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Patient Report

Patient Age/Gender: 1 day Female

Specimen Collected: 25-May-21 12:30

Emery-Dreifuss Muscular Dystrophy by NGS | **Received: 25-May-21 12:30** **Report/Verified: 25-May-21 12:39**

Procedure	Result	Units	Reference Interval
Emery-Dreifuss Muscular Dystrophy Spec	Whole Blood		
Emery-Dreifuss Muscular Dystrophy Interp	Positive [f1 i1]		

Result Footnote

f1: Emery-Dreifuss Muscular Dystrophy Interp

INDICATION FOR TESTING
Not provided

RESULT
One pathogenic variant was detected in the EMD gene.

PATHOGENIC VARIANT
Gene: EMD (NM_000117.2)
Nucleic Acid Change: c.506_507delCT; Hemizygous
Amino Acid Alteration: p.Pro169ArgfsTer40
Inheritance: X-linked

INTERPRETATION
One pathogenic variant, c.506_507delCT; p.Pro169ArgfsTer40 was detected in the EMD gene by massively parallel sequencing and confirmed by Sanger sequencing. Pathogenic EMD variants are inherited in an X-linked recessive manner and are associated with Emery-Dreifuss muscular dystrophy 1 (MIM: 310300). This result is consistent with a diagnosis of Emery-Dreifuss muscular dystrophy. All of this individual's daughters will be carriers, but none of the sons will inherit the pathogenic variant.

No additional pathogenic variants were identified in the targeted genes by massively parallel sequencing. Please refer to the background information included in this report for a list of the genes analyzed and the limitations of this test.

Evidence for variant classification: The EMD c.506_507delCT; p.Pro169ArgfsTer40 variant is reported in the literature in an individual affected with Emery-Dreifuss muscular dystrophy (Bione 1994). This variant is absent from general population databases (Exome Variant Server, Genome Aggregation Database), indicating it is not a common polymorphism. This variant causes a frameshift by deleting two nucleotides, and is predicted to result in a truncated protein or mRNA subject to nonsense-mediated decay. Based on available information, this variant is considered to be pathogenic.

RECOMMENDATIONS
Genetic consultation, including a discussion of medical screening and management, is indicated. At-risk family members should be offered testing for the identified pathogenic variant (Familial Mutation, Targeted Sequencing, ARUP test code 2001961).

COMMENTS
Likely benign and benign variants are not included in this report.

REFERENCES
Bione S et al. Identification of a novel X-linked gene responsible for Emery-Dreifuss muscular dystrophy. Nat Genet. 1994 Dec;8(4):323-7.

*=Abnormal, #=Corrected, C=Critical, f=Result Footnote, H-High, i-Test Information, L-Low, t-Interpretive Text, @=Performing lab

Result Footnote

f1: Emery-Dreifuss Muscular Dystrophy Interp

This result has been reviewed and approved by Rong Mao, M.D.

Test Information

i1: Emery-Dreifuss Muscular Dystrophy Interp

BACKGROUND INFORMATION: Emery-Dreifuss Muscular Dystrophy Panel, Sequencing

CHARACTERISTICS: Emery-Dreifuss muscular dystrophy (EDMD) is characterized by a clinical triad of early onset joint contractures (commonly involving elbows, ankles, and neck), slowly progressive limb muscle weakness and wasting, and cardiac disease. EDMD demonstrates intra- and interfamilial variability in age of onset, severity, and progression; although penetrance is high. Typical presentation includes joint contractures in first two decades of life, followed by muscle weakness and wasting, with cardiac involvement occurring in the second to third decades. Carrier females of X-linked EDMD are usually asymptomatic, but are at risk for developing cardiac disease, and less commonly, mild muscle disease.

EPIDEMIOLOGY: Prevalence 1-2:100,000.

CAUSE: Pathogenic germline variants in EMD, FHL1, or LMNA.

INHERITANCE: X-linked for EMD or FHL1. Typically, autosomal dominant for LMNA; de novo variation is common. Autosomal recessive inheritance for LMNA is rare.

CLINICAL SENSITIVITY: 36 percent for EDMD.

GENES TESTED: EMD, FHL1, LMNA.

METHODOLOGY: Capture of all coding exons and exon-intron junctions of the targeted genes, followed by massively parallel sequencing. Sanger sequencing was performed as necessary to fill in regions of low coverage and confirm reported variants. Human genome build 19 (Hg 19) was used for data analysis.

ANALYTICAL SENSITIVITY/SPECIFICITY: The analytical sensitivity of this test is approximately 99 percent for single nucleotide variants (SNVs) and greater than 93 percent for insertions/duplications/deletions from 1-10 base pairs in size. Variants greater than 10 base pairs may be detected, but the analytical sensitivity may be reduced.

LIMITATIONS: A negative result does not exclude a diagnosis of EDMD. This test only detects variants within the coding regions and intron-exon boundaries of the targeted genes. Regulatory region variants and deep intronic variants will not be identified. Deletions/duplications/insertions of any size may not be detected by massively parallel sequencing. In males, lack of massively parallel sequencing

Test Information

i1: Emery-Dreifuss Muscular Dystrophy Interp

coverage of one or more EMD or FHL1 exons may suggest the presence of large deletions; however, this should be confirmed by a validated method. Diagnostic errors can occur due to rare sequence variations. In some cases, variants may not be identified due to technical limitations in the presence of pseudogenes, repetitive, or homologous regions. This assay may not detect low-level mosaic or somatic variants associated with disease. Interpretation of this test result may be impacted if this patient has had an allogeneic stem cell transplantation. Noncoding transcripts were not analyzed.

This test was developed and its performance characteristics determined by ARUP Laboratories. It has not been cleared or approved by the US Food and Drug Administration. This test was performed in a CLIA certified laboratory and is intended for clinical purposes.

Counseling and informed consent are recommended for genetic testing. Consent forms are available online.