Department of Medical and Molecular Genetics
Division of Diagnostic Genomics

Laboratory Test Directory

**KCNQ1 Sequencing**

**CPT Code(s):** 81406

**Service Code (IU Health):** 53025532

**Ordering Recommendation:** Information about the gene sequence may be used as an aid to clinicians in confirming the clinical diagnosis in symptomatic subjects, determining the risk assessment for asymptomatic first degree relatives, and establishing the most appropriate therapeutic strategy and treatment

**Synonyms:** KCNQ1, LQT1, JLNS1, IKS, KvLQT1, Kv7.1, ATFB3, SQTS2

**Methodology:** Sanger sequencing analysis

**Performed:** weekly

**Reported:** 14-21 days

**Specimen Requirements**

**Patient Preparation:** None required for whole blood

**Collect:** Preferred: Lavender (EDTA); Acceptable: Yellow (ACD Solution A or B), DNA extracted from leukocytes, muscle, or fibroblasts eluted in sterile DNase/RNAse free water or TE and with A260:A280 ratio should of 1.8-2.0

**Specimen Volume/Amount:** Blood: 7mL whole blood (minimum 2mL), Extracted DNA: 3 micrograms

**Storage/Transport:** Refrigerated/Room temperature

**Unacceptable Conditions:** Grossly hemolyzed or clotted

**Remarks:**

**Stability:** 2 weeks refrigerated; 1 month frozen

**Reference Interval:** N/A
Interpretive Data

**Characteristics:** Pathogenic variants in the *KCNQ1* gene cause abnormal function of the alpha subunit of the voltage-gated potassium channel Kv7.1, leading to various forms of cardiac rhythm disturbances in some cases associated with congenital profound bilateral sensorineural hearing loss.

**Inheritance:** Autosomal dominant or autosomal recessive.

**Cause:** *KCNQ1* pathogenic variants such as, but not limited to missense, nonsense, splicing, and insertions and deletions.

**Incidence of long QT syndrome (LQTS):** LQTS is a pan-ethnic disease with a worldwide incidence of the Romano-Ward syndrome (RWS), the autosomal dominant form of LQTS being 1:7,000 people, while the worldwide incidence of Jervell and Lange-Nielsen syndrome (JLNS), the autosomal recessive form of LQTS is 6:1,000,000 people.

**Penetration:** Incomplete.

**Clinical sensitivity:** Pathogenic variants in the *KCNQ1* gene have been identified in approximately 90% patients with JLNS, an autosomal recessive form of LQTS associated with congenital profound bilateral sensorineural hearing loss, and in approximately 46% of RWS, the autosomal dominant forms of LQTS. In addition, pathogenic variants in the *KCNQ1* gene have been identified also in patients with Atrial Fibrillation (AF) and Short QT Syndrome (SQTS).

**Analytical sensitivity and specificity:** 99%

**Limitations:** Only the coding and immediate flanking regions of the *KCNQ1* gene are analyzed by DNA sequencing. Changes in the promoter and other non-coding regions are not detected by this assay. In addition, the presence of a large intragenic deletion of the *KCNQ1* gene (such as the deletion of an exon or multiple exons) will not be detected by sequence analysis. Although rare, false positive or false negative results may occur. All results should be interpreted in context of clinical findings, relevant history, and other laboratory data.

**References:** Genetic Testing Registry, Gene Reviews, OMIM, ACC/AHA/HRS Guidelines.