Sample Report

The Jackson Laboratory
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Patient Name: Shawn Lopez
Order ID: LK037362

Test: JAX SOMASEQ
Report Date: 07/07/2023

PATIENT	SPECIMEN	PHYSICIAN
Name: Shawn Lopez	**Specimen ID:** ADM52A5182	**Name:** Bart Bass
Patient ID: J0000000056	**Source Specimen ID:** CNVST-01	**Affiliation:** JAX-Lab-Internal-Quality
Source Patient ID: 1243568709	**1° Tumor Site:** Left arm	**Collection Date:** 06/05/2023
D.O.B: 06/01/1958	**Specimen Site:** Left arm	
Gender: Male	**Neoplastic Content:** 100.00 %	
Tumor Type: Melanoma	**Received Date:** 06/14/2023	

Sample RNA FAILED quality metrics and therefore the fusion assay was not performed
Sample DNA passed quality control metrics and the DNA assay was executed (see below)

Test Results Summary
The following clinically significant variants were detected in this specimen: ERBB2 amplification, FGFR3 amplification, and MYC amplification. RNA was not analyzed for this specimen and therefore the fusion assay was not performed. The sequencing read depth for the TERT promoter falls below the limit of detection for the assay, however digital droplet PCR (ddPCR) was performed and no variants were detected at the TERT promoter hotspots. Clinical correlation is REQUIRED.

Clinically Significant Findings

Variants with Therapeutic Relevance

Gene	Variant	Significance*	Therapeutic Implications**	Additional Information
ERBB2	Amplification	Tier 2	Associated with drug response; Potentially relevant clinical trials	CN: 5.5
FGFR3	Amplification	Tier 2	Potentially relevant clinical trials	CN: 6.2
MYC	Amplification	Tier 2	Potentially relevant clinical trials	CN: 5.2

Immunotherapy Markers

Biomarker	Result	Therapeutic Implications**	Additional Information
Microsatellite Instability (MSI)	Microsatellite Stable(MSS)	None	Percent Unstable Sites:2.5% Usable Sites: 120
Tumor Mutation Burden (TMB)	Tumor Mutation Burden Low (TMB-L)	None	Mut/Mb:0.00

Associated Therapies

Therapies Associated with Sensitivity for Patient's Tumor Type

Therapy	Alteration(s) Detected	Condition	Source
None			

Therapies Associated with Sensitivity for Other Tumor Types

Therapy	Alteration(s) Detected	Condition	Source
Ado-Trastuzumab Emtansine	ERBB2 Amplification	Breast Cancer	FDA,NCCN
Ado-Trastuzumab Emtansine	ERBB2 Amplification	Head And Neck Cancer	NCCN
Fam-Trastuzumab Deruxtecan	ERBB2 Amplification	Gastric Cancer	FDA,NCCN
Fam-Trastuzumab Deruxtecan	ERBB2 Amplification	Esophageal Cancer	NCCN

Therapy	Alteration(s) Detected	Condition	Source
Fam-Trastuzumab Deruxtecan	ERBB2 Amplification	Colorectal Cancer	NCCN
Fam-Trastuzumab Deruxtecan	ERBB2 Amplification	Breast Cancer	FDA,NCCN
Fam-Trastuzumab Deruxtecan	ERBB2 Amplification	Head And Neck Cancer	NCCN
Lapatinib	ERBB2 Amplification	Breast Cancer	FDA,NCCN
Margetuximab	ERBB2 Amplification	Breast Cancer	FDA,NCCN
Neratinib	ERBB2 Amplification	Breast Cancer	FDA,NCCN
Pembrolizumab, Trastuzumab	ERBB2 Amplification	Gastric Cancer	FDA,NCCN
Pembrolizumab, Trastuzumab	ERBB2 Amplification	Esophageal Cancer	NCCN
Pertuzumab	ERBB2 Amplification	Breast Cancer	FDA,NCCN
Trastuzumab, Lapatinib	ERBB2 Amplification	Colorectal Cancer	NCCN
Trastuzumab, Pertuzumab	ERBB2 Amplification	Colorectal Cancer	NCCN
Trastuzumab, Pertuzumab	ERBB2 Amplification	Cholangiocarcinoma	NCCN
Trastuzumab	ERBB2 Amplification	Breast Cancer	FDA,NCCN
Trastuzumab	ERBB2 Amplification	Gastric Cancer	FDA,NCCN
Trastuzumab	ERBB2 Amplification	Esophageal Cancer	NCCN
Trastuzumab	ERBB2 Amplification	Head And Neck Cancer	NCCN
Trastuzumab	ERBB2 Amplification	Endometrial Adenocarcinoma	NCCN
Tucatinib	ERBB2 Amplification	Breast Cancer	FDA,NCCN

Therapies Associated with Resistance for Patient's Tumor Type

Therapy	Alteration(s) Detected	Condition	Source
None			

Sources: **FDA** = US Food and Drug Administration (www.fda.gov), **NCCN** = National Comprehensive Cancer Network (www.nccn.org), **ASCO** = American Society of Clinical Oncology (www.asco.org), **MCG**: My Cancer Genome (www.mycancergenome.org)

Potential Clinical Trials

Related Biomarkers	Phase	NCT ID	Title	Locations/Contact
ERBB2 Amplification, FGFR3 Amplification	Phase 2	NCT02693535	TAPUR: Testing the Use of Food and Drug Administration (FDA) Approved Drugs That Target a Specific Abnormality in a Tumor Gene in People With Advanced Stage Cancer (NCT02693535)	**Contact:** American Society of Clinical Oncology www.tapur.org **Locations:** South Portland, Maine; Scarborough, Maine; Biddeford, Maine **+123 more**
MYC Amplification	Phase 1	NCT05159518	A Study of PRT2527 in Patients With Advanced Solid Tumors (NCT05159518)	**Contact:** Prelude Therapeutics See Email **Locations:** Philadelphia, Pennsylvania; Fairfax, Virginia; Celebration, Florida **+3 more**

Variants of Biological Significance

Gene	Variant	Significance*	Associated Clinical Outcome	Additional Information
None				

Variants of Unknown Clinical Significance

Gene	Variant	Significance*	Therapeutic Implications**	Additional Information
ARID1A	p.H203Q c.609C>A	Tier 3	N/A	COSMIC: N/A gnomAD Frequency: 0.0% dbSNP: rs558792709 VAF: 47.08%
DNMT3A	p.C911Y c.2732G>A	Tier 3	N/A	COSMIC: COSV104585302 , COSM253390 gnomAD Frequency: 0.0% dbSNP: rs906113912 VAF: 44.98%
EGFR	p.R675Q c.2024G>A	Tier 3	N/A	COSMIC: COSV51862598 , COSM5033534 gnomAD Frequency: 0.0% dbSNP: rs150423237 VAF: 52.17%

***Significance:** Tier according to the AMP/ASCO/CAP somatic variant classification system.
****Therapeutic Implications:** Associated with drug response = related to drug sensitivity or resistance as described in Drug Response section of this report; Potentially relevant clinical trials = gene is related to a trial in the Clinical Trials section of this report
COSMIC: Mutation ID in the Catalogue Of Somatic Mutations in Cancer (http://cancer.sanger.ac.uk/)
gnomAD Frequency: Allele frequency of the alteration from gnomAD (http://gnomad.broadinstitute.org//)
dbSNP: RS number of alteration in dbSNP database (http://www.ncbi.nlm.nih.gov/SNP)

Pertinent Negatives*

ATM, BRAF, BRCA1, BRCA2, EGFR, IDH1, KIT, KRAS, MET, MLH1, MSH2, MSH6, PDGFRA, PIK3CA, PMS2, RET, SMARCB1, TERT Promoter
** please see regions of low coverage listed below*

Genomic Marker Interpretations

COMMENTS
The following clinically significant variants were detected in this specimen: ERBB2 amplification, FGFR3 amplification, and MYC amplification. RNA was not analyzed for this specimen and therefore the fusion assay was not performed. The sequencing read depth for the TERT promoter falls below the limit of detection for the assay, however digital droplet PCR (ddPCR) was performed and no variants were detected at the TERT promoter hotspots. Clinical correlation is REQUIRED.

Gene	Variant	VAF/CN	Depth	Functional Impact	Class	Type
ERBB2	Amplification	5.5	Copy Gain	Overexpression	Tier 2	Therapeutic

Gene Description:ERBB2 (HER2), erb-b2 receptor tyrosine kinase 2, is an EGFR receptor tyrosine kinase that activates PI3K-AKT-mTOR and RAS-RAF-MEK-ERK pathways, therefore regulating growth and transformation (PMID: 17471238). ERBB2 (HER2) amplification and/or overexpression, and activation has been implicated in several tumor types (PMID: 17471238, PMID: 31019892), and is commonly observed in breast cancer (PMID: 31650186, PMID: 32161378), while some ERBB2 mutations have been implicated in resistance to select tyrosine kinase inhibitors (PMID: 32327210). (via The Jackson Laboratory Clinical Knowledgebase, ckb.jax.org)
Pathways: Receptor tyrosine kinase/growth factor signaling
Mutation Description: ERBB2 gene amplification is predicted to result in increased expression of the ERBB2 (HER2) protein. ERBB2 amplification is a major driver of tumor development and progression in a subset of breast cancers (PMID: 24508693) and is correlated with increased tumor size, lymph node positivity and high rates of cellular proliferation (PMID: 1671531). ERBB2 amplification or overexpression is frequently observed in breast cancers as well as many other cancer types, including ovarian, stomach and bladder (PMID: 17993237). The FDA has approved multiple drugs for breast, gastric, and gastro esophageal adenocarcinomas containing ERBB2 amplifications (FDA.gov).

Gene	Variant	VAF/CN	Depth	Functional Impact	Class	Type

References: PMID: 17471238, PMID: 31019892, PMID: 31650186, PMID: 32161378, PMID: 32327210, PMID: 24508693, PMID: 1671531, PMID: 17993237

Gene	Variant	VAF/CN	Depth	Functional Impact	Class	Type
FGFR3	Amplification	6.2	Copy Gain	Overexpression	Tier 2	Therapeutic

Gene Description:FGFR3, fibroblast growth factor receptor 3, is a receptor tyrosine kinase activated upon binding of the FGF ligand, which activates RAS-MAPK and PI3K-AKT pathways (PMID: 22508544). Altered function of FGFR3 in cancer may lead to increased cell proliferation and decreased apoptosis (PMID: 22508544) and mutations and fusions are commonly observed in bladder cancer (PMID: 30975452, PMID: 23175443), while FGFR3 overexpression only in bladder cancer may have different treatment implications (PMID: 32682615). (via The Jackson Laboratory Clinical Knowledgebase, ckb.jax.org)
Pathways: Receptor tyrosine kinase/growth factor signaling
References: PMID: 22508544, PMID: 23175443, PMID: 30975452, PMID: 32682615

Gene	Variant	VAF/CN	Depth	Functional Impact	Class	Type
MYC	Amplification	5.2	Copy Gain	Overexpression	Tier 2	Therapeutic

Gene Description:MYC, MYC proto-oncogene, bHLH transcription factor, is a transcription factor that regulates expression of genes involved in cell cycle progression, apoptosis, cellular transformation (PMID: 25038584, PMID: 32071436) and the immune system (PMID: 29514782). Amplification, overexpression, and rearrangement of MYC is commonly observed in solid and hematological tumors (PMID: 28587062, PMID: 32203465), such as lung cancer (PMID: 32014901) and diffuse large B-Cell lymphoma (PMID: 32074595). (via The Jackson Laboratory Clinical Knowledgebase, ckb.jax.org)
Mutation Description:
MYC amplification is a known mechanism for deregulated expression of the MYC protein, a transcription factor that plays a role in cellular proliferation, cell cycle progression, and genomic stability (PMID: 19029958, PMID: 10378696). Deregulated MYC expression has a documented role in tumor initiation and maintenance (PMID: 22464321, PMID: 16934487, PMID: 16935001). MYC is one of the most highly amplified oncogenes among many different cancer types (PMID: 20164920) and has been observed frequently in solid tumors and hematological cancers (PMID: 10378696).
References: PMID: 25038584, PMID: 28587062, PMID: 29514782, PMID: 32014901, PMID: 32071436, PMID: 32074595, PMID: 32203465, PMID: 19029958, PMID: 10378696, PMID: 22464321, PMID: 16934487, PMID: 16935001, PMID: 20164920

Regions of Low Coverage

TERT Promoter (chr5:1295228)

Test Methods & Limitations

The JAX SOMASEQ™ incorporates two targeted enrichment sequencing assays: a DNA based panel comprising 517 cancer related genes and an RNA based panel evaluating 55 genes known to form fusions in solid tumors. Clinically significant small nucleotide variants (SNVs) and insertion-deletions (indels) are reported across the 517 gene panel. Copy number variants (CNVs) and fusions are reported in 61 and 55 genes, respectively. Additionally, MET exon 14 and EGFR exons 2-7 (EGFRvIII) splicing events are covered.

The JAX SOMASEQ™ uses genomic DNA and RNA extracted from macro dissection enriched FFPE tissue sections (30% neoplastic content), followed by enrichment of target exons and introns by hybrid capture (Illumina). The Illumina NovaSeq 6000 generates 101bp paired end sequence reads with a median exon coverage of greater than or equal to 150X. A minimum coverage of 100X is required for reporting SNVs (single nucleotide variants) and indels (insertions and deletions up to 50 bp in length). Variants within regions that do not meet our coverage thresholds are not reported. For a list of these regions, please contact CGL_CS@jax.org. The LOD (limit of detection) for SNVs and indels was determined as 5% during the analytical validation. The LOD for copy number variants (CNVs) was 5 copies for amplifications and 1 copy for deletions. Mutational analysis is performed using the TSO500 bioinformatic pipeline. Variants are called against human genome build GRCh37.

Digital droplet PCR (ddPCR) is performed at TERT promoter hotspots chr5:1295228 and chr5:1295250 (hg19 coordinates) for all JAX SOMASEQ™ samples. TERT promoter hotspot mutations detected at 5% or greater will be included on the report.

Evidence of association between genomic variants and potential therapeutic (including clinical trials), prognostic and/or diagnostic outcomes is obtained from peer reviewed literature, clinical practice guidelines, FDA labels, publicly available databases and the JAX Clinical Knowledgebase (CKB). Information from these sources is curated into the GenomOncology Pathology Workbench and clinical significance of genomic variants interpreted in the context of each patient's molecular/disease profile. The JAX SOMASEQ™ report reflects the variants determined to be clinically relevant at the time of reporting. Variants are classified into four tiers based on the joint consensus guidelines published by AMP/ASCO/CAP on interpretation of sequence variants in cancer (PMID: 27993330). The four tiers include strong clinical significance (Tier I), potential clinical significance (Tier II), unknown clinical significance (Tier III) and benign or likely benign variants (Tier IV). The patient's complete molecular profile is available to the ordering clinician(s) upon request, up to 18 months after the date of report, including allele frequencies for variants of uncertain significance (VUS) and variants with no current therapeutic correlation.

Tumor mutation burden (TMB) is calculated as the mutations per megabase (mut/Mb) across the ~1.94Mb of coding DNA captured by the JAX SOMASEQ™ panel. Tumors containing 10 mut/Mb are classified as TMB high and may respond to immunotherapy treatment (PMID: 28835386, PMID: 29658845). Microsatellite instability (MSI) status is determined through analysis of 130 MSI marker sites to calculate the percentage of unstable sites. A minimum of 40 analyzed MSI sites are required for classification. Specimens with 10% unstable MSI sites are reported as microsatellite instability high (MSI-H) and specimens with <10% unstable MSI sites are reported as microsatellite stable (MSS).

Disclaimer

Decisions on patient care must be based on the independent medical judgment of the treating physician, taking into consideration all relevant information about the patient's condition, including patient medical and family history, physical examinations, information from other diagnostic tests, and patient preferences.

A treating physician's decisions should not be based on a single test, such as this test, or the information contained in this report alone. Results of this test must always be interpreted in the context of all relevant clinical and pathological data and should not be used alone for diagnosis or patient care decisions.

The JAX SOMASEQ™ uses high throughput sequencing to identify clinically significant variants (SNVs and indels) within 517 cancer related genes including the TERT promoter, CNVs of 61 cancer related genes, fusions across 55 gene partners, and splicing events in MET and EGFR as listed in the appendix of this report. The assay may not detect all potentially relevant variants. Tumor tissue is not homogenous, and its characteristics may differ from sample to sample for the same tumor. Sample neoplastic content levels near the required minimum (30%) may have decreased sensitivity for copy number alterations. It may be possible for a biomarker variant to be present yet go undetected by our assay either due to the heterogeneous nature of the tumor tissue or the limit of detection of our assay (please see “test methods and limitations” section). Therefore, to the extent a particular biomarker variant is not reported, we cannot guarantee that the variant does not exist.

The JAX SOMASEQ™ examines tumor tissue only and does not examine normal tissue (such as tissue adjacent to the tumor). Thus, the origin of a mutation detected by our assay may be a somatic (not inherited) or a germline mutation (inherited) and will not be distinguishable by this assay. If a germline inheritance pattern is suspected, then counseling by a genetic counselor is recommended.

The information presented in the clinical trials section of this report is compiled from public sources believed to be reliable and current. However, the information available in the public domain is continuously updated. While we endeavor to make this information accurate and complete, we cannot guarantee the accuracy or completeness of this information. Accordingly, the patient's physician or research staff should independently investigate the clinical trials information. The clinical trials information was compiled from www.clinicaltrials.gov. The clinical trials are not ranked in order of potential or predicted efficacy. The clinical trial information is to be used for clinical trial guidance and may not include all relevant trials. The clinical trials listed in this report were enrolling at the time of report generation, but the status may change at any time. Specific entrance criteria for each clinical trial should be reviewed as additional inclusion criteria may apply. The clinical trials identified may or may not be suitable for a particular patient and we do not guarantee or suggest that any particular trial will be effective with the treatment of any particular condition. Health care providers should employ independent clinical judgment in interpreting this information for their patients.

This report includes information about therapeutic agents that appear to be associated with clinical benefit based on National Comprehensive Cancer Network (NCCN) Compendium guidelines, relevance of tumor lineage, and published evidence, as available and compiled by The Jackson Laboratory. The Jackson Laboratory expressly disclaims and makes no representation or warranty relating to the published evidence and scientific literature identified in this report, or any of the conclusions and information set forth in this report that is derived from a review thereof, including information and conclusions relating to therapeutic agents that are included or omitted from this report. The therapeutic agents included in this report are not ranked in order of potential or predicted efficacy. Agents with potential clinical benefit (or lack of clinical benefit) are not evaluated for source or level of published evidence and are identified based on the information available at the time of the test. The agents identified may or may not be suitable for use on a particular patient and we do not guarantee or suggest that any particular agent will be effective with the treatment of any particular condition. The selection of any, all or none of the agents associated with potential clinical benefit (or lack of clinical benefit) resides solely within the discretion of the treating physician.

This report includes some clinically relevant interpretation of next generation sequencing data powered by The Jackson Laboratory Clinical Knowledgebase (CKB). This information may include associations between a biomarker variant (or lack of a variant) and one or more therapeutic agents with potential clinical benefit (or lack of clinical benefit), including agents that are being studied in clinical research. A finding of a biomarker variant does not necessarily indicate pharmacologic effectiveness (or lack thereof) of any agent or treatment regimen. A finding of “no biomarker variant” does not necessarily indicate lack of pharmacologic effectiveness (or lack of effectiveness) of any agent or treatment regimen. The Jackson Laboratory expressly disclaims, and makes no representation or warranty of, the accuracy or completeness with respect to the publicly available information included herein or compiled in creating this report.

This test was developed and its performance characteristics determined by The Jackson Laboratory. It has not been cleared or approved by the U.S. Food and Drug Administration (FDA). This test may be used for clinical purposes and should not be regarded as purely investigational or for research only. This laboratory is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA 88) as qualified to perform high complexity clinical testing. The Jackson Laboratory 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 this test.

Appendix I - Additional Genomic Information for Clinically Significant Variants

Variant	Transcript	Genomic Coordinate	Genome Build
FGFR3 Amplification	NM_000142.4	N/A	Hg19
MYC Amplification	NM_002467.4	N/A	Hg19
ERBB2 Amplification	NM_004448.2	N/A	Hg19

Appendix II - Genes Sequenced on the TSO500

Gene	Reference Sequence	Gene	Reference Sequence	Gene	Reference Sequence
ABL1^	NM_005157.4	ABL2	NM_007314.3	ACVR1	NM_001105.4
ACVR1B	NM_020328.3	AKT1	NM_001014432.1	AKT2*	NM_001626.4
AKT3^	NM_005465.4	ALK*^	NM_004304.4	ALOX12B	NM_001139.2
AMER1	NM_152424.3	ANKRD11	NM_001256182.1	ANKRD26	NM_014915.2
APC	NM_000038.5	AR*^	NM_000044.3	ARAF	NM_001654.4
ARFRP1	NM_003224.4	ARID1A	NM_006015.4	ARID1B	NM_020732.3
ARID2	NM_152641.2	ARID5B	NM_032199.2	ASXL1	NM_015338.5
ASXL2	NM_018263.4	ATM*	NM_000051.3	ATR	NM_001184.3
ATRX	NM_000489.3	AURKA	NM_198433.1	AURKB	NM_004217.3
AXIN1	NM_003502.3	AXIN2	NM_004655.3	AXL^	NM_021913.4
B2M	NM_004048.2	BAP1	NM_004656.3	BARD1	NM_000465.2
BBC3	NM_001127240.2	BCL10	NM_003921.4	BCL2^	NM_000633.2
BCL2L1	NM_138578.1	BCL2L11	NM_001204108.1	BCL2L2	NM_001199839.1
BCL6	NM_001706.4	BCOR	NM_001123385.1	BCORL1	NM_021946.4
BCR	NM_004327.3	BIRC3	NM_001165.4	BLM	NM_000057.2
BMPR1A	NM_004329.2	BRAF*^	NM_004333.4	BRCA1*^	NM_007294.3
BRCA2*^	NM_000059.3	BRD4	NM_058243.2	BRIP1	NM_032043.2
BTG1	NM_001731.2	BTK	NM_000061.2	C11orf30	NM_020193.3
CALR	NM_004343.3	CARD11	NM_032415.4	CASP8	NM_001228.4
CBFB	NM_001755.2	CBL	NM_005188.3	CCND1*	NM_053056.2
CCND2	NM_001759.3	CCND3*	NM_001760.3	CCNE1*	NM_001238.2
CD274	NM_014143.3	CD276	NM_001024736.1	CD74	NM_001025159.2
CD79A	NM_001783.3	CD79B	NM_000626.2	CDC73	NM_024529.4
CDH1	NM_004360.3	CDK12	NM_016507.2	CDK4*^	NM_000075.3
CDK6*	NM_001259.6	CDK8	NM_001260.1	CDKN1A	NM_000389.4
CDKN1B	NM_004064.3	CDKN2A*	NM_000077.4	CDKN2B*	NM_004936.3
CDKN2C	NM_001262.2	CEBPA	NM_004364.3	CENPA	NM_001809.3
CHD2	NM_001271.3	CHD4	NM_001273.2	CHEK1*	NM_001114122.2
CHEK2*	NM_007194.3	CIC	NM_015125.3	CREBBP	NM_004380.2
CRKL	NM_005207.3	CRLF2	NM_022148.2	CSF1R^	NM_005211.3
CSF3R	NM_156039.3	CSNK1A1	NM_001025105.2	CTCF	NM_006565.3
CTLA4	NM_005214.4	CTNNA1	NM_001903.2	CTNNB1	NM_001904.3
CUL3	NM_003590.4	CUX1	NM_001913.3	CXCR4	NM_003467.2

Gene	Reference Sequence	Gene	Reference Sequence	Gene	Reference Sequence
CYLD	NM_015247.2	DAXX	NM_001141970.1	DCUN1D1	NM_020640.2
DDR2	NM_001014796.1	DDX41	NM_016222.2	DHX15	NM_001358.2
DICER1	NM_177438.2	DIS3	NM_014953.3	DNAJB1	NM_006145.1
DNMT1	NM_001130823.1	DNMT3A	NM_022552.4	DNMT3B	NM_006892.3
DOT1L	NM_032482.2	E2F3	NM_001949.4	EED	NM_003797.3
EGFL7	NM_016215.4	EGFR*^	NM_005228.3	EIF1AX	NM_001412.3
EIF4A2	NM_001967.3	EIF4E	NM_001130679.1	EML4^	NM_019063.3
EP300	NM_001429.3	EPCAM	NM_002354.2	EPHA3	NM_005233.5
EPHA5	NM_004439.5	EPHA7	NM_004440.3	EPHB1	NM_004441.4
ERBB2*^	NM_004448.2	ERBB3*	NM_001982.3	ERBB4	NM_005235.2
ERCC1*	NM_001983.3	ERCC2*	NM_000400.3	ERCC3	NM_000122.1
ERCC4	NM_005236.2	ERCC5	NM_000123.3	ERG^	NM_001136154.1
ERRFI1	NM_018948.3	ESR1*^	NM_001122742.1	ETS1^	NM_001143820.1
ETV1^	NM_004956.4	ETV4^	NM_001079675.2	ETV5^	NM_004454.2
ETV6	NM_001987.4	EWSR1^	NM_013986.3	EZH2	NM_004456.4
FAM175A	NM_139076.2	FAM46C	NM_017709.3	FANCA	NM_000135.2
FANCC	NM_000136.2	FANCD2	NM_033084.3	FANCE	NM_021922.2
FANCF	NM_022725.3	FANCG	NM_004629.1	FANCI	NM_001113378.1
FANCL	NM_001114636.1	FAS	NM_000043.4	FAT1	NM_005245.3
FBXW7	NM_033632.3	FGF1*	NM_001144934.1	FGF10*	NM_004465.1
FGF14*	NM_175929.2	FGF19*	NM_005117.2	FGF2*	NM_002006.4
FGF23*	NM_020638.2	FGF3*	NM_005247.2	FGF4*	NM_002007.2
FGF5*	NM_004464.3	FGF6*	NM_020996.1	FGF7*	NM_002009.3
FGF8*	NM_033163.3	FGF9*	NM_002010.2	FGFR1*^	NM_023110.2
FGFR2*^	NM_022970.3	FGFR3*^	NM_000142.4	FGFR4*^	NM_213647.1
FH	NM_000143.3	FLCN	NM_144997.5	FLI1^	NM_002017.4
FLT1^	NM_002019.4	FLT3^	NM_004119.2	FLT4	NM_182925.4
FOXA1	NM_004496.3	FOXL2	NM_023067.3	FOXO1	NM_002015.3
FOXP1	NM_032682.5	FRS2	NM_001278351.1	FUBP1	NM_003902.3
FYN	NM_002037.5	GABRA6	NM_000811.2	GATA1	NM_002049.3
GATA2	NM_032638.4	GATA3	NM_001002295.1	GATA4	NM_002052.3
GATA6	NM_005257.4	GEN1	NM_182625.3	GID4	NM_024052.4
GLI1	NM_005269.2	GNA11	NM_002067.2	GNA13	NM_006572.4
GNAQ	NM_002072.3	GNAS	NM_000516.4	GPR124	NM_032777.9

Gene	Reference Sequence	Gene	Reference Sequence	Gene	Reference Sequence
GPS2	NM_004489.4	GREM1	NM_013372.6	GRIN2A	NM_000833.3
GRM3	NM_000840.2	GSK3B	NM_002093.3	H3F3A	NM_002107.4
H3F3B	NM_005324.3	H3F3C	NM_001013699.2	HGF	NM_000601.4
HIST1H1C	NM_005319.3	HIST1H2BD	NM_021063.3	HIST1H3A	NM_003529.2
HIST1H3B	NM_003537.3	HIST1H3C	NM_003531.2	HIST1H3D	NM_003530.4
HIST1H3E	NM_003532.2	HIST1H3F	NM_021018.2	HIST1H3G	NM_003534.2
HIST1H3H	NM_003536.2	HIST1H3I	NM_003533.2	HIST1H3J	NM_003535.2
HIST2H3A	NM_001005464.2	HIST2H3C	NM_021059.2	HIST2H3D	NM_001123375.2
HIST3H3	NM_003493.2	HNF1A	NM_000545.5	HNRNPK	NM_002140.3
HOXB13	NM_006361.5	HRAS	NM_005343.2	HSD3B1	NM_000862.2
HSP90AA1	NM_001017963.2	ICOSLG	NM_015259.4	ID3	NM_002167.4
IDH1	NM_005896.2	IDH2	NM_002168.2	IFNGR1	NM_000416.2
IGF1	NM_001111283.1	IGF1R	NM_000875.3	IGF2	NM_001127598.1
IKBKE	NM_014002.3	IKZF1	NM_006060.4	IL10	NM_000572.2
IL7R	NM_002185.3	INHA	NM_002191.3	INHBA	NM_002192.2
INPP4A	NM_001134224.1	INPP4B	NM_003866.2	INSR	NM_000208.2
IRF2	NM_002199.3	IRF4	NM_002460.3	IRS1	NM_005544.2
IRS2	NM_003749.2	JAK1	NM_002227.2	JAK2*^	NM_004972.3
JAK3	NM_000215.3	JUN	NM_002228.3	KAT6A	NM_001099412.1
KDM5A	NM_001042603.1	KDM5C	NM_004187.3	KDM6A	NM_021140.2
KDR^	NM_002253.2	KEAP1	NM_012289.3	KEL	NM_000420.2
KIF5B^	NM_004521.2	KIT*^	NM_000222.2	KLF4	NM_004235.4
KLHL6	NM_130446.2	KMT2A^	NM_001197104.1	KRAS*	NM_004985.3
LAMP1*	NM_005561.3	LATS1	NM_004690.3	LATS2	NM_014572.2
LMO1	NM_002315.2	LRP1B	NM_018557.2	LYN	NM_002350.3
LZTR1	NM_006767.3	MAGI2	NM_012301.3	MALT1	NM_006785.3
MAP2K1	NM_002755.3	MAP2K2	NM_030662.3	MAP2K4	NM_001281435.1
MAP3K1	NM_005921.1	MAP3K13	NM_004721.4	MAP3K14	NM_003954.3
MAP3K4	NM_005922.2	MAPK1	NM_002745.4	MAPK3	NM_002746.2
MAX	NM_002382.4	MCL1	NM_021960.4	MDC1	NM_014641.2
MDM2*	NM_002392.5	MDM4*	NM_002393.4	MED12	NM_005120.2
MEF2B	NM_001145785.1	MEN1	NM_130799.2	MET*^	NM_001127500.1
MGA	NM_001164273.1	MITF	NM_000248.3	MLH1	NM_000249.3
MLLT3^	NM_004529.2	MPL	NM_005373.2	MRE11A	NM_005591.3

Gene	Reference Sequence	Gene	Reference Sequence	Gene	Reference Sequence
MSH2^	NM_000251.2	MSH3	NM_002439.4	MSH6	NM_000179.2
MST1	NM_020998.3	MST1R	NM_002447.2	MTOR	NM_004958.3
MUTYH	NM_001128425.1	MYB	NM_001130173.1	MYC*^	NM_002467.4
MYCL*	NM_001033082.2	MYCN*	NM_005378.4	MYD88	NM_002468.4
MYOD1	NM_002478.4	NAB2	NM_005967.3	NBN	NM_002485.4
NCOA3	NM_181659.2	NCOR1	NM_006311.3	NEGR1	NM_173808.2
NF1	NM_001042492.2	NF2	NM_000268.3	NFE2L2	NM_006164.4
NFKBIA	NM_020529.2	NKX2-1	NM_001079668.2	NKX3-1	NM_006167.3
NOTCH1^	NM_017617.3	NOTCH2^	NM_024408.3	NOTCH3^	NM_000435.2
NOTCH4	NM_004557.3	NPM1	NM_002520.6	NRAS*	NM_002524.4
NRG1*^	NM_013962.2	NSD1	NM_022455.4	NTRK1^	NM_002529.3
NTRK2^	NM_006180.3	NTRK3^	NM_001012338.2	NUP93	NM_014669.4
NUTM1	NM_175741.1	PAK1	NM_001128620.1	PAK3	NM_002578.3
PAK7	NM_020341.3	PALB2	NM_024675.3	PARK2	NM_004562.2
PARP1	NM_001618.3	PAX3^	NM_181457.3	PAX5	NM_016734.2
PAX7^	NM_001135254.1	PAX8	NM_013953.3	PBRM1	NM_018313.4
PDCD1	NM_005018.2	PDCD1LG2	NM_025239.3	PDGFRA*^	NM_006206.4
PDGFRB*^	NM_002609.3	PDK1	NM_001278549.1	PDPK1	NM_002613.4
PGR	NM_000926.4	PHF6	NM_032458.2	PHOX2B	NM_003924.3
PIK3C2B	NM_002646.3	PIK3C2G	NM_004570.4	PIK3C3	NM_002647.2
PIK3CA*^	NM_006218.2	PIK3CB*	NM_006219.2	PIK3CD	NM_005026.3
PIK3CG	NM_002649.2	PIK3R1	NM_181523.2	PIK3R2	NM_005027.3
PIK3R3	NM_003629.3	PIM1	NM_002648.3	PLCG2	NM_002661.3
PLK2	NM_006622.3	PMAIP1	NM_021127.2	PMS1	NM_000534.4
PMS2	NM_000535.5	PNRC1	NM_006813.2	POLD1	NM_001256849.1
POLE	NM_006231.2	PPARG^	NM_138712.3	PPM1D	NM_003620.3
PPP2R1A	NM_014225.5	PPP2R2A	NM_001177591.1	PPP6C	NM_001123355.1
PRDM1	NM_001198.3	PREX2	NM_024870.2	PRKAR1A	NM_212472.2
PRKCI	NM_002740.5	PRKDC	NM_006904.6	PRSS8	NM_002773.3
PTCH1	NM_000264.3	PTEN*	NM_000314.4	PTPN11	NM_002834.3
PTPRD	NM_002839.3	PTPRS	NM_002850.3	PTPRT	NM_133170.3
QKI	NM_006775.2	RAB35	NM_006861.6	RAC1	NM_018890.3
RAD21	NM_006265.2	RAD50	NM_005732.3	RAD51	NM_002875.4
RAD51B	NM_133509.3	RAD51C	NM_058216.2	RAD51D	NM_002878.3

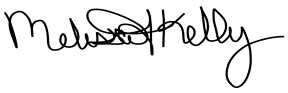
Gene	Reference Sequence	Gene	Reference Sequence	Gene	Reference Sequence
RAD52	NM_134424.2	RAD54L	NM_001142548.1	RAF1*^	NM_002880.3
RANBP2	NM_006267.4	RARA	NM_000964.3	RASA1	NM_002890.2
RB1	NM_000321.2	RBM10	NM_005676.4	RECQL4	NM_004260.3
REL	NM_002908.2	RET*^	NM_020975.4	RFWD2	NM_022457.5
RHEB	NM_005614.3	RHOA	NM_001664.2	RICTOR*	NM_152756.3
RIT1	NM_006912.5	RNF43	NM_017763.4	ROS1^	NM_002944.2
RPS6KA4	NM_003942.2	RPS6KB1*^	NM_003161.3	RPS6KB2	NM_003952.2
RPTOR	NM_020761.2	RUNX1	NM_001754.4	RUNX1T1	NM_175635.2
RYBP	NM_012234.5	SDHA	NM_004168.2	SDHAF2	NM_017841.2
SDHB	NM_003000.2	SDHC	NM_003001.3	SDHD	NM_003002.3
SETBP1	NM_015559.2	SETD2	NM_014159.6	SF3B1	NM_012433.2
SH2B3	NM_005475.2	SH2D1A	NM_002351.4	SHQ1	NM_018130.2
SLIT2	NM_004787.1	SLX4	NM_032444.2	SMAD2	NM_001135937.2
SMAD3	NM_005902.3	SMAD4	NM_005359.5	SMARCA4	NM_001128849.1
SMARCB1	NM_003073.3	SMARCD1	NM_003076.4	SMC1A	NM_006306.3
SMC3	NM_005445.3	SMO	NM_005631.4	SNCAIP	NM_005460.2
SOCS1	NM_003745.1	SOX10	NM_006941.3	SOX17	NM_022454.3
SOX2	NM_003106.3	SOX9	NM_000346.3	SPEN	NM_015001.2
SPOP	NM_001007226.1	SPTA1	NM_003126.2	SRC	NM_005417.4
SRSF2	NM_003016.4	STAG1	NM_005862.2	STAG2	NM_001042749.1
STAT3	NM_139276.2	STAT4	NM_003151.3	STAT5A	NM_003152.3
STAT5B	NM_012448.3	STK11	NM_000455.4	STK40	NM_032017.1
SUFU	NM_016169.3	SUZ12	NM_015355.2	SYK	NM_003177.5
TAF1	NM_004606.3	TBX3	NM_016569.3	TCEB1	NM_005648.3
TCF3	NM_003200.3	TCF7L2	NM_030756.4	TERC	
TERT	NM_198253.2	TET1	NM_030625.2	TET2	NM_001127208.2
TFE3	NM_006521.4	TFRC*	NM_003234.2	TGFBR1	NM_004612.2
TGFBR2	NM_001024847.2	TMEM127	NM_017849.3	TMPRSS2^	NM_001135099.1
TNFAIP3	NM_006290.3	TNFRSF14	NM_003820.2	TOP1	NM_003286.2
TOP2A	NM_001067.3	TP53	NM_000546.5	TP63	NM_003722.4
TRAF2	NM_021138.3	TRAF7	NM_032271.2	TSC1	NM_000368.4
TSC2	NM_000548.3	TSHR	NM_000369.2	U2AF1	NM_006758.2
VEGFA	NM_001025366.2	VHL	NM_000551.3	VTCN1	NM_024626.3
WISP3	NM_003880.3	WT1	NM_024426.4	XIAP	NM_001167.3

Gene	Reference Sequence	Gene	Reference Sequence	Gene	Reference Sequence
XPO1	NM_003400.3	XRCC2	NM_005431.1	YAP1	NM_001130145.2
YES1	NM_005433.3	ZBTB2	NM_020861.1	ZBTB7A	NM_015898.2
ZFHX3	NM_006885.3	ZNF217	NM_006526.2	ZNF703	NM_025069.1
ZRSR2	NM_005089.3				

* : Gene was tested for CNVs
^ : Gene was tested for Fusions

Appendix III - Genes Analyzed for Pertinent Negatives and Low Coverage

The following genes are analyzed for regions of low coverage and reported as pertinent negatives if no clinically significant variants are detected throughout the gene.
ALK Fusions, ATM, BRAF, BRCA1, BRCA2, EGFR , ERBB2 Gene Amplification, FGFR2 Fusions, FGFR3 Fusions, IDH1, KIT, KRAS, MET, MLH1, MSH2, MSH6, NTRK1 Fusions, NTRK2 Fusions, NTRK3 Fusions, PDGFRA, PIK3CA, PMS2, RET, ROS1 Fusions, SMARCB1

Name:  Date: 07/07/2023

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