## Lab Dept: Anatomic Pathology

## Test Name: LONG QT SYNDROME PANEL, SEQUENCING AND DELETION/DUPLICATION

### *General Information*

**Lab Order Codes:** LQTS

**Synonyms:** Ventricular Fibrillation with Prolonged QT interval; Romano-Ward syndrome (RWS); Jervell and Lange-Nielsen syndrome (JLNS)

**CPT Codes:** 81403- Molecular pathology procedure, level 4 (KCNJ2 del/dup)
81404- Molecular pathology procedure, level 5 (CAV3 del/dup)
81406- Molecular pathology procedure, level 6 (KCNQ1 del/dup)
81414- Cardiac Ion del/dup (eg, KCNH2, SCN5A, KCNE1, KCNE2, CACNA1C, SCN4B, AKAP, SNTA1, ANK2); full sequence analysis

**Test Includes:** Sequencing of the entire coding regions of 17 genes: CALM1, CALM2, CALM3, KCNJ5, SCN5A, TRDN, KCNQ1, KCNH2, SCN5A, ANK2, KCNE1, KCNE2, KCNJ2, CACNA1C (through exon 44), CAV3, SCN4B, AKAP9 (only the KCNQ1 binding domains including the Ser1570 residue), and SNTA1.

### *Logistics*

**Test Indications:** Confirmation of a clinical diagnosis in symptomatic patients; Risk assessment for asymptomatic family members of a proband with LQTS; Differentiation of hereditary LQTS from acquired (non-genetic) causes of LQTS; Prenatal diagnosis in families with a known mutation.

Long QT syndrome (LQTS) is a cardiac disorder due to abnormal ion channel function characterized by prolongation of the QT interval on ECG. 75% of cases of LQTS are due to known genetic causes. It is associated with increased risk for syncope (unexplained fainting), ventricular arrhythmia and sudden cardiac death in young adults with normal heart structure.

LQTS is usually inherited in an autosomal dominant manner, and an affected individual with a disease-causing mutation has a 50% chance of transmitting this mutation to a child. Rarely, autosomal recessive inheritance has been described.

Reasons for referral:
1. Confirmation of a clinical diagnosis
2. Genetic counseling

**Lab Testing Sections:** Anatomic Pathology - Sendouts

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| **Referred to:** | GeneDx, Inc. (GDX: 727) |
| **Phone Numbers:** | MIN Lab: 612-813-6280 |
| | STP Lab: 651-220-6550 |
| **Test Availability:** | Daily, 24 hours (Preferred draws are Sunday - Thursday as specimens can only be received at the reference lab Monday - Friday. Specimens collected Friday or Saturday will be held for shipment on Monday.) |
| **Turnaround Time:** | 4 weeks |
| **Special Instructions:** | A signed consent form must be sent with any specimen. |

### *Specimen*

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| **Specimen Type:** | Whole blood |
| **Container:** | Lavender top (EDTA) tube |
| **Draw Volume:** | 2 - 5 mL blood |
| **Processed Volume:** | Same as Draw Volume |
| **Collection:** | Routine venipuncture, invert collection tube gently to mix |
| **Special Processing:** | Lab Staff: Do Not centrifuge. Blood specimen should remain in the original collection container. Store and ship at ambient temperature. Ship overnight at ambient temperature, using a cool pack in hot weather.<br>Note: Specimens may be stored at refrigerated temperatures for up to 7 days prior to shipping. |
| **Patient Preparation:** | None |
| **Sample Rejection:** | Mislabeled or unlabeled specimens |

### *Interpretive*

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| **Reference Range:** | No mutations detected. An interpretive report will be provided. |
| **Critical Values:** | N/A |

**Limitations:** Approximately 75% of individuals with a clinical diagnosis of idiopathic LATS are due to genetic causes. It is currently not known what percentage of these individuals would be expected to harbor a disease-causing mutation in the 17 genes tested for this panel. It is estimated that this panel would detect a disease-causing mutation in at least 70% of patients with LQTS. The technical sensitivity of this testing approach is estimated to be at 98% for mutations identifiable by sequence analysis. This sequencing test will not detect large chromosomal aberrations and deletions, insertions, or rearrangements greater than or equal to 5 base pairs. Deletions or duplications of less than 500 bp are not reliably detected by array CGH. LQTS ExonArray DX analysis is specifically designed to detect partial or whole deletion/duplications of the 17 genes on the LQTS panel. Approximately 10% of patients with LQTS and no sequence abnormality in one of the common LQTS gene have been found to have a large deletion or duplication involving one of those genes.

**Methodology:** Using genomic DNA, the entire coding region of 17 genes are sequenced using a novel sequencing-by-synthesis process that allows sequencing a large number of amplicons in parallel. For analysis, DNA sequence is assembled and compared to the published genomic reference sequences. The presence of any potentially disease-associated sequence variant(s) is confirmed by conventional dideoxy DNA sequence analysis. A reference library of up to 800 alleles is used to evaluate the frequency of novel sequence variants if indicated. Concurrent deletion/duplication testing is performed using exon-level oligo array CGH. Data analysis is performed using gene-specific filtering. If appropriate, testing of one affected relative or, if not available, of both biological parents, is performed to clarify variants of unknown significance at no additional charge.

**References:**

GeneDx, Inc. April 2017