CARDIO Panel Sequencing

**CPT Code(s):** 81406

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

**Ordering Recommendation:** Information about the *KCNQ1, KCNH2, SCN5A, KCNE1, KCNE2, KCNA5, LMNA,* and *KCNJ2* genes 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, KCNH2, SCN5A, KCNE1, KCNE2, KCNA5, LMNA, KCNJ2, LQTS, SQTS, ATF, arrhythmias, conduction defects, long QT syndrome (LQTS), Brugada syndrome (BRS), dilated cardiomyopathy with cardiac conduction disease (DCM), familial atrial fibrillation (AF), Andersen-Tawil syndrome (ATS), sick sinus syndrome (SSS)*

**Methodology:** Sanger sequencing analysis

**Performed:** weekly

**Reported:** 21-28 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, KCNH2, SCN5A, KCNE1, KCNE2, KCNA5, LMNA, and KCNJ2 genes cause abnormal function of cardiac voltage-gated potassium and sodium channels, channel-interacting proteins, and proteins of the nuclear lamina, leading to various forms of primary cardiac muscle diseases, cardiac rhythm disturbances and complex cardiovascular syndromes such as but not limited to long QT syndrome (LQTS), Brugada syndrome (BRS), dilated cardiomyopathy with cardiac conduction disease (DCM), familial atrial fibrillation (AF), Andersen-Tawil syndrome (ATS), and sick sinus syndrome (SSS)

Inheritance: autosomal dominant or autosomal recessive

Cause: Pathogenic variants such as, but not limited to missense, nonsense, splicing, and insertions and deletions

Incidence of CARDIO Panel-related disorders: BRS, LQTS, DCM, AF, ATS, and SSS are pan ethnic diseases with a worldwide incidence of 5:10,000 (BRS) people, 1:7,000 (LQTS - autosomal dominant), est. 1:675 (DCM), 1:168 (AF) people, and 1:600 (SSS) people respectively. The worldwide incidence of ATS is unknown

Penetrance: Incomplete

Clinical sensitivity: Pathogenic variants in the genes of the CARDIO panel (KCNQ1, KCNH2, SCN5A, KCNE1, KCNE2, KCNA5, LMNA, and KCNJ2) have been identified in approximately 75% patients with a definitive diagnosis of long QT syndrome (CARDIO), 99% patients with Jervell and Lange-Nielsen syndrome (JLNS), 60% patients with Andersen-Tawil syndrome (ATS), 8-10% patients with Dilated Cardiomyopathy (DCM) with or without Atroventricular Block (AVB) along with other forms of arrhythmias such as Atrial Fibrillation (AF) and Short QT Syndrome (SQTS). In addition, pathogenic variants in the KCNQ1, KCNH2, SCN5A, KCNE1, KCNE2, KCNA5, LMNA, and KCNJ2 genes 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, KCNH2, SCN5A, KCNE1, KCNE2, KCNA5, LMNA, and KCNJ2 genes 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, KCNH2, SCN5A, KCNE1, KCNE2, KCNA5, LMNA, and KCNJ2 genes (such as the deletion of an exon or multiple exons) will not be detected by sequence analysis. Although rare, false positive or false negative
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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