ARUP LABORATORIES
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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	5/16/1990
Gender:	Male
Patient Identifiers:	01234567890ABCD, 012345
Visit Number (FIN):	01234567890ABCD
Collection Date:	00/00/0000 00:00

Exome Sequencing, Familial Control

ARUP test code 2006340

Exome Sequencing, Familial Control

Negative

Section 79-1 of New York State Civil Rights Law requires informed consent be obtained from patients (or their legal guardians) prior to pursuing genetic testing. These forms must be kept on file by the ordering physician. Consent forms for genetic testing are available at www.aruplab.com. Incidental findings are not reported unless clinically significant but are available upon request.

Result: No secondary pathogenic variants were detected.

Interpretation: The American College of Medical Genetics and Genomics (ACMG) recommends analysis of specific genes in all individuals undergoing exome sequencing even though these variants may not be related to the primary indication for testing. Please see the list of genes below for which ACMG recommends reporting disease-causing variants. Although no known secondary pathogenic variants were identified in the ACMG-recommended genes in this individual, this result does not exclude the possibility this individual may carry a pathogenic variant in one of these genes, or in another gene that is not included on this list. Note that single pathogenic variants in recessive ACMG genes are not reported. The genes on the ACMG-recommended list for reporting are evaluated to the extent that standard exome sequencing will allow, and the clinical significance of the variants detected are evaluated using evidence from current literature and variant databases.

Recommendation: Medical management should rely on clinical findings and family history. If there is clinical suspicion or family history of a genetic condition associated with one of the ACMG-recommended genes, additional targeted testing should be considered as exome sequencing will not identify all pathogenic variants in these genes.

This result has been reviewed and approved by [redacted]

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

BACKGROUND INFORMATION: Exome Sequencing, Familial Control

CHARACTERISTICS: DNA coding regions and intron/exon boundaries of the human exome are sequenced to identify the cause(s) of a disorder in a family member. The American College of Medical Genetics (ACMG) recommends analysis of the following genes for pathogenic mutations in all individuals undergoing exome sequencing:

GENES ASSOCIATED WITH AN INCREASED RISK FOR TUMORS/CANCER: hereditary breast and ovarian cancer (BRCA1, BRCA2), Li-Fraumeni syndrome (TP53), Peutz-Jeghers syndrome (STK11), Lynch syndrome (MLH1, MSH2, MSH6, PMS2), familial adenomatous polyposis (APC), MUTYH-associated polyposis, Von Hippel Lindau syndrome (VHL), multiple endocrine neoplasia type 1 (MEN1), multiple endocrine neoplasia type 2/familial medullary thyroid cancer (RET), PTEN hamartoma tumor syndrome (PTEN), retinoblastoma (RB1), hereditary paraganglioma-pheochromocytoma syndrome (SDHD, SDHAF2, SDHC, SDHB), tuberous sclerosis complex (TSC1, TSC2), WT1-related Wilms (WT1), neurofibromatosis type 2 (NF2). GENES ASSOCIATED WITH CARDIOVASCULAR (HEART) PROBLEMS: EDS IV (COL3A1), Marfan syndrome (FBN1), Loeys-Dietz syndrome (TGFBR1 and TGFBR2), familial thoracic aortic aneurysms and dissections (SMAD3, ACTA2, MYLK, MYH11), hypertrophic cardiomyopathy/dilated cardiomyopathy (MYBPC3, MYH7, TNNT2, TNNI3, TPM1, MYL3, ACTC1, PRKAG2, GLA ,MYL2, LMNA), catecholaminergic polymorphic ventricular tachycardia (RYR2), arrhythmogenic right ventricular cardiomyopathy (PKP2, DSP, DSC2, TMEM43, DSG2), Romano-Ward long QT syndromes types 1, 2, and 3, Brugada syndrome (KCNQ1, KCNH2, SCN5A), familial hypercholesterolemia (LDLR, APOB, PCSK9).

GENES INFLUENCING RESPONSE TO ANESTHESIA: malignant hyperthermia (RYR1, CACNA1S).

INHERITANCE: Varies depending on the specific gene and variant.

CLINICAL SENSITIVITY: Varies by gene.

METHODOLOGY: Targeted capture of all coding exons and exon-intron junctions of the targeted genes, followed by massively parallel sequencing. Sanger sequencing was performed as necessary to confirm reported variants. Human genome build 19 (Hg 19) was used for data analysis.

LIMITATIONS OF ANALYSIS: Not all pathogenic variants occur in the coding regions of genes. Some genes, or parts of genes, may not be adequately sequenced to allow for confident analysis. The following types of variants may not be detectable: those located in genes with corresponding pseudogenes, those in repetitive or high GC rich regions, large deletions / duplications / rearrangements, and mosaic mutations. Rare variants in probe hybridization sites may compromise analytical sensitivity. Mode of inheritance, reduced penetrance,and genetic heterogeneity could reduce the clinical sensitivity.

LIMITATIONS OF REPORTING: Only known pathogenic variants identified in genes on the ACMG-recommended panel are reported. Variants of unknown significance will not be reported. Single pathogenic variants in autosomal recessive genes will not be reported.

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

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VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
Exome Sequencing, Familial Control	19-137-104862	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00

END OF CHART

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