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

Physician: Doctor, Example

Patient: Patient, Example

DOB	6/18/1982
Gender:	Male
Patient Identifiers:	01234567890ABCD, 012345
Visit Number (FIN):	01234567890ABCD
Collection Date:	00/00/0000 00:00

Hereditary Gastrointestinal Cancer Panel, Sequencing and Deletion/Duplication

ARUP test code 2013449

Gastrointestinal Cancer Panel - Spcmn: Whole Blood

Gastrointestinal Cancer Panel - Interp: Negative

INDICATION FOR TESTING
Personal and family history of colorectal polyps.

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

INTERPRETATION
No pathogenic variants were identified by massively parallel sequencing of the coding regions and exon-intron boundaries of the genes tested. 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 gastrointestinal or other 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 reported.
Variants in the following region(s) may not be detected by NGS with sufficient confidence in this sample due to technical limitations; reportable variants are confirmed by Sanger sequencing:
NONE

This result has been reviewed and approved by [redacted]

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

CHARACTERISTICS: Pathogenic variants in multiple genes have been implicated in hereditary gastrointestinal (GI) cancer. Germline variants in genes associated with hereditary GI cancer may also confer risk for other non-GI cancers. Common signs of a hereditary GI cancer syndrome include a GI cancer diagnosed at a young age (less than 50 years old), multiple and/or rare tumors in a single individual, and a family history of the same or

related types of cancer. Lynch syndrome is caused by pathogenic variants in the MLH1, MSH2, MSH6, PMS2, and EPCAM genes. Individuals with Lynch syndrome are at an increased risk for colorectal, endometrial, stomach, ovarian, and other cancers.

EPIDEMIOLOGY: Approximately 300,000 new cases of cancer within the digestive organs are diagnosed in the U.S. per year. Prevalence of Lynch syndrome in the general population has been estimated at 1 in 440 individuals.

CAUSE: At least 2-4 percent of colorectal cancers are associated with a hereditary cause.

INHERITANCE: Autosomal dominant, with the exception of the SDHD gene which is autosomal dominant with parent-of-origin effect, and the MUTYH gene which is autosomal recessive but may also have autosomal dominant risks that are not well-defined. Additionally, some genes are also associated with autosomal recessive childhood cancer predisposition or other syndromes.

PENETRANCE: Varies, depending on the gene and specific variant.

GENES TESTED: APC, AXIN2**, BMPR1A, CDH1, CHEK2*, EPCAM****, MLH1, MSH2, MSH3**, MSH6, MUTYH, NTHL1, PMS2, POLD1, POLE, PTEN, SDHB, SDHC*, SDHD*, SMAD4, STK11, TP53

* - 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.
**** - 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
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;BMPR1A(NM_004329) 9;CDH1(NM_004360) 1;CHEK2(NM_001005735) 3;CHEK2(NM_007194) 11,12,14,15;MSH2(NM_000251) 1;MSH2(NM_001258281) 2;MSH6(NM_000179) 10;MUTYH(NM_001128425) 1;NTHL1(NM_002528) 3,4,5,6;POLD1(NM_002691) 6,18,25;PTEN(NM_000314) 8,9;PTEN(NM_001304717) 1;SDHD(NM_001276506) 4;TP53(NM_001126113) 10;TP53(NM_001126114) 10

This test was developed and its performance characteristics determined by ARUP Laboratories. It has not been cleared or approved by the US Food and Drug Administration. This test was performed in a CLIA certified laboratory and is intended for clinical purposes.

Counseling and informed consent are recommended for genetic testing. Consent forms are available online.

VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
Gastrointestinal Cancer Panel - Spcmn	22-035-139210	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Gastrointestinal Cancer Panel - Interp	22-035-139210	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00

END OF CHART

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