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

Physician: Doctor, Example

Patient: Patient, Example

DOB	Unknown
Gender:	Male
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	**Duplication**	*
Duchenne/Becker MD (DMD) Reflex Interp	See Note	

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

INDICATION FOR TESTING
Not provided.

RESULT
One likely pathogenic duplication was detected in the DMD gene.

LIKELY PATHOGENIC VARIANT

Gene: DMD (NM_004006.2)
Nucleic Acid Change: Exon 45-62 duplication; Hemizygous

INTERPRETATION
One likely pathogenic variant, a contiguous duplication of exons 45-62, was detected in the DMD gene by multiplex ligation-dependent probe amplification (MLPA). Although the MLPA assay does not indicate the location within the genome that the duplicated region is positioned, in the case of a tandem duplication event, the identified duplication is expected to result in an out-of-frame product. However, as this assay does not determine breakpoint positions, it is uncertain whether all or part of the identified exons are duplicated. Pathogenic variants in DMD are causative for Duchenne/Becker muscular dystrophy (MIM: 310200 / 300376); therefore, this individual is predicted to be affected. Female offspring will be carriers of the disease and may be variably affected; male offspring will be neither carriers of nor affected with the disease.
Due to the large duplication detected by MLPA, DMD sequencing was not performed.
Evidence for variant classification:
Duplication of exons 45-62 has been reported in individuals affected with Duchenne muscular dystrophy (DMD) (see link to UMD-DMD database and references therein, Kalman 2011). Other duplication events in this region (exons 44-63, exons 45-60) have also been reported in individuals affected with DMD (Dastur 2011, Mah 2011). Based on the above information, duplication of exons 45-62 is considered likely pathogenic.
RECOMMENDATIONS

Genetic consultation is recommended, including a discussion of medical screening and management. At-risk family members should be offered testing for the identified likely pathogenic duplication (Duchenne/Becker Muscular Dystrophy (DMD) Deletion/Duplication; ARUP test code 2011235).
Reference Sequence: GenBank # NM_004006 (DMD)
REFERENCES
Link to UMD-DMD Database: http://www.umd.be/DMD/4DACTION/WV/1635
Dastur R et al. Identification of deletions and duplications in the Duchenne muscular dystrophy gene and female carrier status in western India using combined methods of multiplex polymerase chain reaction and multiplex ligation-dependent probe amplification. Neurol India. 2011 Nov-Dec;59(6):803-9.
Kalman L et al. Quality assurance for Duchenne and Becker muscular dystrophy genetic testing: development of a genomic DNA reference material panel. J Mol Diagn. 2011 Mar;13(2):167-74.
Mah J et al. A population-based study of dystrophin mutations in Canada. Can J Neurol Sci. 2011 May;38(3):465-74.

This result has been reviewed and approved by [redacted]

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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.

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VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
Duchenne/Becker MD (DMD) Reflex Specimen	22-195-102621	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Duchenne/Becker MD (DMD) DelDup MLPA	22-195-102621	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Duchenne/Becker MD (DMD) Reflex Interp	22-195-102621	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00

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