Patient
Name: Mary Smith
Patient ID: H23/028662
Sex at birth: Female
Date of birth: Nov 20, 1987

Physician
Name: John Doe
Institution:
Heritage Medical Center
Contact: +82-10-0000-0000
Address:
1600 Amphitheatre Parkway, Mountain View, CA 94043

Specimen
Specimen ID: C346399(9)
Specimen type: FFPE
Collected: Nov 20, 2023 14:10
Received: Nov 24, 2023
Normal sample:
Matched blood
Normal obtained:
Nov 20, 2023 20:20
Primary site: Breast, left
Sampling site: Breast, left
Diagnosis:
Breast cancer, triple negative

Test Information
Test name:
Target-enhanced whole genome analysis and interpretation
Quality: Satisfactory
Tumor Proportion: 48%

Sequencing mean depth
Tumor (WGS): 48.2x
Tumor (target): 523.2x
Normal (WGS): 25.2x

KEY FINDINGS SUMMARY - POTENTIALLY ACTIONABLE*

Therapeutics, in current diagnosis

Somatic alteration		
BRCA1 rearrangement	**Talazoparib**	Evidence B
	Olaparib	Evidence B
	Potential clinical trials: **Matched****	
Germline alteration		
RAD51C rearrangement	Potential clinical trials: **Matched****	

Therapeutics, In other indications

Somatic alteration	
BRCA1 rearrangement	**Rucaparib**
	Niraparib
	Olaparib
	Olaparib + Bevacizumab
	(+ 3 more options)
Genomic instability***	
HR deficiency	**Rucaparib**
	Niraparib

Cancer-related germline alteration

RAD51C rearrangement	Genetic counseling may be beneficial.

*The prescribing information for the FDA-approved therapeutic option may not include the associated alterations and it should be noted this information does not pertain to pediatric indications. Therapeutic options with evidence level A or B according to the ASCO/CAP guideline, are reported.

** See details in following pages.

*** While the TMB/MSI/HRD scores have been validated, this test is not FDA-approved as a companion diagnostic for therapeutic selection, including Anti-PD-1, and PARP inhibitor treatments.

Genomic instability

Tumor mutational burden	Low	0 **4.7** 10 >20	High
Microsatellite instability	Stable	0 **2.4** 20 100	Instable
Homologous recombination	Proficient	0 0.7 **0.99**	**Deficient**

Somatic driver alteration

Point mutation	
CDKN2A p.P81R	Missense variant
ATR p.W1471*	Stop-gain
PPARG p.A414P	Missense variant
ROS1 p.V1261L	Missense variant
ERCC2 p.I244F	Missense variant

Somatic driver alteration, cont'd

Structural variation

PTEN	Rearrangement (Disruption)
BRIP1	Rearrangement (Disruption)
ARID1A	Rearrangement (Disruption)
BRCA1	Rearrangement (Disruption)
KMT2C	Rearrangement (Disruption)

Copy number variation

Gain	***CALR, LYL1, PRKACA***

KEY FINDINGS - POTENTIALLY ACTIONABLE

Therapeutics, in current diagnosis

Alteration	Treatment	Predicted response*	Evidence level
BRCA1 rearrangement somatic alteration	Talazoparib	Sensitive	B
	Olaparib	Sensitive	B

The prescribing information for the FDA-approved therapeutic option may not include the associated alteration and it should be noted this information does not pertain to pediatric indications. Therapeutic options with evidence level A or B according to the ASCO/CAP guideline, are reported.
*The Predictive Response Type reports treatment response likelihood across five categories: decreased response, predictive-resistant, predictive-sensitive, resistant, and sensitive.

Clinical trial

Alteration	ID / phase	Title
BRCA1 rearrangment	NCT04890613 Phase I	Study of CX-5461 in Patients With Solid Tumours and BRCA1/2, PALB2 or Homologous Recombination Deficiency (HRD) Mutation
RAD51C rearrangment	NCT05340413 Phase II	Predicting Olaparib Sensitivity in Patients With Unresectable Locally Advanced/Metastatic HER2-negative Breast Cancer With BRCA1, BRCA2, PALB2, RAD51C or RAD51D Mutations or RAD51-foci Low

A list of clinical trials, recruiting as of November 25, 2023, in the United States, was provided, taking into account the patient's genomic findings and cancer type. See https://clinicaltrials.gov/ for more detailed and real-time information.

Therapeutics, in other indications

Alteration	Treatment	Predicted response*	Evidence level**
BRCA1 rearrangement	Rucaparib	Sensitive	A
	Niraparib	Sensitive	A
	Olaparib	Sensitive	A
	Olaparib + Bevacizumab	Sensitive	A
	Talazoparib + Enzalutamide	Sensitive	A
	Niraparib + Abiraterone Acetate + Predisone	Sensitive	A
	Olaparib + Abiraterone + Predisolone	Sensitive	A
Homologous recombination deficiency***	Rucaparib	Sensitive	A
	Niraparib	Sensitive	A

*The Predictive Response Type reports treatment response likelihood across five categories: decreased response, predictive-resistant, predictive-sensitive, resistant, and sensitive.
**The Evidence levels are derived on the assumption that the patient's cancer type matches the drug indication, according to the ASCO/CAP guidelines.
***While the TMB/MSI/HRD scores have been validated, this test is not FDA-approved as a companion diagnostic for therapeutic selection, including Anti-PD-1, and PARP inhibitor treatments. The evidence level is associated with results from FDA-approved companion diagnostic tests.

Cancer-related germline alteration

Alteration	Type	Interpretation	Genotype	Note
RAD51C rearrangement	SV (DEL)	Pathogenic	Heterozygous	Loss of heterogyzosity in cancer

GENOMIC INSTABILITY

Tumor mutational burden

Single nucleotide variation	11,479
Small insertion / deletion	2,063

The Tumor Mutational Burden (TMB) score represents the number of mutations per Mb across the whole genome of the tumor. It is calculated by summing all the number of somatic SNVs and indels divided by the effective genome size (~2.9Gb). A tumor is considered to have a high TMB if the score is > 10mut/mb.

Microsatellite status

Number of microsatellite site	2,041
Somatically altered site	53
Percentage of altered site	2.4%

The microsatellite instability (MSI) score represents the number of somatic insertions and deletions per Mb in microsatellite regions across the whole genome of the tumor. A tumor is considered microsatellite stable (MSS) if the score is < 20, and MSI-High if > 20.

Homologous recombination deficiency score

The homologous recombination deficiency (HRD) score is calculated by our proprietary algorithm. Tumors with HRD score greater than or equal to 0.7 are considered HR-deficient.

The sum of loss of heterozygosity(LOH), telomeric allelic imbalance(TAI), and large-scale state transitions (LST) scores, is **56.**

SOMATIC DRIVER ALTERATION

Point mutation

Alteration*	Type	Functional effect	Loss of heterozygosity	Variant allele frequency, (cancer cell fraction**)
CDKN2A p.Pro81Arg	Missense variant	Tumor suppresor	Positive	78%, (99%)
ATR p.Trp1471Ter	Stop-gain	Tumor suppresor	Negative	26%, (92%)
PPARG p.Ala414Pro	Missense variant	Tumor suppresor	Positive	52%, (90%)
ROS1 p.Val1261Leu	Missense variant	Oncogene	Not applicable	34%, (89%)
ERCC2 p.Ile244Phe	Missense variant	Tumor suppresor	Positive	9%, (30%)

*See the appendix to check the detail genome coordinate information of alterations.
** See the test information to check the definition of cancer cell fraction

Structural variantion

Alteration*	Breakpoint 1	Breakpoint 2	Functional effect	Loss of heterozygosity	Cancer cell fraction**
PTEN	*PTEN* (NM_00314) intron 2/8 (+)	*SWP70* (NM_015055) Intron 10/11(+)	Tumor suppresor	Negative	99%
BRIP1	*BRIP1* (NM_032043) Intron 17/19 (-)	chr17:61,656,237 intergenic region (+)	Tumor suppresor	Positive	99%
ARID1A	*ARID1A* (NM_006015) Intron 1/19 (+)	chr22:30,223,968 intergenic region (+)	Tumor suppresor	Positive	98%
BRCA1	*BRCA1* (NM_007294) Intron 8/22 (-)	NBR1 (NM_005899) Intron 5/20 (+)	Tumor suppresor	Positive	98%
KMT2C	*KMT2C* (NM_170606) Intron 3/58 (-)	chr2:120,606,494 intergenic region (+)	Tumor suppresor	Negative	72%

*See the appendix to check the detail genome coordinate information of alterations.
** See the test information to check the definition of cancer cell fraction

Copy number variation

Gene	Location	Functional effect	Consequence*	Copy number
CALR	chr19	Oncogene	Amplification	12
LYL1	chr19	Oncogene	Amplification	11
PRKACA	chr19	Oncogene	Amplification	11

*Gene amplification indicates that the gene's copy number is a minimum of five higher than the average ploidy level.

MUTATIONAL SIGNATURE

Major single base substitution signatures

Signature	Count	Proportion	Etiology
SBS3	5925	52.3%	Component of HRD phenotype
SBS5	3548	31.3%	Aging, presumable (clock-like signature)

The mutational signature analysis is primarily based on the COSMIC mutational signatures of SNVs.[1]

APPENDIX I: DETAILS OF GENES AND BIOMARKERS FOUND IN THE PATIENT

CDKN2A
Gene

CDKN2A, cyclin-dependent kinase inhibitor 2A, is a tumor suppressor (PMID: 30562755) that encodes p16 and p14ARF from alternate reading frames, which function to inhibit Cdk4 and Cdk6 and regulate Tp53 activity to promote cell-cycle arrest (PMID: 23875803, PMID: 17055429, PMID: 27428416). CDKN2A germline mutations are associated with familial atypical multiple mole melanoma and somatic mutations are highest in pancreatic (PMID: 32273725), HNSCC, NSCLC, and melanoma (PMID: 27283171), and deletion of CDKN2A may be prognostic in IDH-mutant glioma (PMID: 32385699).

ATR
Gene

ATR, ATR serine/threonine kinase, is involved in regulation of the DNA damage response and mediation of cell-cycle checkpoints (PMID: 25512053). Loss of function ATR mutations have been identified in melanoma (PMID: 28273450), and inhibition of Atr selectively sensitizes cancerous cells to radiation and chemotherapy (PMID: 23583268, PMID: 31836456, PMID: 29054375).

PPARG
Gene

PPARG, peroxisome proliferator-activated receptor gamma, is a transcription factor and member of the proliferator-activated receptor family of nuclear receptors and regulates adipocyte differentiation and glucose homeostasis (PMID: 9209705, PMID: 30651555). PPARG fusions are frequently observed with PAX8 in follicular thyroid carcinoma (PMID: 25069464) and missense mutations and amplification have been reported in luminal bladder cancer (PMID: 30651555).

ROS1
Gene

ROS1, ROS proto-oncogene 1, receptor tyrosine kinase, is an orphan receptor tyrosine kinase that may activates multiple pathways involved in cell survival and transformation (PMID: 23719267, PMID: 32327173). ROS1 fusion proteins frequently lead to constitutive activation of Ros1 signaling and have been identified in glioblastoma, non-small cell lung cancer, cholangiocarcinoma, ovarian cancer, gastric adenocarcinoma, colorectal cancer, inflammatory myofibroblastic tumor, angiosarcoma, glioma, and epithelioid hemangioendothelioma (PMID: 23719267, PMID: 30262706, PMID: 30171048, PMID: 3004937), and ROS1 mutations are often associated with acquired resistance to inhibition (PMID: 31256210).

ERCC2
Gene

ERCC2, ERCC excision repair 2 TFIIH core complex helicase subunit, is an ATP-dependent 5'-3' DNA helicase that plays a role in nucleotide excision repair, RNA transcription, and chromosome segregation (PMID: 20797633). ERCC2 variants have been associated with susceptibility to gastric cancer (PMID: 24338713) and lung cancer (PMID: 20627704) and somatic Ercc2 loss of function mutations may confer sensitivity to cisplatin (PMID: 29980530).

PTEN
Gene

PTEN, phosphatidylinositol 3,4,5-trisphosphate 3-phosphatase and dual-specificity protein phosphatase PTEN, is a tumor suppressor (PMID: 30562755) with roles in the cell cycle, growth, DNA repair, cell survival and regulation of the Akt-mTOR pathway (PMID: 24656806, PMID: 30145641). PTEN germline mutations are common in Cowden syndrome (PMID: 30562755) and PTEN somatic alterations resulting in loss of function have been found in many types of cancer including, but not limited to endometrial (PMID: 30142194), melanoma (PMID: 30148988), and prostate (PMID: 18767981, PMID: 30153654).

BRIP1
Gene

BRIP1, BRCA1 interacting protein C-terminal helicase 1, is involved in DNA repair and aids the tumor suppressor function of Brca1 (PMID: 14983014). BRIP1 germline mutations are associated with breast and ovarian cancers and somatic mutations are highest in endometrial, colon, and NSCLC (PMID: 27283171), while expression may promote breast cancer cell invasion (PMID: 32888398).

ARID1A
Gene

ARID1A, AT-rich interaction domain 1A, is a member of the cBaF subunit (PMID: 32303701) of the SWI/SNF chromatin remodeling complex and is involved in cell-cycle activation (PMID: 29136504). ARID1A has been reported to influence PI3K/AKT pathways (PMID: 24618703), and loss of function is commonly found in ovarian clear cell carcinoma (PMID: 32020380, PMID: 32027624), gastric, colorectal (PMID: 28937020), and bladder cancers (PMID: 28583311), while in liver cancer, Arida1a has a context dependent role (PMID: 29136504) and ARID1A promoter hypermethylation has been observed in squamous cell carcinoma (PMID: 32015157).

BRCA1
Gene

BRCA1, BRCA1 DNA repair associated, is a tumor suppressor (PMID: 30562755) involved in the DNA damage response and DNA repair (PMID: 21203981). BRCA1 germline mutations increase the risk of developing ovarian and/or breast cancer (PMID: 21285145) and somatic mutations are highest in NSCLC, pancreatic, and colon cancers (PMID: 27283171).

KMT2C
Gene

KMT2C, lysine methyltransferase 2C, is a H3K4 histone methyltransferase (PMID: 31128216) that is involved in transcriptional coactivation and functions in chromatin modification (PMID: 31337554) and epigenetic gene regulation (PMID: 31128216). KMT2C mutations are associated with various tumor types (PMID: 24965397; PMID: 23429989; PMID: 24670651), including breast cancer (PMID: 31128216), diffuse-type gastric adenocarcinoma (PMID: 30108106), and urothelial carcinoma (PMID: 30665945).

APPENDIX I: DETAILS OF GENES AND BIOMARKERS FOUND IN THE PATIENT, CONT'D

CALR
Gene

CALR, calreticulin, is a Ca2+ binding chaperone protein that plays a role in multiple biological processes, including protein folding and quality control, calcium homeostasis, immune response, cell adhesion and migration, and cell signaling (PMID: 19940256, PMID: 28470469, PMID: 22959412). CALR frameshift mutations have been identified in myeloproliferative neoplasms, including essential thrombocytothemia and myelofibrosis (PMID: 24365789, PMID: 28470469).

LYL1
Gene

LYL1 (LYL1 Basic Helix-Loop-Helix Family Member) is a Protein Coding gene. Diseases associated with LYL1 include Leukemia and T-Cell Acute Lymphoblastic Leukemia. Among its related pathways are Signaling by NTRKs and Nuclear Events (kinase and transcription factor activation). Gene Ontology (GO) annotations related to this gene include protein dimerization activity. An important paralog of this gene is TAL1.

PRKACA
Gene

PRKACA, protein kinase cAMP-activated catalytic subunit alpha, encodes the catalytic subunit of protein kinase A, which activates cAMP-dependent signaling pathways and is involved in diverse biological processes including cardiovascular and adrenal cortex functions (PMID: 26042218, PMID: 26687711, PMID: 29205368). PRKACA mutations have been identified in cardiac (PMID: 28369983) and adrenal (PMID: 26042218) tumors, and a DNAJB1-PRKACA fusion has been identified in fibrolamellar hepatocellular carcinoma (PMID: 24578576), and in pancreatic and bile duct cancer (PMID: 31676785).

RAD51C
Gene

RAD51C, RAD51 paralog C, functions in homologous recombination in DNA repair and plays a role in cell cycle checkpoint signaling in response to DNA damage (PMID: 21821141). Germline mutations in RAD51C are associated with increased susceptibility to breast and ovarian cancers (PMID: 21821141, PMID: 31446535) and overexpression of Rad51c has been observed in ovarian cancer (PMID: 32055267).

APPENDIX II: DETAILS OF ALTERATIONS FOUND IN THE PATIENT

Details of point mutations

Gene	Position	Ref	Alt	Transcript alteration	Protein change	Note
CDKN2A	chr9:21971117	G	C	NM_000077.5:c.(242C>G)	NP_478102.2:p.(Pro81Arg)	Exon 2/3
ATR	chr3:142515485	C	T	NM_001184.4:c.(4413G>A)	NP_001175.2:p.(Trp1471Ter)	Exon 25/47
PPARG	chr3:12433957	G	C	NM_138711.6:c.(1240G>C)	NP_619725.3:p.(Ala414Pro)	Exon 8/8
ROS1	chr6:117357862	C	A	NM_001378902.1:c.(3781G>T)	NP_002935.2:p.(Val1261Leu)	Exon 25/44
ERCC2	chr19:45364320	T	A	NM_000400.4:c.(730A>T)	NP_000391.1:p.(Ile244Phe)	Exon 9/23

Details of structural variations

Alteration	Breakpoint 1 position	Breakpoint 2 position	DNA Connection Type	Breakpoint 1 gene strand	Breakpoint 2 gene strand
PTEN	chr10:87,896,877	chr11:9,748,484	3to3	Positive	Negative
BRIP1	chr17:164,711,167	chr17:61,656,237	3to5	Positive	Negative
ARID1A	chr1:26,703,059	chr22:30,223,968	3to3	Positive	Negative
BRCA1	chr17:43,096,101	chr17:43,184,166	3to3	Positive	Positive
KMT2C	chr7:152,321,594	chr2:120,606,494	3to5	Positive	Positive
RAD51C	chr17:58,716,036	chr17:58,750,897	3to5	Positive	Positive

TEST INFORMATION

1. The CancerVision test is a target-enhanced whole-genome assay that pairs a tumor with its matched normal, that provides a list of detected single nucleotide variants (SNVs), multiple nucleotide variants (MNVs), small insertions and deletions (indels), copy number alterations (CNAs), and structural variations (SVs) in tumor tissue, along with an analysis report of mutational signature, tumor mutational burden (TMB), microsatellite instability (MSI), and homologous recombination deficiency (HRD).
2. The genomic DNA is extracted from the patient's normal and tumor samples via the ThermoFisher KingFisher Apex and prepared using the Watchmaker Genomics enzymatic library preparation which includes end repair, purification, adapter ligation and PCR amplification. A portion of the library is hybridized to targeted probes. The libraries are sequenced using the Illumina NovaSeq X+. For whole-genome sequencing, the mean genome-wide read-depth is 40x for tumor and 20x for its matched-normal sample (deduplicated unique reads). For target-enhanced panel sequencing, on-target read-depth is 500x on average. The gene list is provided at the end of this section.
3. The sequence data are analyzed using various validated bioinformatics tools and a custom data-processing pipeline that have been established by a team of experts in genomics and engineering and powered by AI algorithms. For formalin-fixed paraffin-embedded (FFPE) specimens, AI-powered data correction algorithms developed by Inocras are used to mitigate data-quality issues commonly encountered in FFPE-derived samples. GRCh38 is used for human reference genome.
4. Each tumor's cancer-specific mutations are then queried against a proprietary gene-drug database based on peer-reviewed literature to identify potential therapeutic associations; however, this information should be considered in conjunction with other clinical and diagnostic findings.
5. Potential actionable findings encompass the identification of on-label drugs pertinent to the patient's reported diagnosis, detection of off-label drugs associated with genomic findings not approved for the patient's disease state, alignment with clinical trials (accessible via clinicaltrials.gov), and the identification of likely or pathogenic germline findings.
6. Tumor cellularity is a proportion of tumor cells in the specimen of whole-genome sequencing. Somatic mutations may be under-detected when tumor cellularity is low. Samples with a tumor content of less than 20% may have reduced sensitivity, potentially leading to false negative results.
7. SNVs and indels whose consequences are predicted to activate oncogenes and reported as hotspot mutations by COSMIC were categorized as oncogenic mutations. Those whose consequences cause loss of function of tumor suppressor genes (TSGs) were classified as TSG-disrupting mutations.
8. CNAs that amplify oncogenes more than five copies above the average ploidy were classified as oncogene amplification, whereas those that delete both copies of TSGs were categorized as biallelic deletion of TSGs.
9. SVs that generate known fusion oncogenes or disrupt TSGs were classified as driver events. SVs that produce known fusion oncogenes by connecting two independent genes were classified as fusion oncogene-generating SVs. SVs that alter the arrangement of exons of TSGs were classified as TSG-disrupting SVs.
10. The term 'indirect fusion' describes a condition in which the pair of genes subject to fusion are not directly connected but are linked through another DNA component. It is important to exercise caution in interpreting the results, as the efficacy of therapeutic agents may vary in cancer tissues containing indirect fusion findings compared to those with conventional fusion alterations.
11. Variant allele frequency (VAF) is the fraction of variant-supporting reads among total sequencing reads and is dependent on tumor cellularities. Cancer cell fraction accounts for contamination by normal cells, providing a more accurate estimate of the mutation’s prevalence and its clonality.
12. The TMB score represents the number of mutations per Mb across the whole genome of the tumor. It is calculated by summing all the number of somatic SNVs and indels divided by the effective genome size (2.9Gb). A tumor is considered to have a high TMB if the score is > 10mut/ mb. While the TMB score has been validated, it is not FDA approved as a companion diagnostic for therapeutic selection, such as Anti-PD-1 treatments.
13. The MSI score represents the number of somatic insertions and deletions per Mb in microsatellite regions across the whole genome of the tumor. A tumor is considered microsatellite stable (MSS) if the score is < 20, and MSI-High if > 20. While the MSI score has been validated, it is not FDA approved as a companion diagnostic for therapeutic selection, such as Anti-PD-1 treatments.
14. The HRD score is calculated by our proprietary algorithm. Tumors with HRD score greater than or equal to 0.7 are considered HR deficient. While the HRD score has been validated, it is not FDA approved as a companion diagnostic for therapeutic selection, such as PARP inhibitor treatments.
15. A lack of a variant call does not necessarily indicate the absence of a variant, as technical limitations may restrict data acquisition in certain genetic regions. Additionally, it is possible that the sample contains a mutation below our established limit of detection (1% allele frequency in hotspots, 5% in other regions), or in a gene excluded by our assay. Alterations present in repetitive or high GC content region may not be detected. The inherent DNA fragmentation, damage, and background noise in FFPE samples can reduce the sensitivity and specificity of copy number alterations (amplifications/deletions) and structural variations.

16. The Predictive Response Type reports treatment response likelihood across five categories: decreased response, predictive-resistant, predictive-sensitive, resistant, and sensitive. A decreased response implies diminished efficacy compared to alternative therapies or molecular profiles, without meeting resistance criteria. Predictive-Resistant indicates literature-backed resistance of a variant or pathway to therapy, potentially including resistance. Predictive-Sensitive suggests literature-supported sensitivity of an unspecified variant or pathway to therapy. Resistant denotes explicit resistance of a molecular profile to therapy due to biochemical mechanisms, while Sensitive indicates literature-supported therapy sensitivity. Efficacy evidence levels are determined based on AMP/CAP/ASCO criteria.

Gene list (target)

The list below is for target-enhanced panel sequencing.

A-B
ABL1, ABL2, ABRAXAS1, ACVR1, ACVR1B, ADGRA2, AKT1, AKT2, AKT3, ALK, ALOX12B, AMER1, ANKRD11, ANKRD26, APC, AR, ARAF, ARFRP1, ARID1A, ARID1B, ARID2, ARID5B, ASXL1, ASXL2, ATM, ATR, ATRX, AURKA, AURKB, AXIN1, AXIN2, AXL, B2M, BAP1, BARD1, BBC3, BCL10, BCL2,BCL2L1, BCL2L11, BCL2L2, BCL6, BCOR, BCORL1, BCR, BIRC3, BLM, BMPR1A, BRAF, BRCA1, BRCA2, BRD4, BRIP1, BTG1, BTK

C-D
CALR, CARD11, CASP8, CBFB, CBL, CCN6, CCND1, CCND2, CCND3, CCNE1, CD274, CD276, CD74, CD79A, CD79B, CDC73, CDH1, CDK12, CDK4, CDK6, CDK8, CDKN1A, CDKN1B, CDKN2A, CDKN2B, CDKN2C, CEBPA, CENPA, CHD2, CHD4, CHEK1, CHEK2, CIC, COP1, CREBBP, CRKL, CRLF2, CSF1R, CSF3R, CSNK1A1, CTCF, CTLA4, CTNNA1, CTNNB1, CUL3, CUX1, CXCR4, CYLD, DAXX, DCUN1D1, DDR2, DDX41, DHX15, DICER1, DIS3, DNAJB1, DNMT1, DNMT3A, DNMT3B, DOT1L

E-F
E2F3, EED, EGFL7, EGFR, EIF1AX, EIF4A2, EIF4E, ELOC, EML4, EMSY, EP300, EPCAM, EPHA3, EPHA5, EPHA7, EPHB1, ERBB2, ERBB3, ERBB4, ERCC1, ERCC2, ERCC3, ERCC4, ERCC5, ERG, ERRFI1, ESR1, ETS1, ETV1, ETV4, ETV5, ETV6, EWSR1, EZH2, FAM46C, FANCA, FANCC, FANCD2, FANCE, FANCF, FANCG, FANCI, FANCL, FAS, FAT1, FBXW7, FGF1, FGF10, FGF14, FGF19, FGF2, FGF23, FGF3, FGF4, FGF5, FGF6, FGF7, FGF8, FGF9, FGFR1, FGFR2, FGFR3, FGFR4, FH, FLCN, FLI1, FLT1, FLT3, FLT4, FOXA1, FOXL2, FOXO1, FOXP1, FRS2, FUBP1, FYN

G-H
GABRA6, GATA1, GATA2, GATA3, GATA4, GATA6, GEN1, GID4, GLI1, GNA11, GNA13, GNAQ, GNAS, GPS2, GREM1, GRIN2A, GRM3, GSK3B, H1-2, H2BC5, H3-3A, H3-3B, H3-4, H3-5, H3C1, H3C10, H3C11, H3C12, H3C13, H3C14, H3C15, H3C2, H3C3, H3C4, H3C6, H3C7, H3C8, HGF, HLA-A, HLA-B, HLA-C, HNF1A, HNRNPK, HOXB13, HRAS, HSD3B1, HSP90AA1

I-M
ICOSLG, ID3, IDH1, IDH2, IFNGR1, IGF1, IGF1R, IGF2, IKBKE, IKZF1, IL10, IL7R, INHA, INHBA, INPP4A, INPP4B, INSR, IRF2, IRF4, IRS1, IRS2, JAK1, JAK2, JAK3, JUN, KAT6A, KDM5A, KDM5C, KDM6A, KDR, KEAP1, KEL, KIF5B, KIT, KLF4, KLHL6, KMT2A, KMT2B, KMT2C, KMT2D, KRAS, LAMP1, LATS1, LATS2, LMO1, LRP1B, LYN, LZTR1, MAGI2, MALT1, MAP2K1, MAP2K2, MAP2K4, MAP3K1, MAP3K13, MAP3K14, MAP3K4, MAPK1, MAPK3, MAX, MCL1, MDC1, MDM2, MDM4, MED12, MEF2B, MEN1, MET, MGA, MITF, MLH1, MLLT3, MPL, MRE11, MSH2, MSH3, MSH6, MST1, MST1R, MTOR, MUTYH, MYB, MYC, MYCL, MYCL1, MYCN, MYD88, MYOD1

N-P
NAB2, NBN, NCOA3, NCOR1, NEGR1, NF1, NF2, NFE2L2, NFKBIA, NKX2-1, NKX3-1, NOTCH1, NOTCH2, NOTCH3, NOTCH4, NPM1, NRAS, NRG1, NSD1, NTRK1, NTRK2, NTRK3, NUP93, NUTM1, PAK1, PAK3, PAK5, PALB2, PARP1, PAX3, PAX5, PAX7, PAX8, PBRM1, PDCD1, PDCD1LG2, PDGFRA, PDGFRB, PDK1, PDPK1, PGR, PHF6, PHOX2B, PIK3C2B, PIK3C2G, PIK3C3, PIK3CA, PIK3CB, PIK3CD, PIK3CG, PIK3R1, PIK3R2, PIK3R3, PIM1, PLCG2, PLK2, PMAIP1, PMS1, PMS2, PNRC1, POLD1, POLE, PPARG, PPM1D, PPP2R1A, PPP2R2A, PPP6C, PRDM1, PREX2, PRKAR1A, PRKCI, PRKDC, PRKN, PRSS8, PTCH1, PTEN, PTPN11, PTPRD, PTPRS, PTPRT

Q-R
QKI, RAB35, RAC1, RAD21, RAD50, RAD51, RAD51B, RAD51C, RAD51D, RAD52, RAD54L, RAF1, RANBP2, RARA, RASA1, RB1, RBM10, RECQL4, REL, RET, RHEB, RHOA, RICTOR, RIT1, RNF43, ROS1, RPS6KA4, RPS6KB1, RPS6KB2, RPTOR, RUNX1, RUNX1T1, RYBP

S-T
SDHA, SDHAF2, SDHB, SDHC, SDHD, SETBP1, SETD2, SF3B1, SH2B3, SH2D1A, SHQ1, SLC7A8, SLIT2, SLX4, SMAD2, SMAD3, SMAD4, SMARCA4, SMARCB1, SMARCD1, SMC1A, SMC3, SMO, SNCAIP, SOCS1, SOX10, SOX17, SOX2, SOX9, SPEN, SPOP, SPTA1, SRC, SRSF2, STAG1, STAG2, STAT3, STAT4, STAT5A, STAT5B, STK11, STK40, STT3A, SUFU, SUZ12, SYK, TAF1, TBX3, TCF3, TCF7L2, TENT5C, TERC, TERT, TET1, TET2, TFE3, TFRC, TGFBR1, TGFBR2, TMEM127, TMPRSS2, TNFAIP3, TNFRSF14, TOP1, TOP2A, TP53, TP63, TRAF2, TRAF7, TSC1, TSC2, TSHR,

U-Z
U2AF1, VEGFA, VHL, VTCN1, WT1, XIAP, XPO1, XRCC2, YAP1, YES1, ZBTB2, ZBTB7A, ZFHX3, ZNF2, ZNF217, ZNF703, ZRSR2

Gene list (cancer-related germline genes)

The following is a list of genes that we report when a pathogenic or likely pathogenic germline mutation is found.

ABCC11, ALK, APC, AR, ATM, ATR, AXIN2, BAP1, BARD1, BLM, BMPR1A, BRCA1, BRCA2, BRIP1, BUB1B, CBL, CDC73, CDH1, CDK4, CDKN1B, CDKN2A (p14ARF), CDKN2A (p16INK4a), CEBPA, CHEK2, COL7A1, CTNNA1, CTR, CYLD, DDB2, DICER1, DIS3L2, DKC1, DOCK8, EGFR, ELANE, EPCAM, ERCC1, ERCC2, ERCC3, ERCC4, ERCC5, EXT1, EXT2, FAH, FANCA, FANCC, FANCE, FANCG, FANCI, FANCM, FH, FLCN, GALNT3, GATA2, GBA, GJB2, GPC3, GREM1, HFE, HMBS, HNF1A, HOXB13, HRAS, ITK, JMJD1C, KIT, MAX, MEN1, MET, MITF, MLH1, MSH2, MSH3, MSH6, MTAP, MUTYH (alpha3), MUTYH (alpha5), NBN, NF1, NF2, NTHL1, PALB2, PAX5, PDGFRA, PHOX2B, PMS2, POLD1, POLE, POLH, PRDM9, PRKAR1A, PRSS1, PTCH1, PTEN, PTPN11, RAD51C, RAD51D, RB1, RECQL, RECQL4, RET, RHBDF2, RMRP, RUNX1, SBDS, SDHA, SDHAF2, SDHB, SDHC, SDHD, SERPINA1, SETBP1, SH2B3, SH2D1A, SLC25A13, SMAD4, SMARCA4, SMARCB1, SMARCE1, SOS1, SRGAP1, SRY, STAT3, STK11, SUFU, TERT, TGFBR1, TMEM127, TNFRSF6, TP53, TRIM37, TSC1, TSC2, UROD, VHL, WAS, WRN, WT1, XPA, XPC

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1. Catalogue of Somatic Mutations in Cancer (COSMIC, cancer.sanger.ac.uk). Tate, J.G, et al. (2019) COSMIC: the catalogue of somatic mutations in cancer. *Nucleic Acids Research* 47(D1):D941–D947 (https://doi.org/10.1093/nar/gky1015)

DISCLAIMER

This report is intended to provide information to the treating physician and is not intended to guarantee or promise the efficacy or usefulness of any particular drug or treatment regimen for any patient. The potential clinical benefit of any drug listed in this report may vary based on a variety of factors, including the patient's specific tumor type and other clinical considerations.

This test was developed, and quality-assured by Inocras. It has not been cleared or approved by the US Food and Drug Administration. The test has been validated as a Laboratory Developed Test per institutional and applicable CLIA regulation (CLIA# 05D2280195) as qualified to perform high complexity clinical laboratory testing. Data interpretations are based on our current understanding of genes and variants as of the report date. When the report does identify variants with therapeutic implications, this does not promise or guarantee that a particular drug or treatment regimen will be effective or helpful in the treatment of disease in any patient, and the selection of any drug for patient treatment is done at the discretion of the treating physician. Genomic alterations should be considered in the context of the patient's history, risk factors and any previous genomic testing.

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For germline alterations, Inocras strongly suggests that the patient receive appropriate genetic counseling to explain the implications of this test result, its residual risks and uncertainties, and the reproductive or medical options it raises for the patient.

TRACKING INFORMATION

Sample tracking ID: 2401-034.001
Analysis ID: GINS-0000-0000-01AD
Pipeline version: Somatic 1.2.0