Inherited Disorders Deletion/Duplication Test

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Patient Name	:	**Zayyan Jagfar Ali**	Test	:	**MLPA (multiplex ligation-dependent probe amplification) test for the *DMD* gene**
Gender	:	**Male**	Referring Center	:	**Gulf Care Diagnostic Centre**
Age	:	**6 Years**	Referred by	:	**Dr. Vivek Mundada**
MRN #	:	**NA**	Sample Collected	:	**28-Apr-2025**
Sample ID	:	**STRAN-2025-72841**	Sample Received	:	**05-May-2025**
Specimen	:	**Blood**	Report Generated	:	**14-May-2025**

Indications for test

This individual manifested elevated serum creatine kinase (CK) levels, motor difficulties and falls during walking. Suspected of Duchenne muscular dystrophy (DMD).

Test details

MLPA (Multiplex Ligation-dependent Probe Amplification) Test: To detect large deletions or duplications in the *DMD* gene (RefSeq id: NM_004006.3).

Results

Positive for the variant, c.(7660+1_7661-1)_(8027+1_8028-1)del, (Deletion of exon 53-54), in the *DMD* gene (RefSeq id: NM_004006.3). The variant was detected in hemizygous state and it has been labeled as **'pathogenic'.**

Interpretation summary

- The individual carries one copy (hemizygous) of a 'pathogenic' variant in the *DMD* gene (Fig. 2), which may be associated with Duchenne muscular dystrophy (DMD) or Becker muscular dystrophy (BMD).
- Germline pathogenic variations in the *DMD* gene have been shown to be associated with DMD and BMD, which manifest as progressive muscle weakness, calf hypertrophy and atrophy. Other features include waddling gait, delayed motor skills such as difficulty in sitting, standing and walking [Gene Reviews, PMID: 20301298].
- DMD and BMD, caused due to pathogenic variations in the *DMD* gene, are inherited in an X-linked manner. However, skewed X-inactivation in females, new variations (*de novo*) and genetic mosaicism have also been reported in this gene [Gene Reviews, PMID: 20301298].

Gene name: *DMD1* **Genetic Alteration:** None

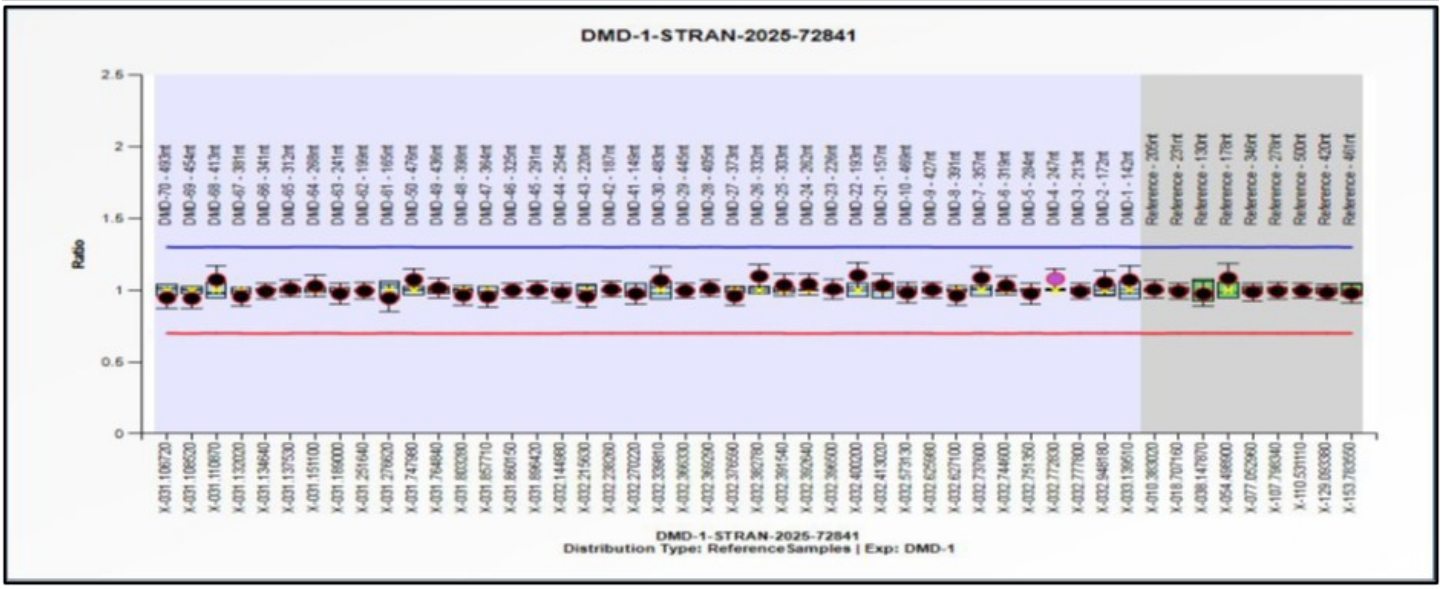


Figure 1: MLPA (multiplex ligation-dependent probe amplification) data from the individual showing normal copy of exons 1-10, 21-30, 41-50 and 61-70 of the *DMD* gene (RefSeq id: NM_004006.3).

Gene name: *DMD2* **Genetic Alteration:** chrX:(31645980_31676106)_ (31697704_31747747)del; c.(7660+1_7661-1)_(8027+1_8028-1)del, (Deletion of exon 53-54)

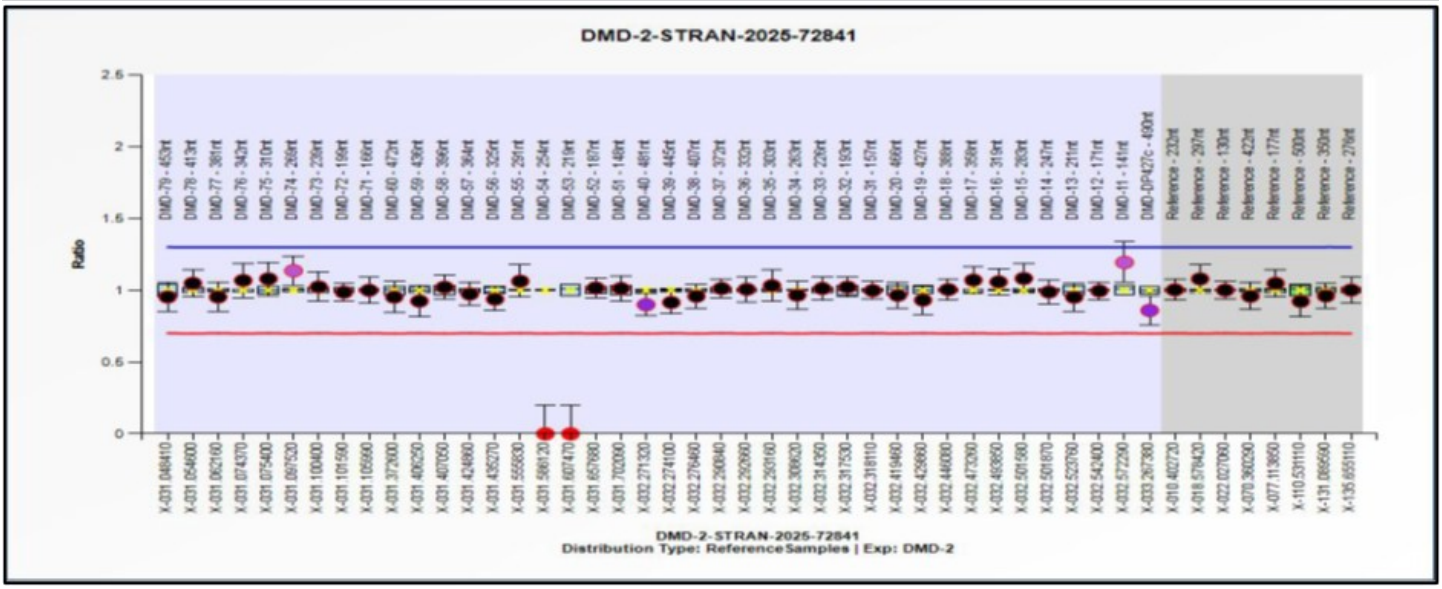
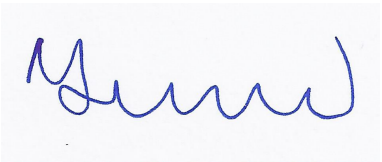


Figure 2: MLPA (multiplex ligation-dependent probe amplification) data from the individual showing hemizygous deletion of exon 53-54 [c.(7660+1_7661-1)_(8027+1_8028-1)del], of the *DMD* gene (RefSeq id: NM_004006.3).

Recommendations

- Genetic counselling is recommended to discuss the implications of this test result for this individual.Test results should be interpreted in the context of this individual's clinical history of disease.
- Kindly consult with the referring physician to discuss about surveillance measures.
- Genetic testing for the identified *DMD* variant in the **mother by using MLPA test is recommended** to ascertain if the identified variant is a *de novo* variant in this individual or transmitted from the mother.
- For further details, kindly contact: report.strandx@strandls.com

Signatures



Sameer Phalke
PhD, Director- Laboratory Sciences

Dayananda S Biligi
MBBS, MD (Path), Consulting Pathologist

Supplementary information

Genomic Regions Evaluated

The *DMD* gene (RefSeq id: NM_004006.3) gene consisting of 79 exons.

Background

The *DMD* gene encodes for the dystrophin protein, which is primarily expressed in skeletal and cardiac muscles. It is involved in the formation of dystrophin-glycoprotein (DGC) complex, which is required for connecting the structural framework of the cell and bridging the inner cytoskeleton with the extracellular matrix. Germline pathogenic variations in the *DMD* gene have been shown to be associated with Duchenne muscular dystrophy (DMD), Becker muscular dystrophy (BMD) and dilated cardiomyopathy (DCM) [MedlinePlus].

Methodology

The test is performed using the Multiplex Ligation-dependent Probe Amplification (MLPA) methodology using SALSA MLPA P034-DMD-1-B2-0422 (B2) kit for the *DMD*-1 gene contains 40 exons and P035-DMD-2-B1-0422 (B1) kit for the *DMD*-2 gene contains 39 exons corresponding to the RefSeq transcript NM_004006.3 (MRC-Holland, the Netherlands). MLPA is a semi-quantitative technique that is used to determine the relative copy number of up to 60 DNA sequences in probe hybridization to all target regions, followed by single multiplex PCR-based reaction. Probe amplification products were run on the Genetic Analyzer (3500 DX, Lifetech Inc., USA) and MLPA peak plots were visualized, normalized and the dosage ratios were calculated by using the Coffalyser software provided by the vendor. MLPA results are interpreted using Coffalyser software (version v.140721.1958) which has a normal range for probes with final ratio (FR) between 0.80 < FR < 1.20. FR distribution of 0.80 < FR < 1.20 represent normal copy in both male and female samples. FR = 0 represents hemizygous deletion and 1.65 < FR < 2.25 represents duplication in male samples. In females samples, FR=0 represents homozygous deletion, 0.40 < FR < 0.65 represent heterozygous deletion, 1.30 < FR < 1.65 represent heterozygous duplication and 1.75 < FR < 2.15 represent heterozygous triplication/homozygous duplication. The presence of any large deletion or duplication was evaluated by comparing the data from individual sample with control samples. For further details, kindly contact: report.strandx@strandls.com

Limitations and Disclaimer

As with any laboratory test, there is a small chance that this result may be inaccurate due to any reason, such as an error during specimen collection and labelling (incorrect patient identification), an error in processing, data collection or interpretation, sub-optimal sample quality or a technical error, and you agree that we shall not be liable for any claim, loss, or liability arising out of or in connection with this test, including but not limited to the accuracy of the test. Currently available data indicates that technical error rate for analysis involving DNA tests is anywhere between 1-2%. Variants that have not been confirmed by an independent analysis could represent technical artifacts. Many factors such as genetic mosaicism, PCR allele bias or allele drop-out due to variation at the primer binding site etc. can influence the quality of sequencing and may result in an occasional technical error. For an autosomal dominant condition, if the variant does not seem to be inherited from parents, it could be due to a *de novo* (new) event or due to a germline mosaicism in an unaffected parent. In case of germline mosaicism, there is a risk of the disease recurrence in the family. However, due to technical limitations of this test, germline mosaicism cannot be determined by this test. Accurate interpretation of this report is dependent on detailed clinical history of the patient and other laboratory reports, and you agree that we shall not be liable for any claim, loss, or liability arising out of or in connection with any medical advice or treatment provided by any person to you based on this test conducted or report provided by us. We cannot guarantee the accuracy of the interpretation of this report. The variant annotation of the detected variant in the report is with respect to Human Genome build GRCh37 (hg19). This report does not constitute medical advice and you will not rely on the report as a substitute for medical advice. You should consult with a qualified healthcare professional for a comprehensive evaluation and interpretation of your test result.

This report is generated within a specific timeframe known as the turnaround time (TAT). However, the actual TAT may differ based on the complexity of the test and information provided along with the sample. We cannot be held liable for any delays that occur beyond the mentioned TAT.

This report is strictly not a medical diagnostic report and shall not be construed as the medical certificate or medical laboratory report or diagnostic report.

Compliance statement

This assay is used for clinical purposes and was developed, and its performance validated by Strand Life Sciences Pvt. Ltd. It has not been cleared or approved by the US Food and Drug Administration (FDA). The FDA has determined that such clearance or approval is not necessary. Genetic counselling is recommended for all patients undergoing genetic testing. We follow the American College of Medical Genetics and Genomics (ACMG) guidelines regarding guidelines for test validation, variant classification and clinical reporting.

End of report