Client: ARUP Example Report Only
500 Chipeta Way
Salt Lake City, UT 84108
UNITED STATES

Physician: TEST, DR

Patient: LQT NGS, NEG

DOB
Sex: Female
Patient Identifiers: 41748
Visit Number (FIN): 42073
Collection Date: 8/17/2022 10:48

Long QT Panel, Sequencing and Deletion/Duplication

ARUP test code 3001603

Long QT Specimen	Whole Blood
Long QT Interp	Negative

INDICATION FOR TESTING
Prolonged QT interval

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. This result decreases the likelihood of, but does not exclude, a heritable form of long QT syndrome (LQTS). 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 of this individual should rely on clinical findings and family history. Genetic consultation is recommended.

COMMENTS
Likely benign and benign variants are not reported.
BACKGROUND INFORMATION: Long QT Panel, Sequencing and Deletion/Duplication
CHARACTERISTICS: Long QT syndrome (LQTS) is characterized by prolongation of the QTc interval and T-wave abnormalities on electrocardiogram that are associated with tachyarrhythmias, often torsade de pointes. Cardiac events including syncope, ventricular fibrillation, or sudden cardiac death may occur from infancy to middle age but are most common in preteens and young adults. Forms of LQTS associated with additional noncardiac features include Andersen-Tawil syndrome (muscle weakness and distinctive facial features), Timothy syndrome (cutaneous syndactyly, neurodevelopmental and facial features), and Jervell and Lange-Nielsen syndrome (congenital sensorineural hearing loss).

EPIDEMIOLOGY: Prevalence of congenital LQTS is approximately 1 in 2,500.

CAUSE: Pathogenic germline variants in genes associated with LQTS

INHERITANCE: Typically autosomal dominant with incomplete penetrance. Autosomal recessive inheritance for Jervell and Lange-Nielsen syndrome.

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

PENETRANCE: Variable, influenced by gene involved

CLINICAL SENSITIVITY: 60-75 percent

GENES TESTED: CACNA1C, CALM1*, CALM2, CALM3, KCNE1*, KCNE2*, KCNH2*, KCNJ2, KCNQ1, SCN5A, TRDN
*One or more exons are not covered by sequencing and/or deletion/duplication analysis for the indicated gene; see limitations section below.

METHODOLOGY: Probe hybridization-based 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 fill in regions of low coverage and to confirm reported variants that do not meet acceptable quality metrics. A proprietary bioinformatic algorithm was used to detect large (single exon-level or larger) deletions or duplications in the indicated genes. Large deletions/duplications confirmed using an orthogonal exon-level microarray. Human genome build 19 (Hg 19) was used for data analysis.

ANALYTICAL SENSITIVITY/SPECIFICITY: The analytical sensitivity is approximately 99 percent for single nucleotide variants (SNVs) and greater than 93 percent for insertions/duplications/deletions (indels) from 1-10 base pairs in size. Indels greater than 10 base pairs may be detected, but the analytical sensitivity may be reduced. Deletions of 2 exons or larger are detected with sensitivity greater than 97 percent; single exon deletions are detected with 62 percent sensitivity. Duplications of 3 exons or larger are detected at greater than 83 percent sensitivity. Specificity is greater than 99.9 percent for all variant classes.

LIMITATIONS: A negative result does not exclude a heritable form of LQTS. This test only detects variants within the coding regions and intron-exon boundaries of the targeted genes. Deletions/duplications/insertions of any size may not be detected by massively parallel sequencing. Regulatory region variants and deep intronic variants will not be identified. Precise breakpoints for large deletions or duplications are not determined in this assay and single exon deletions/duplications may not be detected based on the breakpoints of the rearrangement. The actual breakpoints for the deletion or duplication may extend beyond or be within the exon(s) reported. This test is not intended to detect duplications of 2 or fewer exons in size, though these may be identified. Single exon deletions are reported but called at a lower sensitivity. Diagnostic errors can occur due to rare sequence variations. In some cases, variants may not be identified due to technical limitations caused by the presence of pseudogenes, repetitive, or homologous regions. This test is not intended to detect low-level mosaic or somatic variants, gene conversion events, complex inversions, translocations, mitochondrial DNA (mtDNA) mutations, or repeat expansions. Interpretation of this test result may be impacted if this patient has had an allogeneic stem cell transplantation. Noncoding transcripts were not analyzed.

The following regions are not sequenced due to technical limitations of the assay:
CALM1 (NM_001363670) exon(s) 1

Single exon deletions/duplications will not be called for the following exons: KCNH2 (NM_000238, NM_172056) 6; KCNH2 (NM_001204798, NM_172057) 2; TRDN (NM_006073, NM_001251987, NM_001256020, NM_001256021, NM_001256022) 5; CALM1 (NM_001363670) 1
Duplications may not be called for the following genes: CAV3,

KCNE1, KCNE2

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
Long QT Specimen	22-229-104326	8/17/2022 10:48:00 AM	8/17/2022 10:48:47 AM	8/17/2022 10:54:00 AM
Long QT Interp	22-229-104326	8/17/2022 10:48:00 AM	8/17/2022 10:48:47 AM	8/17/2022 10:54:00 AM

END OF CHART

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