

## Overview

### Useful For

Establishing a molecular diagnosis for patients with hereditary neuralgic amyotrophy

Identifying variants within *SEPTIN9* known to be associated with hereditary neuralgic amyotrophy, allowing for predictive testing of at-risk family members

### Genetics Test Information

[This test utilizes next-generation sequencing to detect single nucleotide and copy number variants in one gene associated with hereditary neuralgic amyotrophy: \*SEPTIN9\*. See Method Description for additional details.](#)

Identification of a disease-causing variant may assist with diagnosis, prognosis, clinical management, recurrence risk assessment, familial screening, and genetic counseling for hereditary neuralgic neuropathy.

### Special Instructions

- [Informed Consent for Genetic Testing](#)
- [Molecular Genetics: Neurology Patient Information](#)
- [Informed Consent for Genetic Testing \(Spanish\)](#)

### 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

Targeted testing (also called site-specific or known variants testing) is available for variants identified in the *SEPTIN9* gene. See FMTT / Familial Mutation, Targeted Testing, Varies. To obtain more information about this testing option, call 800-533-1710.

Testing for *SEPTIN9* gene as part of a customized panel is available. For more information see CGPH / Custom Gene Panel, Hereditary, Next-Generation Sequencing, Varies.

### Shipping Instructions

Specimen preferred to arrive within 96 hours of collection.

**Specimen Required**

**Patient Preparation:** A previous bone marrow transplant from an allogenic donor will interfere with testing. Call 800-533-1710 for instructions for testing patients who have received a bone marrow transplant.

**Specimen Type:** Whole blood

**Container/Tube:**

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

**Acceptable:** Any anticoagulant

**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)/Refrigerated

**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:

- [Informed Consent for Genetic Testing \(T576\)](#)
- [Informed Consent for Genetic Testing \(Spanish\) \(T826\)](#)
- 2. [Molecular Genetics: Neurology Patient Information](#)

**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 | Special Container |
|---------------|-------------|------|-------------------|
| Varies        | Varies      |      |                   |

**Clinical & Interpretive****Clinical Information**

Hereditary neuralgic amyotrophy (HNA) is an autosomal dominant disorder characterized by periods of severe pain involving the brachial plexus followed by muscle atrophy and weakness. These recurrent episodes can also be accompanied by decreased sensation and paresthesias. Individuals with this disease are generally symptom-free between pain attacks, though many patients experience lingering effects with repeated attacks. The pain episodes are frequently triggered by physical, emotional, or immunological stress. Less commonly, affected individuals can exhibit non-neurological features including short stature, skin folds, hypotelorism, and cleft palate.

Variants in the *SEPTIN9* gene cause the clinical manifestations of HNA. *SEPTIN9* is currently the only known gene

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associated with HNA, although approximately 15% of HNA families do not show linkage to this gene.

**Reference Values**

An interpretive report will be provided.

**Interpretation**

All detected variants are evaluated according to American College of Medical Genetics and Genomics recommendations.(1) 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 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.

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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:

At this time, it is not standard practice for the laboratory to systematically review previously classified variants on a regular basis. The laboratory encourages healthcare providers to contact the laboratory at any time to learn how the classification of a particular variant may have changed over time. Due to broadening genetic knowledge, it is possible that the laboratory may discover new information of relevance to the patient. Should that occur, the laboratory may issue an amended report.

#### 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.(1) 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. These findings will be carefully reviewed to determine whether they will be reported.

#### Clinical Reference

1. 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 May;17(5):405-424
2. Klein CJ, Duan X, Shy ME. Inherited neuropathies: clinical overview and update. *Muscle Nerve*. 2013 Oct;48(4):604-22

## 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 *SEPTIN9*, 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), above 95% for deletions up to 75 bp and insertions up

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to 47 bp. NGS and/or a polymerase chain reaction (PCR)-based quantitative method is performed to test for the presence of deletions and duplications in *SEPTIN9*.

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 *SEPTIN9* gene is NM\_006640.4. 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**

28 to 42 days

**Specimen Retention Time**

Whole blood: 2 weeks (if available); Extracted DNA: 3 months

**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. This test has not been cleared or approved by the US Food and Drug Administration.

**CPT Code Information**

81479

**LOINC® Information**

| Test ID | Test Order Name                  | Order LOINC® Value |
|---------|----------------------------------|--------------------|
| SEP9Z   | SEPTIN9 Gene, Full Gene Analysis | 77067-7            |

| Result ID | Test Result Name       | Result LOINC® Value |
|-----------|------------------------|---------------------|
| 617715    | Test Description       | 62364-5             |
| 617716    | Specimen               | 31208-2             |
| 617717    | Source                 | 31208-2             |
| 617718    | Result Summary         | 50397-9             |
| 617719    | Result                 | 82939-0             |
| 617720    | Interpretation         | 69047-9             |
| 618191    | Additional Results     | In Process          |
| 617721    | Resources              | 99622-3             |
| 617722    | Additional Information | 48767-8             |
| 617723    | Method                 | 85069-3             |
| 617724    | Genes Analyzed         | 48018-6             |
| 617725    | Disclaimer             | 62364-5             |
| 617726    | Released By            | 18771-6             |