MAYO CLINIC

1-800-533-1710

SEPTIN9 Gene, Full Gene Analysis

SEP9Z

PATIENT NAME				ORDER NUMBER
TESTING, SEP9Z_ABNORMAL				**M311000153**
PATIENT ID SA00154784	DATE OF BIRTH 05/05/2005	AGE 17 Y	SEX Male	REQUESTED BY CLIENT CLIENT
COLLECTED 10/11/2022, 12:00 AM	RECEIVED 10/13/2022, 3:30 PM	REPORTED 10/17/2022, 2:14 PM		
The collected, received, and reported dates and times on the report are in the time zone of the performing location. 7028846 MCL RochesterCampus Rochester MN 55901				CLIENT ORDER NUMBER SA00154784 CLIENT MRN SA00154784

TEST DESCRIPTION

Evaluation of the SEPTIN9 gene associated with hereditary neuralgic amyotrophy

SPECIMEN

WB Whole Blood

RESULT SUMMARY

Pathogenic Variant Detected

RESULT

Gene (Transcript)	Variant	Zygosity	Classification
SEPTIN9 (NM_006640.5)	c.262C>T p.Arg88Trp (p.R88W) chr17(GRCh37):g.75398380C>T	heterozygous	PATHOGENIC

The following heterozygous PATHOGENIC variant was detected:
SEPTIN9 (NM_006640.5), chr17(GRCh37):g.75398380C>T, c.262C>T, p.Arg88Trp (p.R88W)

No additional reportable variants were detected within all other tested genes. See the Genes Analyzed section for a complete list of genes evaluated by this assay.

INTERPRETATION

SEPTIN9 c.262C>T (p.Arg88Trp), PATHOGENIC
The heterozygous c.262C>T (p.Arg88Trp) missense variant in the SEPTIN9 gene (MIM:604061) is classified as pathogenic. Pathogenic variants in the SEPTIN9 gene have been associated with autosomal dominant hereditary neuralgic amyotrophy (HNA). This variant has been reported in individuals with HNA and has been shown to track with disease in families with HNA (1-4). However, functional studies have not been performed to either support or refute the pathogenicity of this variant. This variant is absent from large control databases (5,6). This result is supportive of a diagnosis of HNA for this individual. Clinical correlation is recommended.

This result should be interpreted in the context of clinical findings, family history, and other laboratory testing.

Consultation with a genetics professional is recommended for interpretation of this result and to determine whether reproductive risk assessment and familial testing may be of benefit to this family. Genetic testing for family members is available by ordering FMTT / Familial Mutation, Targeted Testing for the specific variant(s) detected. Please contact the laboratory at 1-800-533-1710 or the online test catalog at www.mayocliniclabs.com for information about FMTT.

REFERENCES:
1) Kuhlenbäumer G, Hannibal MC, Nelis E, et al. Mutations in SEPT9 cause hereditary neuralgic amyotrophy. Nat Genet. 2005;37(10):1044-1046. doi:10.1038/ng1649 (PMID 16186812)
2) Hannibal MC, Ruzzo EK, Miller LR, et al. SEPT9 gene sequencing analysis reveals recurrent mutations in hereditary

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neuralgic amyotrophy. Neurology. 2009;72(20):1755-1759. doi:10.1212/WNL.0b013e3181a609e3 (PMID 19451530)
3) Leshinsky-Silver E, Ginzberg M, Dabby R, Sadeh M, Lev D, Lerman-Sagie T. Neonatal vocal cord paralysis-an early presentation of hereditary neuralgic amyotrophy due to a mutation in the SEPT9 gene. Eur J Paediatr Neurol. 2013;17 (1):64-67. doi:10.1016/j.ejpn.2012.08.006 (PMID 22981636)
4) Ueda M, Kawamura N, Tateishi T, et al. Phenotypic spectrum of hereditary neuralgic amyotrophy caused by the SEPT9 R88W mutation. J Neurol Neurosurg Psychiatry. 2010;81(1):94-96. doi:10.1136/jnnp.2008.168260 (PMID 20019224)
5) dbSNP: www.ncbi.nlm.nih.gov/snp; Sherry ST, Ward M and Sirotkin K. dbSNP-Database for Single Nucleotide Polymorphisms and Other Classes of Minor Genetic Variation. Genome Res. 1999;9:677-679 (PMID 10447503)
6) gnomAD Browser: gnomad.broadinstitute.org/; Karczewski K, Francioli LC, MacArthur DG, et al. The mutational constraint spectrum quantified from variation in 141,456 humans. Nature. 2020; 581(7809):434-443 (PMID 32461654)

METHOD

Next generation sequencing (NGS) and/or Sanger sequencing was performed to test for the presence of variants in coding regions and intron/exon boundaries of the gene analyzed. 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 >30X. Sensitivity is estimated at >99% for single nucleotide variants, >94% for indels up to 39 base pairs, >95% for deletions up to 75 base pairs and insertions up to 47 base pairs. NGS and/or a PCR-based quantitative method was performed to test for the presence of deletions and duplications in the gene analyzed. See the Genes Analyzed field for a list of gene(s) tested.

There may be regions of genes that cannot be effectively evaluated for sequencing or deletion and duplication analysis as a result of technical limitations of the assay, including regions of homology, high GC content, and repetitive sequences. Confirmation of select reportable variants was performed by alternate methodologies based on internal laboratory criteria. See www.mayocliniclabs.com (TEST ID SEP9Z) for details regarding genes with regions not routinely covered.

GENES ANALYZED

SEPTIN9

DISCLAIMER

Clinical Correlations
An online research opportunity called GenomeConnect (genomeconnect.org), a project of ClinGen, is available for the recipient of this genetic test. This patient registry collects de-identified genetic and health information to advance the knowledge of genetic variants. Mayo Clinic is a collaborator of ClinGen. This may not be applicable for all tests.

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(s) in an affected family member would allow for more informative testing of at risk individuals.

To discuss the availability of further testing options or for assistance in the interpretation of these results, Mayo Clinic Laboratory genetic counselors can be contacted at 1-800-533-1710.

Technical Limitations
Next generation sequencing may not detect all types of genomic variants. In rare cases, false negative or false positive

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results may occur. The depth of coverage may be variable for some target regions, but 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 for sequencing or deletion and duplication analysis as a result of technical limitations of the assay, including regions of homology, high GC content, and repetitive sequences. Confirmation of select reportable variants was performed by alternate methodologies based on internal laboratory criteria.

Additionally, low level mosaic variants may not be detected.

This test is not designed 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.

Reclassification of Variants Policy
See www.mayocliniclabs.com (TEST ID SEP9Z) for information regarding the laboratory's policy for reclassification of variants.

Variant Evaluation
Variant curation is performed using published ACMG-AMP recommendations as a guideline. Other gene-specific guidelines may also be considered. Variants classified as benign or likely benign are not reported.

Results from in silico evaluation tools may change over time and should be interpreted with caution and professional clinical judgment.

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.

RELEASED BY

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