

Client: Example Client ABC123
123 Test Drive
Salt Lake City, UT 84108
UNITED STATES

Physician: Doctor, Example

Patient: Patient, Example

DOB 12/9/2011
Gender: Male
Patient Identifiers: 01234567890ABCD, 012345
Visit Number (FIN): 01234567890ABCD
Collection Date: 01/01/2017 12:34

Duchenne/Becker Muscular Dystrophy (DMD) Sequencing

ARUP test code 2011153

DMD Sequencing Specimen whole Blood

DMD Sequencing Interpretation Positive

H=High, L=Low, *=Abnormal, C=Critical

Unless otherwise indicated, testing performed at:

INDICATION FOR TESTING

CK >4000 U/L, calf hypertrophy, calf pain

RESULT

One pathogenic variant was detected in the DMD gene.

PATHOGENIC VARIANT

Gene: DMD (NM_004006.2)
Nucleic Acid Change: c.1259dupT; Hemizygous
Amino Acid Alteration: p.Gln421fs
Inheritance: X-linked

INTERPRETATION

One pathogenic variant, c.1259dupT; p.Gln421fs, was detected in the DMD gene by massive parallel sequencing and confirmed by Sanger sequencing. No additional pathogenic variants were detected in DMD by massive parallel sequencing. Variants in DMD are causative for Duchenne/Becker muscular dystrophy (MIM: 310200 / 300376).

Evidence for variant classification: The DMD c.1259dupT; p.Gln421fs variant, to our knowledge, is not described in the medical literature or gene-specific databases. It is also absent from general population databases (1000 Genomes Project, Exome Variant Server, and Genome Aggregation Database), indicating it is not a common polymorphism. This variant causes a frameshift by duplicating a single nucleotide, so it is predicted to result in a truncated protein or mRNA subject to nonsense-mediated decay. Additionally, several downstream truncating variants have been described in individuals affected with Duchenne muscular dystrophy and are considered pathogenic (Flanigan 2009, Mah 2011, Okubo 2017). Based on available information, the p.Gln421fs variant is considered pathogenic.

RECOMMENDATIONS

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

COMMENTS

Benign variants are not included in this report, but are available upon request.

REFERENCES

Flanigan K et al. Mutational spectrum of DMD mutations in dystrophinopathy patients: application of modern diagnostic techniques to a large cohort. Hum Mutat. 2009 Dec;30(12):1657-66.

Mah J et al. A population-based study of dystrophin mutations in Canada. Can J Neurol Sci. 2011 May;38(3):465-74.

Okubo M et al. Genetic diagnosis of Duchenne/Becker muscular dystrophy using next-generation sequencing: validation analysis of DMD mutations. J Hum Genet. 2016 Jun;61(6):483-9.

This result has been reviewed and approved by [REDACTED]

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Unless otherwise indicated, testing performed at:

ARUP LABORATORIES | 800-522-2787 | aruplab.com
500 Chipeta Way, Salt Lake City, UT 84108-1221
Tracy I. George, MD, Laboratory Director

Patient: Patient, Example
ARUP Accession: 18-344-110629
Patient Identifiers: 01234567890ABCD, 012345
Visit Number (FIN): 01234567890ABCD
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BACKGROUND INFORMATION: Duchenne/Becker Muscular Dystrophy (DMD) Sequencing

CHARACTERISTICS: Symptoms of Duchenne muscular dystrophy (DMD) usually begin in childhood and include fatigue, learning difficulties, muscle weakness, progressive difficulty walking with eventual wheelchair dependency, breathing difficulties and heart disease. Symptoms of Becker muscular dystrophy (BMD) are similar to DMD but begin at a later age and progress at a slower rate. Dilated cardiomyopathy has been observed in nearly all affected males and many female carriers of DMD and BMD.

EPIDEMIOLOGY: Incidence of DMD: 1 in 3,500 male births, BMD: 1 in 19,000 male births.

INHERITANCE: X-linked; de novo variants occur in 1/3 of cases.

PENETRANCE: Males: 100 percent. Females: Varies with X-chromosome inactivation.

CLINICAL SENSITIVITY: DMD 20-35 percent. BMD: 10-20 percent.

METHODOLOGY: Targeted capture of all coding exons and exon-intron junctions of the DMD gene, 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: 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 heritable form of muscular dystrophy. This test only detects variants within the coding regions and intron-exon boundaries of the DMD gene. Regulatory region variants and deep intronic variants will not be identified. Deletions/duplications/insertions of any size may not be detected by massive parallel sequencing. 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 somatic variants associated with disease. Interpretation of this test result may be impacted if this patient has had an allogeneic stem cell transplantation. Non-coding transcripts were not analyzed.

Test developed and characteristics determined by ARUP Laboratories. See Compliance Statement C: aruplab.com/CS

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4848

VERIFIED/REPORTED DATES				
Procedure	Accession	Collected	Received	Verified/Reported
DMD Sequencing Specimen	18-344-110629	12/10/2018 1:05:00 PM	12/10/2018 1:05:44 PM	12/10/2018 1 09:00 PM
DMD Sequencing Interpretation	18-344-110629	12/10/2018 1:05:00 PM	12/10/2018 1:05:44 PM	12/10/2018 1 09:00 PM

END OF CHART

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