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

Physician: Doctor, Example

Patient: Patient, Example

DOB	12/31/1752
Gender:	Female
Patient Identifiers:	01234567890ABCD, 012345
Visit Number (FIN):	01234567890ABCD
Collection Date:	01/01/2017 12:34

HNPCC/Lynch Syndrome (MSH2) Sequencing and Deletion/Duplication

ARUP test code 0051654

MSH2 FGA Specimen	Whole Blood	
MSH2 Full Gene Analysis	**Positive**	*

H – high L – low * – abnormal C – critical

TEST PERFORMED - 0051654
TEST DESCRIPTION - HNPCC/Lynch Syndrome (MSH2) Sequencing and Deletion/Duplication
INDICATION FOR TEST - Not Provided

RESULT
One pathogenic variant was detected in the MSH2 gene.

DNA VARIANT(S)
Classification: Pathogenic
Gene: MSH2
Nucleic Acid Change: c.2038C>T; Heterozygous
Amino Acid Alteration: p.Arg680Ter

INTERPRETATION
One pathogenic variant, .2038C>T, p.Arg680Ter, was detected in the MSH2 gene by sequencing. No pathogenic MSH2 variants were detected by deletion/duplication analysis. This result is consistent with a diagnosis of Lynch syndrome/HNPCC. This individual's offspring have a 50 percent chance of inheriting the causative variant.

Evidence for variant classification(s): The MSH2 c.2038C>T, p.Arg680Ter variant (rs63749932) is a recurrent alteration in families with Lynch syndrome (Brieger 2011, Wijnen 1997, InSiGHT LOVD database). It is listed as pathogenic in ClinVar (Variation ID: 36572) by the International Society for Gastrointestinal Hereditary Tumours (Thompson 2014), and observed once in the Genome Aggregation Database general population database (1/246216 alleles). The variant introduces a premature termination codon, and predicted to result in a truncated protein or an absent transcript. Based on the above information, the variant is classified as pathogenic.

RECOMMENDATIONS
Genetic consultation is indicated, including a discussion of medical screening and management. Targeted sequencing for the identified pathogenic variant is recommended for at-risk adult family members (Familial Mutation, Targeted Sequencing, ARUP test code 2001961).

COMMENTS
Reference Sequence: GenBank # NM_000251.1 (MSH2)
Nucleotide numbering begins at the "A" of the ATG initiation codon.
Benign variants are not included in this report but are available upon request.

REFERENCES
InSiGHT LOVD database: http://chromium.lovd.nl/LOVD2/colon_cancer/variants.php?action=search_unique
Brieger A et al. Malignant fibrous histiocytoma is a rare Lynch syndrome-associated tumor in two German families. Fam Cancer. 2011; 10(3):591-5.
Thompson B et al. Application of a 5-tiered scheme for standardized classification of 2,360 unique mismatch repair gene variants in the InSiGHT locus-specific database. Nat Genet. 2014; 46(2):107-15.
Wijnen J et al. Hereditary nonpolyposis colorectal cancer families not complying with the Amsterdam criteria show extremely low frequency of mismatch-repair-gene mutations. Am J Hum Genet. 1997; 61(2):329-35.

This result has been reviewed and approved by Rong Mao, M.D.

BACKGROUND INFORMATION: HNPCC/Lynch Syndrome (MSH2)
Sequencing and Deletion/Duplication
CHARACTERISTICS: Increased risk of colorectal and extra-colonic cancers including endometrial, renal pelvis, ureter, ovary, stomach, small intestine and hepatobiliary tract.
INCIDENCE: 1-2 percent of colorectal cancer is due to mismatch repair gene mutations.
INHERITANCE: Autosomal dominant
PENETRANCE: 80 percent lifetime risk of colorectal cancer; 20-60 percent risk for endometrial cancer.
CAUSE: Pathogenic Germline MLH1 MSH2, MSH6, and PMS2 gene mutations.
METHODS: Bi-directional sequencing of MSH2 coding regions and intron-exon boundaries; multiplex ligation-dependent probe amplification (MLPA) to detect large MSH2 exonic deletions and EPCAM (TACSTD1) exon 9 deletions.
TEST LIMITATIONS: Diagnostic errors can occur due to rare sequence variations. The breakpoints of large/duplications will not be determined. Regulatory region mutations, deep intronic mutations and mutations in genes other than MSH2 will not be detected.

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

VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
MSH2 FGA Specimen	17-313-105391	11/9/2017 11:06:00 AM	11/13/2017 11:20:14 AM	11/13/2017 11:33:10 AM
MSH2 Full Gene Analysis	17-313-105391	11/9/2017 11:06:00 AM	11/13/2017 11:20:14 AM	11/13/2017 11:33:10 AM

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