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

Physician: Doctor, Example

Patient: Patient, Example

DOB	9/12/1981
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	**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 - Confirm Diagnosis

RESULT
One pathogenic variant was detected in the DMD gene.

DNA VARIANT
Classification: Pathogenic
Gene: DMD
Nucleic Acid Change: Deletion of exons 45-50; Hemizygous Out-of-frame deletion

INTERPRETATION
One copy of a pathogenic variant, deletion of exons 45-50, was detected by deletion/duplication analysis. This deletion is expected to alter the reading frame. Thus, this result is consistent with a diagnosis of Duchenne/Becker muscular dystrophy (DMD/BMD). Female offspring of this individual will be carriers of the condition and may be variably affected; male offspring will be neither carriers of nor affected with the disease.

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

Evidence for variant classification: The deletion of exons 45-50 variant is frequently reported in the literature in many individuals affected with DMD/BMD (selected references: Dent 2009, Ankala 2012 and Nallamilli 2021). This deletion is predicted to alter the DMD reading frame; in agreement with the DMD reading frame hypothesis (Monaco 1988), this variant predicted to be associated with the more severe Duchenne muscular dystrophy (MIM: 310200). 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
Ankala et al. Aberrant firing of replication origins potentially explains intragenic nonrecurrent rearrangements within genes, including the human DMD gene. Genome Res. 2012 Jan;22(1):25-34. PMID: 22090376

Dent et al. Improved molecular diagnosis of dystrophinopathies in an unselected clinical cohort. Am J Med Genet A. 2005 Apr 30;134(3):295-8. doi: 10.1002/ajmg.a.30617. PMID: 15723292.

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

Nallamilli et al. A single NGS-based assaycovering the entire genomic sequence of the DMD gene facilitates diagnostic and newborn screening confirmatory testing. Hum Mutat. 2021 May;42(5):626-638. PMID: 33644936.

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	22-153-403021	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Duchenne/Becker MD (DMD) DelDup MLPA	22-153-403021	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Duchenne/Becker MD (DMD) Reflex Interp	22-153-403021	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00

END OF CHART

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