



1-800-533-1710

NOTCH3 Gene, Full Gene Analysis

NTC3Z

PATIENT NAME TESTRNV, IMPLEMENTATION				ORDER NUMBER L624000478
PATIENT ID X100383798	DATE OF BIRTH 02/19/1968	AGE 54 Y	SEX Male	REQUESTED BY PROVIDER UNKNOWN
COLLECTED 3/24/2022, 1:00 PM	RECEIVED 3/25/2022, 10:15 AM	REPORTED 4/12/2022, 4:58 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 X100383798 CLIENT MRN 321

TEST DESCRIPTION

Evaluation of the NOTCH3 gene associated with Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy (CADASIL) and other NOTCH3-related disorders

SPECIMEN

WB Whole Blood

RESULT SUMMARY

Pathogenic Variant Detected

RESULT

The following heterozygous PATHOGENIC variant was detected:

NOTCH3 (NM_000435.2), chr19(GRCh37):g.15303053G>A, c.397C>T, p.Arg133Cys (p.R133C)

INTERPRETATION

NOTCH3 c.397C>T (p.R133C): The heterozygous c.397C>T (p.R133C) missense variant in the NOTCH3 gene (MIM:600276) is an established pathogenic variant. Pathogenic variants in the gene are associated with autosomal dominant cerebral arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL), autosomal dominant lateral meningocele syndrome, and autosomal dominant infantile myofibromatosis. This result is supportive of a diagnosis of a NOTCH3-related disorder 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.

RESOURCES

Disease specific information, including current therapies may be available at:

1. GeneReviews: <https://www.ncbi.nlm.nih.gov/books/NBK1500/>
2. <https://www.fda.gov/drugs>

Information regarding clinical trials, if available, can be found at the following sites:

1. ClinicalTrials.gov: <http://clinicaltrials.gov/ct2/search/advanced>

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



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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 NTC3Z) for details regarding genes with regions not routinely covered.

GENES ANALYZED

NOTCH3

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 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**PATIENT NAME** TESTRNV, IMPLEMENTATION

22-14845



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See www.mayocliniclabs.com (TEST ID NTC3Z) 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 Cherisse A. Marcou, Ph.D.				

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