



1-800-533-1710

F13A1 and B Genes, Full Gene NGS

GNF13

PATIENT NAME GNF13, AB				ORDER NUMBER M724000373
PATIENT ID SA00158418	DATE OF BIRTH 11/11/1987	AGE 35 Y	SEX Female	REQUESTED BY CLIENT CLIENT
COLLECTED 2/22/2023, 12:00 AM	RECEIVED 2/24/2023, 2:39 PM	REPORTED 2/28/2023, 10:35 AM		
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 SA00158418
				CLIENT MRN SA00158418

TEST DESCRIPTION

Evaluation of the F13A1 and F13B genes associated with factor XIII deficiency.

SPECIMEN

WB Whole Blood

RESULT SUMMARY

Pathogenic Variant Detected

RESULT

Gene (Transcript)	Variant	Zygosity	Classification
F13A1	c.27del	heterozygous	PATHOGENIC
NM_000129.4	p.Phe9Leufs*67		
	Chr6:g.6318871del		

The following heterozygous PATHOGENIC variant was detected:

F13A1 (NM_000129.4), chr6(GRCh37):g.6318871del, c.27del, p.Phe9Leufs*67 (p.F9Lfs*67)

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

F13A1 c.27del (p.Phe9Leufs*67), PATHOGENIC

The heterozygous c.27del (p.Phe9Leufs*67) deletion in the F13A1 gene (MIM:134570) is classified as pathogenic. Pathogenic variants in the F13A1 gene have been associated with autosomal recessive factor XIII deficiency. This variant has been reported in several unrelated individuals with a clinical diagnosis of factor XIII deficiency (1-3). Furthermore, functional studies have been performed to support the pathogenicity of this variant. It is an inactivating (loss of function) alteration (1). This alteration is observed in the large population genetics database gnomAD in the heterozygous state in 9 out of 56849 European (non-Finnish) individuals (minor allele frequency [MAF] = 0.008%) and not in any other population (4,5). This result is supportive of carrier status for factor XIII deficiency. However, the presence of an undetectable second variant cannot be ruled out. Clinical correlation is recommended.

Individuals may have a pathogenic variant in one of the interrogated genes that is not detectable by the methods utilized. Additionally, the clinical phenotype that is observed in this individual and/or family may be due to a pathogenic variant or variants in another gene not targeted by this test.

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



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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) Mikkola H, Yee VC, Syrjälä M, et al. Four novel mutations in deficiency of coagulation factor XIII: consequences to expression and structure of the A-subunit. *Blood*. 1996;87(1):141-151. (PMID 8547636)
- 2) Maron JL, Kingsmore SF, Wigby K, et al. Novel Variant Findings and Challenges Associated With the Clinical Integration of Genomic Testing: An Interim Report of the Genomic Medicine for Ill Neonates and Infants (GEMINI) Study [published correction appears in *JAMA Pediatr*. 2021 Aug 1;175(8):871]. *JAMA Pediatr*. 2021;175(5):e205906. doi:10.1001/jamapediatrics.2020.5906 (PMID 33587123)
- 3) Ivaškevičius V, Biswas A, Garly ML, Oldenburg J. Comparison of F13A1 gene mutations in 73 patients treated with recombinant FXIII-A2. *Haemophilia*. 2017;23(3):e194-e203. doi:10.1111/hae.13233 (PMID 28520207)
- 4) 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)
- 5) 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 genes analyzed, as well as some other regions that have known pathogenic variants. NGS and/or a polymerase chain reaction (PCR)-based quantitative method was performed to test for the presence of deletions and duplications in the genes 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 over 30X. Sensitivity is estimated at above 99% for single nucleotide variants, above 94% for indels less than 40 base pairs (bp), above 95% for deletions up to 75 bp and insertions up to 47 bp. See the Genes Analyzed field for a list of genes 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 GNF13) for details regarding genes with regions not routinely covered.

GENES ANALYZED

F13A1 and F13B

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23-11925



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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.

Genes may be added or removed based on updated clinical relevance. Please refer to the Targeted Genes and Methodology Details for the F13A1 and B Genes, Full Gene NGS in the Special Instructions section of the Test Catalog for the most up to date list of genes included in this test.

Reclassification of Variants Policy

See www.mayocliniclabs.com (TEST ID GNF13) for information regarding the laboratory's policy for reclassification of variants.

Variant Evaluation**PATIENT NAME** GNF13, AB

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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

SHANDA VOELTZ

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