Test Definition: BRGGP

Brugada Syndrome Multi-Gene Panel,B

Overview

Useful For

Providing a genetic evaluation for patients with a personal or family history suggestive of Brugada syndrome (BrS)

Establishing a diagnosis of a BrS, in some cases, allowing for appropriate management and surveillance for disease features based on the gene involved

Identifying variants 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.

Highlights

This test uses next generation sequencing to test for variants in the *CACNA1C, CACNA2D1, GPD1L, KCNE3, KCNJ8, SCN3B, CACNB2, SCN1B,* and *SCN5A* genes.

This test may aid in the diagnosis of Brugada syndrome.

Identification of a pathogenic variant may assist with prognosis, clinical management, familial screening, and genetic counseling.

Special Instructions

- Informed Consent for Genetic Testing
- Brugada Syndrome Multi-Gene Panel Prior Authorization Ordering Instructions
- Hereditary Cardiomyopathies and Arrhythmias: Patient Information
- Informed Consent for Genetic Testing (Spanish)

Method Name

Custom Sequence Capture and Targeted Next Generation Sequencing Followed by Polymerase Chain Reaction (PCR) and Supplemental Sanger Sequencing

NY State Available

Yes

Specimen

Specimen Type

Whole Blood EDTA

Advisory Information

Targeted testing for familial variants (also called site-specific or known mutation testing) is available for the genes on this panel. See:

-KVAR1 / Known Variant Analysis-1 Variant, Varies

-KVAR2 / Known Variant Analysis-2 Variants, Varies

-KVAR3 / Known Variant Analysis-3+ Variants, Varies

Call 800-533-1710 to confirm the appropriate test for targeted testing.

Necessary Information

Include physician name and phone number with the specimen.

Specimen Required

Container/Tube: Lavender top (EDTA)

Specimen Volume: 3 mL

Collection Instructions: Send specimen in original tube.

Additional Information: Prior Authorization is available for this test. **Submit the required form with the specimen.**

Forms

1. Hereditary Cardiomyopathies and Arrhythmias: Patient Information **(T725) is required.** See Special Instructions.

2. **New York Clients-Informed consent is required.** Document on the request form or electronic order that a copy is on file. The following documents are available in Special Instructions:

-Informed Consent for Genetic Testing (T576)

-Informed Consent for Genetic Testing-Spanish (T826)

3. Brugada Syndrome Multi-Gene Panel Prior Authorization Ordering Instructions in Special Instructions

4. If not ordering electronically, complete, print, and send a Cardiovascular Test Request (T724) with the specimen.

Specimen Minimum Volume

1 mL

Reject Due To

All specimens will be evaluated at Mayo Clinic Laboratories for test suitability.

Specimen Stability Information

Specimen Type	Temperature	Time
Whole Blood EDTA	Ambient (preferred)	
	Refrigerated	

Clinical and Interpretive

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% to 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 posttest genetic counseling is an important factor in the diagnosis and management of BrS and is supported by expert consensus statements.

Reference Values

An interpretive report will be provided.

Interpretation

Evaluation and categorization of variants is performed using the most recent published American College of Medical Genetics and Genomics (ACMG) 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.

Cautions

Clinical Correlations:

Some individuals who have involvement of 1 or more of the genes on the panel may have a variant that is not identified by the methods performed (eg, promoter variants, deep intronic variants). The absence of a variant, therefore, does not eliminate the possibility of Brugada syndrome (BrS) or a related disorder.

Test results should be interpreted in context of clinical findings, family history, and other laboratory data. Misinterpretation of results may occur if the information provided is inaccurate or incomplete.

If testing was performed because of a family history of BrS or a related disorder, it is often useful to first test an

affected family member. Identification of a pathogenic variant in an affected individual allows for more informative testing of at-risk individuals.

Technical Limitations:

Next-generation sequencing may not detect all types of genetic variants. Additionally, rare polymorphisms may be present that could lead to false-negative or false-positive results. If results do not match clinical findings, consider alternative methods for analyzing these genes, such as Sanger sequencing or large deletion/duplication analysis. If the patient has had an allogeneic blood or marrow transplant or a recent (ie, less than 6 weeks from time of sample collection) heterologous blood transfusion, results may be inaccurate due to the presence of donor DNA.

Reclassification of Variants Policy:

At this time, it is not standard practice for the laboratory to systematically review likely pathogenic variants or variants of uncertain significance that are detected and reported. The laboratory encourages health care providers to contact the laboratory at any time to learn how the status of a particular variant may have changed over time. Consultation with a genetics professional should be considered for interpretation of this result.

A list of benign and likely benign variants detected for this patient is available from the lab upon request.

Contact the laboratory if additional information is required regarding the transcript or human genome assembly used for the analysis of this patient's results.

Clinical Reference

1. Brugada R, Campuzano O, Brugada P, et al: Brugada Syndrome. In GeneReviews. Edited by RA Pagon, MP Adam, HH Ardinger, et al. University of Washington, Seattle. Seattle, WA. 1993-2018. Updated 2016 Nov 17. Accessed June 2018. Available at www.ncbi.nlm.nih.gov/books/NBK1517/

2. Priori SG, Wilde AA, Horie M, et al: HRS/EHRA/APHRS expert consensus statement on the diagnosis and management of patients with inherited primary arrhythmia syndromes. Heart Rhythm 2013;10:12:1932-1963

3. Ackerman MJ, Priori SG, Willems S, et al: HRS/EHRA expert consensus statement on the state of genetic testing for the channelopathies and cardiomyopathies. Heart Rhythm 2011;8:1308-1339

4. Neilsen MW, Holst AG, Olesen SP, Olesen MS: The genetic component of Brugada syndrome. Front Physiol 2013;4:179:1-11

Performance

Method Description

Next-generation sequencing (NGS) is performed using an Illumina instrument with paired-end reads. The DNA is prepared for NGS using a custom Agilent SureSelect Target Enrichment System. Data is analyzed with a bioinformatics software pipeline. Supplemental and confirmatory Sanger sequencing are performed when necessary.(Unpublished Mayo method)

The following genes are evaluated in this multigene panel: *CACNA1C, CACNA2D1, GPD1L, KCNE3, KCNJ8, SCN3B, CACNB2, SCN1B*, and *SCN5A.*

PDF Report

No

Day(s) and Time(s) Test Performed

Wednesday; Varies

Analytic Time

4 weeks after prior authorization approved

Maximum Laboratory Time

6 weeks

Specimen Retention Time

Extracted DNA: 2 months

Performing Laboratory Location

Rochester

Fees and Codes

Fees

- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their Regional Manager. For assistance, contact Customer Service.

Test Classification

This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the U.S. Food and Drug Administration.

CPT Code Information

81479

81406

81404

81407

81479 (if appropriate for government payers)

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
BRGGP	Brugada Syndrome Multi-Gene Panel,B	In Process

Result ID	Test Result Name	Result LOINC Value
36831	Gene(s) Evaluated	36908-2
36832	Result Summary	50397-9
36833	Result Details	82939-0

Result ID	Test Result Name	Result LOINC Value
36834	Interpretation	69047-9
36959	Additional Information	48767-8
36960	Method	49549-9
36961	Disclaimer	62364-5
36835	Reviewed by	18771-6

Prior Authorization

Insurance preauthorization is available for this testing; forms are available in Special Instructions.

Patient financial assistance may be available to those who qualify.Patients who receive a bill from Mayo Clinic Laboratories will receive information on eligibility and how to apply.