MAYO CLINIC

1-800-533-1710

Ehlers-Danlos Syndrome Gene Panel

EDSGG

PATIENT NAME				ORDER NUMBER
ABNORMAL, EDSGG				**M229000223**
PATIENT ID SA00154625	DATE OF BIRTH 01/01/1980	AGE 42 Y	SEX Female	REQUESTED BY CLIENT CLIENT
COLLECTED 9/28/2022, 11:00 AM	RECEIVED 9/29/2022, 9:05 AM	REPORTED 9/30/2022, 10:22 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
SA00154625

CLIENT MRN
SA00154625

TEST DESCRIPTION

Evaluation of 22 genes associated with Ehlers-Danlos syndrome and related conditions

SPECIMEN

DNA (ul)

RESULT SUMMARY

Pathogenic Variant Detected

RESULT

Gene (Transcript)	Variant	Zygosity	Classification
COL3A1 (NM_000090.3)	c.2534dup p.Gly846Trypfs*17 (p.G846Wfs*17) Chr2(GRCh37):g.189867769dup	Heterozygous	Pathogenic

The following heterozygous PATHOGENIC variant was detected: COL3A1 (NM_000090.3), Chr2 (GRCh37):g.189867769dup, c.2534dupC, p.Gly846Trpfs*17 (p.G846Wfs*17)

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

INTERPRETATION

COL3A1: c.4087C>T (p.Arg1363*): The heterozygous c.4087C>T (p.Arg1363*) variant in the COL3A1 gene (MIM: 120180) is classified as pathogenic. The COL3A1 gene encodes the pro-alpha1 chains of type III collagen. Pathogenic variants in this gene have mainly been associated with autosomal dominant vascular Ehlers-Danlos syndrome (also known as vEDS or EDS type IV). This variant has been previously reported in one individual from a cohort of individuals with vEDS (vascular EDS), however no additional clinical or family history information was available on that individual (1). Other truncating variants in the COL3A1 gene have been reported in association with vascular EDS (vEDS). Finally, the p.Gly846Trpfs*17 variant has not been observed in exome and/or genome sequencing data gathered from large, multi-ethnic cohorts, suggesting it is a rare variant (2). Taken together, this result is supportive of a diagnosis of vascular Ehlers Danlos syndrome 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. Pepin MG, Schwarze U, Rice KM, Liu M, Leistritz D, Byers PH. Survival is affected by mutation type and molecular

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mechanism in vascular Ehlers-Danlos syndrome (EDS type IV). Genet Med. 2014;16(12):881-888. doi:10.1038/gim.2014.72 (PMID: 24922459)
2. gnomAD Browser: gnomad.broadinstitute.org/; Karczewski K, Francioli LC, MacArthur DG, et al. The mutationalconstraint 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. 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. 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. 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 EDSGG) for details regarding genes with regions not routinely covered.

GENES ANALYZED

ADAMTS2, AEBP1, ATP7A, B3GALT6, B3GAT3, B4GALT7, CHST14, COL12A1, COL1A1, COL1A2, COL3A1, COL5A1, COL5A2, DSE, FKBP14, FLNA, PLOD1, PRDM5, SLC39A13, SPARC, TNXB, ZNF469

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.

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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 Ehlers-Danlos Syndrome Gene Panel 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 EDSGG) 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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