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

Physician: Doctor, Example

Patient: Patient, Example

DOB	11/10/1998
Gender:	Female
Patient Identifiers:	01234567890ABCD, 012345
Visit Number (FIN):	01234567890ABCD
Collection Date:	00/00/0000 00:00

Duchenne/Becker Muscular Dystrophy (DMD) Deletion/Duplication with Reflex to Sequencing

ARUP test code 2011241

Duchenne/Becker MD (DMD) Reflex Specimen	Whole Blood	
Duchenne/Becker MD (DMD) DelDup MLPA	**Deletion**	*
Duchenne/Becker MD (DMD) Reflex Interp	Positive	

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

TEST PERFORMED - 2011241
TEST DESCRIPTION - Duchenne/Becker Muscular Dystrophy (DMD) Deletion/Duplication with Reflex to Sequencing
INDICATION FOR TESTING - Not Provided

RESULT
One pathogenic variant was detected in the DMD gene.

DNA VARIANT
Classification: Pathogenic
Gene: DMD
Nucleic Acid Change: Deletion of exons 8-15; Heterozygous
Out-of-frame deletion

INTERPRETATION
One pathogenic variant, deletion of exons 8-15, was detected by deletion/duplication analysis. This deletion is expected to alter the reading frame. This individual is a carrier of Duchenne/Becker muscular dystrophy and may be variably affected. Although females are usually asymptomatic, approximately 5-20 percent of carrier females may develop symptoms including variable degrees of muscle weakness and/or cardiomyopathy. This individuals male offspring have a 50 percent chance of being affected and female offspring have a 50 percent chance of being a carrier and variably affected.

A pathogenic variant was detected by deletion/duplication analysis, therefore, DMD sequencing was not performed.

Evidence for variant classification: The DMD exon 8-15 deletion has been described in the literature in individuals affected with Duchenne muscular dystrophy (Flanigan 2009 and Zamani 2022). This deletion is predicted to alter the reading frame of the dystrophin protein and based on the DMD reading frame hypothesis (Monaco 1988), this deletion is predicted result in the classical Duchenne muscular dystrophy. Based on available information, this deletion is classified as 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 variant (Duchenne/Becker Muscular Dystrophy (DMD) Deletion/Duplication; ARUP test code 2011235).

COMMENTS
Reference Sequence: GenBank # NM_004006.2

REFERENCES
American Academy of Pediatrics Section on Cardiology and Cardiac Surgery. Cardiovascular health supervision for individuals affected by Duchenne or Becker muscular dystrophy. Pediatrics. 2005; 116(6):1569-73.

Flanigan KM 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. PMID: 19937601.

Monaco et al. An explanation for the phenotypic differences between patients bearing partial deletions of the DMD locus. Genomics. 1988; 2(1): 90-95.

Zamani G et al. Characteristics of disease progression and genetic correlation in ambulatory Iranian boys with Duchenne muscular dystrophy. BMC Neurol. 2022 May 2;22(1):162. PMID: 35501714.

This result has been reviewed and approved by [redacted]

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

BACKGROUND INFORMATION: Duchenne/Becker Muscular Dystrophy (DMD) Deletion/Duplication with Reflex to 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 is 1 in 3,500 male births; Incidence of BMD is 1 in 19,000 male births.

INHERITANCE: X-linked; de novo variants occur in one-third of cases.

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

CLINICAL SENSITIVITY: Approximately 95 percent.

METHODOLOGY: Multiplex ligation-dependent probe amplification (MLPA) of the DMD gene. If results were negative or inconclusive, testing was reflexed to 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 for MLPA is greater than 99 percent. The analytical sensitivity for sequencing 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 by sequencing, 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 and breakpoints of large deletions/duplications will not be determined. 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.

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.

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

VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
Duchenne/Becker MD (DMD) Reflex Specimen	23-221-402676	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Duchenne/Becker MD (DMD) DelDup MLPA	23-221-402676	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Duchenne/Becker MD (DMD) Reflex Interp	23-221-402676	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00

END OF CHART

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