PMID: 26470729
116. Spruill MD, et al. J. Toxicol. Environ. Health Part A (2002) PMID: 12515591

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