USEFUL FOR

- Providing a genetic evaluation for patients with a personal or family history suggestive of Brugada syndrome
- Establishing a diagnosis of a Brugada syndrome, in some cases, allowing for appropriate management and surveillance for disease features based on the gene involved
- Identifying mutations within genes known to be associated with increased risk for disease features and allowing for predictive testing of at-risk family members

GENETICS TEST INFORMATION

This test includes next-generation sequencing and supplemental Sanger sequencing to evaluate the genes tested on this panel.

Prior Authorization is available for this assay; see Special Instructions.

Targeted testing for familial variants (also called site-specific or known mutation testing) is available for all genes on this panel; however, the test code varies based on the gene requested. Contact Mayo Medical Laboratories to confirm the appropriate test code for targeted testing of additional family members.

CLINICAL INFORMATION

Brugada syndrome (BrS) is a genetic cardiac disorder characterized by ST segment elevation in leads V1-V3 on electrocardiography (EKG) with a high risk for ventricular arrhythmias that can lead to sudden cardiac death. BrS is inherited in an autosomal dominant manner and is caused by pathogenic variants in genes that encode cardiac ion channels. The diagnosis of BrS is established based on the characteristic EKG abnormality along with personal and family health history, and also requires exclusion of other causes including cardiac structural abnormalities, medications, and electrolyte imbalances.

BrS has also been called sudden unexplained nocturnal death syndrome (SUNDS) due to the tendency for syncope and sudden cardiac death to occur at rest or during sleep. The most common presentation of BrS is a male in his 40s with a history of syncopal episodes and malignant arrhythmias. However, presentation may occur at any age including infancy, where BrS may present as SIDS (sudden infant death syndrome). Published studies indicate that BrS is responsible for 4%–12% of unexpected sudden deaths and for up to 20% of all sudden death in individuals with a structurally normal heart.
The prevalence of BrS in the general population is difficult to determine due to the challenges of diagnosing the condition. In Southeast Asia where SUNDS is endemic, the prevalence of BrS is estimated to be 1 in 2,000. Of note, men are 8 to 10 times more likely to express symptoms of BrS, but the disease affects females as well and both sexes are at risk for ventricular arrhythmia and sudden death.

Approximately 25% to 30% of BrS is accounted for by pathogenic variants in the genes known to cause the disorder, with the majority of cases attributed to the SCN5A gene. Although the majority of pathogenic variants identified to date have been detected by sequence analysis, large deletions in the SCN5A, SCN3B, CACNA1C, and KCNE3 genes have been reported in BrS. Genetic testing for BrS is supported by multiple consensus statements to confirm the diagnosis and identify at-risk family members. This is particularly important because the majority of patients with BrS are asymptomatic, but asymptomatic individuals may still be at increased risk for cardiac events. Pre- and post-test genetic counseling is an important factor in the diagnosis and management of BrS and is supported by expert consensus statements.

**Genes included in the Brugada Syndrome Multi-Gene Panel:**
CACNA1C, CACNA2D1, GPD1L, KCNE3, KCNJ8, SCN3B, CACNB2, SCN1B, and SCN5A.

**SPECIMEN REQUIRED**

**Specimen Type**
Whole Blood EDTA

**Container/Tube**
Lavender top (EDTA)

**Specimen Volume**
3 mL

**INTERPRETATION**

Evaluation and categorization of variants is performed using the most recent published American College of Medical Genetics recommendations as a guideline. Variants are classified based on known, predicted, or possible pathogenicity and reported with interpretive comments detailing their potential or known significance.

Multiple in silico evaluation tools may be used to assist in the interpretation of these results. The accuracy of predictions made by in silico evaluation tools is highly dependent upon the data available for a given gene, and predictions made by these tools may change over time. Results from in silico evaluation tools should be interpreted with caution and professional clinical judgment.