

Overview

Useful For

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

Establishing a diagnosis of Brugada syndrome

Reflex Tests

| Test Id | Reporting Name | Available Separately | Always Performed |
|---------|---------------------------------------|----------------------|------------------|
| CULAF | Amniotic Fluid Culture/Genetic Test | Yes | No |
| _STR1 | Comp Analysis using STR (Bill only) | No, (Bill only) | No |
| _STR2 | Add'l comp analysis w/STR (Bill Only) | No, (Bill only) | No |
| CULFB | Fibroblast Culture for Genetic Test | Yes | No |
| MATCC | Maternal Cell Contamination, B | Yes | No |

Genetics Test Information

This test utilizes next-generation sequencing to detect single nucleotide and copy number variants in the *SCN5A* gene associated with Brugada syndrome. See Method Description for additional details.

Identification of a disease-causing variant may assist with diagnosis, prognosis, clinical management, familial screening, and genetic counseling for Brugada syndrome.

[Prior Authorization](#) is available for this assay.

Testing Algorithm

For skin biopsy or cultured fibroblast specimens, fibroblast culture testing will be performed at an additional charge. If viable cells are not obtained, the client will be notified.

Special Instructions

- [Informed Consent for Genetic Testing](#)
- [Hereditary Cardiomyopathies and Arrhythmias: Patient Information](#)
- [Informed Consent for Genetic Testing \(Spanish\)](#)
- [Brugada Syndrome Test \(SCN5A\) Prior Authorization Ordering Instructions](#)

Method Name

Sequence Capture and Targeted Next-Generation Sequencing followed by Polymerase Chain Reaction (PCR) and Sanger

Sequencing.

NY State Available

Yes

Specimen**Specimen Type**

Varies

Ordering Guidance

This single gene test is intended for genetic screening for and diagnosis of Brugada syndrome. For comprehensive inherited cardiac arrhythmia genetic testing, order CARGG / Comprehensive Arrhythmia Gene Panel, Varies.

Testing for *SCN5A* as part of a customized panel is available. For more information see CGPH / Custom Gene Panel, Hereditary, Next-Generation Sequencing, Varies.

Targeted testing for familial variants (also called site-specific or known mutations testing) is available for variants identified in the *SCN5A* gene. See FMTT / Familial Variant, Targeted Testing, Varies. To obtain more information about this testing option, call 800-533-1710.

Necessary Information

[Prior Authorization](#) is available, **but not required**, for this test. If proceeding with the prior authorization process, submit the required form with the specimen.

Specimen Required

Patient Preparation: A previous bone marrow transplant from an allogeneic donor will interfere with testing. For instructions for testing patients who have received a bone marrow transplant, call 800-533-1710.

Submit only 1 of the following specimens:

Specimen Type: Whole blood

Container/Tube:

Preferred: Lavender top (EDTA) or yellow top (ACD)

Acceptable: None

Specimen Volume: 3 mL

Collection Instructions:

1. Invert several times to mix blood.
2. Send whole blood specimen in original tube. **Do not aliquot.**

Specimen Stability Information: Ambient (preferred) 4 days/Refrigerated 4 days/Frozen 4 days

Additional Information:

1. Specimens are preferred to be received within 4 days of collection. Extraction will be attempted for specimens

received after 4 days, and DNA yield will be evaluated to determine if testing may proceed.

2. To ensure minimum volume and concentration of DNA is met, the preferred volume of blood must be submitted.

Testing may be canceled if DNA requirements are inadequate.

Specimen Type: Cord blood

Container/Tube:

Preferred: Lavender top (EDTA) or yellow top (ACD)

Acceptable: Green top (Sodium heparin)

Specimen Volume: 3 mL

Collection Instructions:

1. Invert several times to mix blood.

2. Send specimen in original tube. **Do not aliquot.**

Specimen Stability Information: Ambient (preferred) 4 days/Refrigerated 4 days/Frozen 4 days

Additional Information:

1. Specimens are preferred to be received within 4 days of collection. Extraction will be attempted for specimens received after 4 days, and DNA yield will be evaluated to determine if testing may proceed.

2. To ensure minimum volume and concentration of DNA is met, the preferred volume of blood must be submitted.

Testing may be canceled if DNA requirements are inadequate.

3. While a properly collected cord blood sample may not be at risk for maternal cell contamination, unanticipated complications may occur during collection. Therefore, maternal cell contamination studies are recommended to ensure the test results reflect that of the patient tested and are available at an additional charge. Order MATCC / Maternal Cell Contamination, Molecular Analysis, Varies on the maternal specimen.

Specimen Type: Saliva

Patient Preparation: Patient should not eat, drink, smoke, or chew gum 30 minutes prior to collection.

Supplies: Saliva Collection Kit (T786)

Specimen Volume: 1 Swab

Collection Instructions: Collect and send specimen per kit instructions.

Specimen Stability Information: Ambient (preferred) 30 days/Refrigerated 30 days

Additional information: Saliva specimens are acceptable but not recommended. Due to lower quantity/quality of DNA yielded from saliva, some aspects of the test may not perform as well as DNA extracted from a whole blood sample.

When applicable, specific gene regions that were unable to be interrogated will be noted in the report. Alternatively, additional specimen may be required to complete testing.

Specimen Type: Tissue biopsy

Supplies: Hank's Solution (T132)

Container/Tube: Sterile container with sterile Hank's balanced salt solution, Ringer's solution, or normal saline

Specimen Volume: 0.5 to 3 cm(3) or larger

Specimen Stability Information: Ambient (preferred) <24 hours/Refrigerated <24 hours

Additional Information:

1. Specimens are preferred to be received within 24 hours of collection. Culture and/or extraction will be attempted for specimens received after 24 hours and will be evaluated to determine if testing may proceed.

2. A separate culture charge will be assessed under CULFB / Fibroblast Culture for Biochemical or Molecular Testing. An

additional 3 to 4 weeks are required to culture fibroblasts before genetic testing can occur.

Specimen Type: Cultured fibroblasts

Source: Skin

Container/Tube: T-25 flask

Specimen Volume: 2 Flasks

Collection Instructions: Submit confluent cultured fibroblast cells from a skin biopsy. Cultured cells from a prenatal specimen will not be accepted.

Specimen Stability Information: Ambient (preferred) <24 hours/Refrigerated <24 hours

Additional Information:

1. Specimens are preferred to be received within 24 hours of collection. Culture and/or extraction will be attempted for specimens received after 24 hours and will be evaluated to determine if testing may proceed.
2. A separate culture charge will be assessed under CULFB / Fibroblast Culture for Biochemical or Molecular Testing. An additional 3 to 4 weeks are required to culture fibroblasts before genetic testing can occur

Specimen Type: Blood spot

Supplies: Card-Blood Spot Collection (Filter Paper) (T493)

Container/Tube:

Preferred: Collection card (Whatman Protein Saver 903 Paper)

Acceptable: PerkinElmer 226 filter paper or blood spot collection card

Specimen Volume: 2 to 5 Blood spots

Collection Instructions:

1. An alternative blood collection option for a patient older than 1 year is a fingerstick. For detailed instructions, see [How to Collect a Dried Blood Spot Sample](#).
Samples.
2. Let blood dry on the filter paper at ambient temperature in a horizontal position for a minimum of 3 hours.
3. Do not expose specimen to heat or direct sunlight.
4. Do not stack wet specimens.
5. Keep specimen dry.

Send Ambient (preferred)/Refrigerated

Additional Information:

1. Blood spot specimens are acceptable but not recommended. Due to lower quantity/quality of DNA yielded from blood spots, some aspects of the test may not perform as well as DNA extracted from a whole blood sample. When applicable, specific gene regions that were unable to be interrogated will be noted in the report. Alternatively, additional specimen may be required to complete testing.
2. Due to lower concentration of DNA yielded from blood spot, it is possible that additional specimen may be required to complete testing.
3. For collection instructions, see [Blood Spot Collection Instructions](#).
4. For collection instructions in Spanish, see [Blood Spot Collection Card-Spanish Instructions](#) (T777).
5. For collection instructions in Chinese, see [Blood Spot Collection Card-Chinese Instructions](#) (T800).

Specimen Type: Extracted DNA

Container/Tube:

Preferred: Screw Cap Micro Tube, 2mL with skirted conical base

Acceptable: Matrix tube, 1mL

Collection Instructions:

- 1. The preferred volume is at least 100 mL at a concentration of 75 ng/mL.
- 2. Include concentration and volume on tube.

Specimen Stability Information: Frozen (preferred) 1 year/Ambient/Refrigerated

Additional Information: DNA must be extracted in a CLIA-certified laboratory or equivalent and must be extracted from a specimen type listed as acceptable for this test (including applicable anticoagulants). Our laboratory has experience with Chemagic, Puregene, Autopure, MagnaPure, and EZ1 extraction platforms and cannot guarantee that all extraction methods are compatible with this test. If testing fails, one repeat will be attempted, and if unsuccessful, the test will be reported as failed and a charge will be applied. If applicable, specific gene regions that were unable to be interrogated due to DNA quality will be noted in the report.

Forms

- 1. **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:
[-Informed Consent for Genetic Testing \(T576\)](#)
[-Informed Consent for Genetic Testing \(Spanish\) \(T826\)](#)
- 2. [Hereditary Cardiomyopathies and Arrhythmias: Patient Information \(T725\)](#)
- 3. If not ordering electronically, complete, print, and send a [Cardiovascular Test Request Form \(T724\)](#) with the specimen.
- 4. [Brugada Syndrome Test \(SCN5A\) Prior Authorization Ordering Instructions](#)

Specimen Minimum Volume

See Specimen Required

Reject Due To

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

Specimen Stability Information

| Specimen Type | Temperature | Time | Special Container |
|---------------|-------------|------|-------------------|
| Varies | Varies | | |

Clinical & Interpretive

Clinical Information

Brugada syndrome (BrS) is a genetic cardiac disorder characterized by ST segment elevation in leads V1-V2 on electrocardiography (ECG) occurring spontaneously or after administration of sodium-channel blockers.(1) BrS leads to a high risk for ventricular arrhythmias, which can result in sudden cardiac arrest and sudden cardiac death including sudden unexpected nocturnal death syndrome and sudden infant death syndrome.(2) The diagnosis of BrS is established based on the characteristic ECG abnormality along with personal and family health history and requires exclusion of other causes including cardiac structural abnormalities, medications, and electrolyte imbalances.(2)

Brugada syndrome has an estimated prevalence of 1:2000 to 1:5000.(1) Currently, BrS is definitively associated with

gain-of-function variants in the *SCN5A* gene⁽³⁾ and the condition follows an autosomal dominant pattern of inheritance. Approximately 20% of individuals meeting clinical diagnostic criteria for BrS are found to carry a causative variant in the *SCN5A* gene.⁽³⁾ While variants in other genes have been reported in association with BrS, current evidence is not sufficient to define the role of these genes in BrS.⁽³⁾

Reference Values

An interpretive report will be provided.

Interpretation

All detected variants are evaluated according to American College of Medical Genetics and Genomics recommendations.⁽⁴⁾ Variants are classified based on known, predicted, or possible pathogenicity and reported with interpretive comments detailing their potential or known significance.

Cautions

Clinical Correlations:

Test results should be interpreted in the 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 clinically significant family history, it is often useful to first test an affected family member. Detection of a reportable variant in an affected family member would allow for more informative testing of at-risk individuals.

To discuss the availability of additional testing options or for assistance in the interpretation of these results, contact the Mayo Clinic Laboratories genetic counselors at 800-533-1710.

Technical Limitations:

Next-generation sequencing may not detect all types of genomic variants. In rare cases, false-negative or false-positive results may occur. The depth of coverage may be variable for some target regions; assay performance below the minimum acceptable criteria or for failed regions will be noted. Given these limitations, negative results do not rule out the diagnosis of a genetic disorder. If a specific clinical disorder is suspected, evaluation by alternative methods can be considered.

There may be regions of genes that cannot be effectively evaluated by sequencing or deletion and duplication analysis as a result of technical limitations of the assay, including regions of homology, high guanine-cytosine (GC) content, and repetitive sequences. Confirmation of select reportable variants will be performed by alternate methodologies based on internal laboratory criteria.

This test is validated to detect 95% of deletions up to 75 base pairs (bp) and insertions up to 47 bp. Deletions-insertions (delins) of 40 or more bp, including mobile element insertions, may be less reliably detected than smaller delins.

Deletion/Duplication Analysis:

This analysis targets single and multi-exon deletions/duplications; however, in some instances single exon resolution cannot be achieved due to isolated reduction in sequence coverage or inherent genomic complexity. Balanced structural rearrangements (such as translocations and inversions) may not be detected.

This test is not designed to detect low levels of mosaicism or to differentiate between somatic mutations and germline variants. If there is a possibility that any detected variant is somatic, additional testing may be necessary to clarify the significance of results.

For detailed information regarding gene specific performance and technical limitations, see Method Description or contact a laboratory genetic counselor.

If the patient has had an allogeneic hematopoietic stem cell transplant or a recent blood transfusion, results may be inaccurate due to the presence of donor DNA. Call Mayo Clinic Laboratories for instructions for testing patients who have received a bone marrow transplant.

Reclassification of Variants:

Currently, it is not standard practice for the laboratory to systematically review previously classified variants on a regular basis. The laboratory encourages healthcare professionals to contact the laboratory at any time to learn how the classification of a particular variant may have changed over time.

Variant Evaluation:

Evaluation and categorization of variants are performed using published American College of Medical Genetics and Genomics and the Association for Molecular Pathology recommendations as a guideline.⁽⁴⁾ Other gene-specific guidelines may also be considered. Variants are classified based on known, predicted, or possible pathogenicity and reported with interpretive comments detailing their potential or known significance. Variants classified as benign or likely benign are not reported.

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 periodic updates to these tools may cause predictions to change over time. Results from in silico evaluation tools should be interpreted with caution and professional clinical judgment.

Rarely, incidental or secondary findings may implicate another predisposition or presence of active disease. Incidental findings may include, but are not limited to, results related to the sex chromosomes. These findings will be carefully reviewed to determine whether they will be reported.

Clinical Reference

1. Brugada J, Campuzano O, Arbelo E, Sarquella-Brugada G, Brugada R. Present status of Brugada syndrome: JACC state-of-the-art review. *J Am Coll Cardiol*. 2018;72(9):1046-1059. doi:10.1016/j.jacc.2018.06.037
2. Brugada R, Campuzano O, Sarquella-Brugada G, Brugada P, Brugada J, Hong K. Brugada syndrome. In: Adam MP, Feldman J, Mirzaa GM, et al, eds. *GeneReviews* [Internet]. University of Washington, Seattle; 2005. Updated August 25, 2022. Accessed October 10, 2024. Available at www.ncbi.nlm.nih.gov/books/NBK1517/
3. Schwartz PJ, Ackerman MJ, Antzelevitch C, et al. Inherited cardiac arrhythmias. *Nat Rev Dis Primers*. 2020;6(1):58. doi:10.1038/s41572-020-0188-7
4. Richards S, Aziz N, Bale S, et al: Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. *Genet Med*. 2015;17(5):405-424. doi:10.1038/gim.2015.30

Performance

Method Description

Next generation sequencing (NGS) and/or Sanger sequencing are performed to test for the presence of variants in coding regions and intron/exon boundaries of *SCN5A*, as well as some other regions that have known disease-causing variants. The human genome reference GRCh37/hg19 build was used for sequence read alignment. At least 99% of the bases are covered at a read depth over 30X. Sensitivity is estimated at above 99% for single nucleotide variants, above 94% for deletion-insertions (delins) less than 40 base pairs (bp), and above 95% for deletions up to 75 bp and insertions up to 47 bp. NGS and/or a polymerase chain reaction-based quantitative method is performed to test for the presence of deletions and duplications in *SCN5A*.

There may be regions of genes that cannot be effectively evaluated by sequencing or deletion and duplication analysis as a result of technical limitations of the assay, including regions of homology, high guanine-cytosine (GC) content, and repetitive sequences.(Unpublished Mayo method)

The reference transcript for the *SCN5A* gene is NM_198056.2. Reference transcript numbers may be updated due to transcript re-versioning. Always refer to the final patient report for gene transcript information referenced at the time of testing. Confirmation of select reportable variants may be performed by alternate methodologies based on internal laboratory criteria.

PDF Report

Supplemental

Day(s) Performed

Varies

Report Available

14 to 21 days

Specimen Retention Time

Whole blood: 28 days (if available); Saliva: 30 days (if available); Extracted DNA: 3 months , Blood spots: 1 year (if available)

Performing Laboratory Location

Rochester

Fees & 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 account representative. 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. It has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information

81407

Prior Auhtorization

Insurance preauthorization is available for this testing; forms are available.

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.

LOINC® Information

| Test ID | Test Order Name | Order LOINC® Value |
|---------|-----------------------------------|--------------------|
| SCN5A | Brugada Syndrome, SCN5A Full Gene | 55139-0 |

| Result ID | Test Result Name | Result LOINC® Value |
|-----------|------------------------|---------------------|
| 617450 | Test Description | 62364-5 |
| 617451 | Specimen | 31208-2 |
| 617452 | Source | 31208-2 |
| 617453 | Result Summary | 50397-9 |
| 617454 | Result | 82939-0 |
| 617455 | Interpretation | 69047-9 |
| 617456 | Additional Results | 82939-0 |
| 617457 | Resources | 99622-3 |
| 617458 | Additional Information | 48767-8 |
| 617459 | Method | 85069-3 |
| 617460 | Genes Analyzed | 48018-6 |
| 617461 | Disclaimer | 62364-5 |
| 617462 | Released By | 18771-6 |