Client: Example Client ABC123
123 Test Drive
Salt Lake City, UT 84108
UNITED STATES

Physician: Doctor, Example

Patient: Patient, Example

DOB	12/9/1958
Gender:	Female
Patient Identifiers:	01234567890ABCD, 012345
Visit Number (FIN):	01234567890ABCD
Collection Date:	01/01/2017 12:34

Hereditary Cancer Panel, Sequencing and Deletion/Duplication

ARUP test code 2012032

Cancer Panel, Hereditary, Spcm	Whole Blood
Cancer Panel, Hereditary, Interp	Negative

INDICATION FOR TESTING
Patient with a meningioma and a family history of breast cancer.

RESULT
No pathogenic variants were detected in any of the genes tested.

INTERPRETATION
No pathogenic variants were detected by massively parallel sequencing of the coding regions and intron-exon boundaries in any of the genes analyzed. No large exonic deletions and duplications were identified in the genes tested. No sequence variants and large exonic deletions or duplications were detected in PMS2 by Sanger sequencing and by multiplex ligation dependent probe amplification (MLPA). This result decreases the likelihood of, but does not exclude, a hereditary form of cancer. Please refer to the background information included in this report for a list of the genes analyzed and limitations of this test.

RECOMMENDATIONS
Medical screening and management should rely on clinical findings and family history. Genetic consultation is recommended.

COMMENTS
Likely benign and benign variants are not included in this report.

This result has been reviewed and approved by [redacted]

BACKGROUND INFORMATION: Hereditary Cancer Panel, Sequencing and Deletion/Duplication

CHARACTERISTICS: Pathogenic variants in multiple genes have been implicated in hereditary cancer, often characterized by early age of onset (typically before 50 years), and the development of two or more cancers, multifocal cancers, or similar cancers in an individual or closely related family member(s). Pathogenic variants in the genes analyzed by this panel cause variable phenotypes and cancer risks.

EPIDEMIOLOGY: Approximately 1,700,000 new cases of cancer are diagnosed in the U.S. each year.

CAUSE: Approximately 5-10 percent of cancer is associated with a

hereditary cause.

INHERITANCE: Varies depending on the gene and specific variant.

GENES TESTED: ALK, APC, ATM, ATR, AXIN2**, BAP1, BARD1, BMPR1A, BRCA1, BRCA2, BRIP1, CDH1, CDK4, CDKN1B, CDKN2A, CHEK2*, DICER1, EPCAM****, FH, FLCN, MAX, MEN1, MET, MLH1, MRE11, MSH2, MSH3**, MSH6, MUTYH, NBN, NF1**, NF2, NTHL1, PALB2, PHOX2B, PMS2, POLD1, POLE, PTEN, RAD51C, RAD51D, RB1, RECQL***, RET, SDHAF2, SDHB, SDHC*, SDHD*, SMAD4, SMARCA4**, SMARCB1, STK11, SUFU, TMEM127, TP53, TSC1, TSC2, VHL, WT1**

* - One or more exons are not covered by sequencing for the indicated gene; see limitations section below.
** - Deletion/duplication detection is not available for this gene.
*** - One or more exons are not covered by sequencing, and deletion/duplication detection is not available for this gene; see limitations section below.
**** - Deletion/duplication only; sequencing is not available for this gene.

METHODOLOGY: Targeted capture of all coding exons and exon-intron junctions of the targeted genes, including the PTEN promoter region, followed by massively parallel sequencing. Sanger sequencing was performed as necessary to fill in regions of low coverage and confirm reported variants. A custom tiled comparative genomic hybridization array (aCGH) was used to detect large deletions or duplications in the indicated subset of genes. Human genome build 19 (Hg 19) was used for data analysis. Analysis of the PMS2 gene was performed by bidirectional Sanger sequencing of coding regions and their respective exon intron boundaries as well as multiplex ligation-dependent probe amplification (MLPA). Targeted sequencing was performed for the CHEK2 c.1100delC variant.

ANALYTICAL SENSITIVITY: The analytical sensitivity of this test is approximately 99 percent for single nucleotide variants (SNVs) and greater than 93 percent for insertions/duplications/deletions from 1-10 base pairs in size. Variants greater than 10 base pairs may be detected, but the analytical sensitivity may be reduced.

LIMITATIONS: A negative result does not exclude a heritable form of cancer. This test only detects variants within the coding regions and intron-exon boundaries of the targeted genes. Regulatory region variants and deep intronic variants will not be identified and breakpoints of large deletions/duplications will not be determined. Single exon deletions/duplications or deletions/duplications less than 1kb may not be detected. Deletions/duplications/insertions of any size may not be detected by massive parallel sequencing. Diagnostic errors can occur due to rare sequence variations. In some cases, variants may not be identified due to technical limitations in the presence of pseudogenes, repetitive, or homologous regions. This assay may not detect low-level somatic variants associated with disease. Interpretation of this test result may be impacted if this patient has had an allogeneic stem cell transplantation. Non-coding transcripts were not analyzed.

The following regions are not sequenced due to technical limitations of the assay:
CHEK2(NM_001349956) exon(s) 4
CHEK2(NM_001005735) exon(s) 3
CHEK2(NM_007194) exon(s) 10,12,13,14,15
RECQL(NM_002907) exon(s) 14,15
SDHC(NM_001035511) exon(s) 5
SDHD(NM_001276506) exon(s) 4

Single exon deletions/duplications will not be called for the following exons:

APC(NM_001127511) 1;BAP1(NM_004656) 1;BARD1(NM_000465)
1;BMPR1A(NM_004329) 9;BRCA1(NM_007300) 13;CDH1(NM_004360)
1;CDKN2A(NM_000077) 2;CDKN2A(NM_058195) 2;CHEK2(NM_001005735)
3;CHEK2(NM_007194) 11,12,14,15;FH(NM_000143) 1; FLCN(NM_144997)
8;MAX(NM_001320415) 5;MAX(NM_145113) 5;MRE11(NM_005591)
2;MSH2(NM_000251) 1;MSH2(NM_001258281) 2;MSH6(NM_000179)
10;MUTYH(NM_001128425) 1;NF2(NM_000268) 7,13,16;NTHL1(NM_002528)
3,4,5,6;PALB2(NM_024675) 1;POLD1(NM_002691)
6,18,25;PTEN(NM_000314) 8,9;PTEN(NM_001304717)
1;RAD51D(NM_002878) 1;RB1(NM_000321) 1;RET(NM_020975)
1;SDHD(NM_001276506) 4;SMARCB1(NM_003073) 5;SUFU(NM_001178133)
11;SUFU(NM_016169) 1;TP53(NM_001126113) 10;TP53(NM_001126114)
10;TSC2(NM_000548) 17,29,41;VHL(NM_000551) 1

Test developed and characteristics determined by ARUP Laboratories. See Compliance Statement C: aruplab.com/CS

VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
Cancer Panel, Hereditary, Spcm	19-028-148011	1/28/2019 11:35:00 AM	2/2/2019 1:03:00 PM	3/15/2019 9:04:00 PM
Cancer Panel, Hereditary, Interp	19-028-148011	1/28/2019 11:35:00 AM	2/2/2019 1:03:00 PM	3/15/2019 9:04:00 PM

END OF CHART

H=High, L=Low, *=Abnormal, C=Critical