

## DEPARTMENT OF GENOMICS AND MOLECULAR DIAGNOSTICS

Patient Name	Ms. ITISHREE MOHAPATRA	Visit ID	0652405200210	Collection Date	20-05-2024 05:49 PM
Age / Gender	14 Y / FEMALE	UHID	SELF	Registration Date	21-05-2024 05:49PM
Ref Doctor	Dr. SELF	Hospital Name	SELF	Received Date	21-05-2024 08:48 AM
Barcode	A0710824	Sample Type	WHOLE BLOOD EDTA	Reported Date	13-06-2024 06:46 PM

### DMD Analysis by MLPA

#### Referral Reason

I/V/O congenital dystrophin myopathy ,she was referred for deletion/duplication testing by MLPA for DMD gene to rule out **DUCHENNE MUSCULAR DYSTROPHY (DMD)** .

#### Test Result

Duplication of Exon 49 detected in DMD gene.

#### Interpretation

The analysis has identified **duplication of exon 49** in this individual for DMD gene. Most females with a DMD gene duplication are carriers. Carriers usually do not show symptoms. However, there are exceptions where carrier females may exhibit mild to moderate symptoms.Clinical correlation is recommended.

**Note:**DMD gene duplications in females are primarily due to genetic mutations occurring during meiosis, de novo mutations, or inherited mutations. The clinical manifestations can vary greatly, influenced by factors such as skewed X-inactivation and mosaicism. Proper genetic counseling, alternative testing, and monitoring are essential for managing and understanding the implications of DMD gene duplications in females [7-9].

#### Analyzed by

Kanaka Durga Devi.Y




Kanaka Durga Devi.Y  
Technical Lead -Molecular  
Diagnostics.

#### Approved by



A. Radhika  
Co-Head Genomics

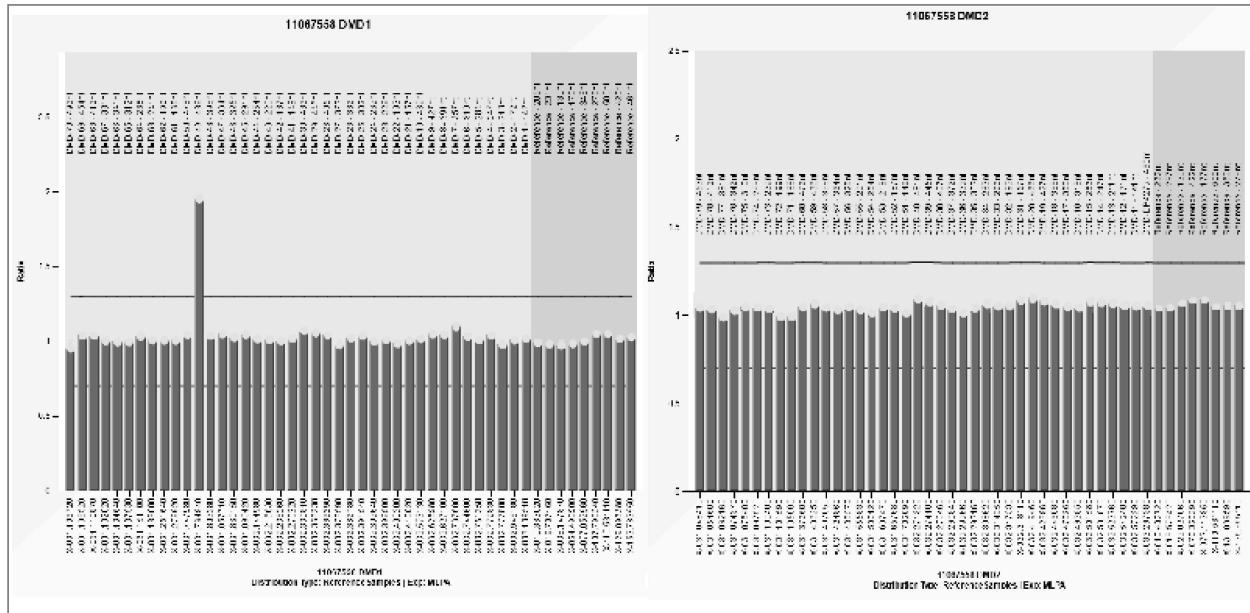


Dr. NAUSHAD  
CHIEF SCIENTIFIC OFFICER  
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<p><b>Kanaka Durga Devi.Y</b> Technical Lead -Molecular Diagnostics.</p>	<p><b>Dr. NAUSHAD</b> CHIEF SCIENTIFIC OFFICER Reg No.: 43432</p>

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### DMD Analysis by MLPA

#### Recommendations

- Genetic Counselling is recommended.
- **Clinical Correlation is strongly recommended.**
- Whole exome sequencing is recommended to rule out related single gene disorders.

#### Methodology

Multiplex Ligation-dependent probe amplification (MLPA) method is used for detection of deletion and duplication in 79 exons on DMD gene using SALSA MLPA probe mix available from MRC (Holland). Coffalyser. Net software is used for data analysis. The exon numbering used in this P034-B2 DMD-1 and P035-B1 DMD-2 product description is the exon numbering from the RefSeq transcript NM\_004006.2, which is identical to the LRG\_199 sequence.

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### DMD Analysis by MLPA

#### Clinical features

The dystrophinopathies include Duchenne muscular dystrophy (DMD, OMIM 310200), Becker muscular dystrophy (BMD, OMIM 300376), and dilated cardiomyopathy, type 3B (CMD3B, OMIM 302045). Duchenne muscular dystrophy is the most common form of congenital muscular dystrophy in all ethnic groups. DMD presents in affected boys in early childhood with difficulty walking and climbing stairs, progressive proximal weakness, pseudohypertrophy of the calves, and greatly elevated serum creatine phosphokinase (CK) levels (Darras et al. 2011). Patients become wheelchair dependent by age 13. Dilated cardiomyopathy and congestive heart failure occur in nearly all patients by their late teens or early 20s. DMD muscle biopsies show a dystrophic process with fibrosis and fatty infiltration. Dystrophin protein content in DMD patients is less than 5% of controls when measured by Western blot or immunohistochemistry (Hoffman et al. 1988).

Becker muscular dystrophy is a relatively mild form of dystrophinopathy with later onset of proximal weakness and preservation of ambulation into the third decade of life. The minimum age for wheelchair dependency in BMD is age 16. As in DMD, cardiomyopathy is a significant cause of morbidity, however, serum CK levels are less elevated than in DMD (Zatz et al. 1991). Dystrophin protein content in BMD patients varies from 20% of control levels to normal levels when measured by Western blot or immunohistochemistry (Hoffman et al. 1988). Both DMD and BMD can be associated with intellectual deficits, involving working memory and executive function (Darras et al. 2011).

DMD-related cardiomyopathy in the absence of skeletal muscle disease is a less common form of dystrophinopathy which presents in affected males between 20 and 40 years of age and later in carrier females (Beggs 1997). In some mild BMD patients, cardiomyopathy can be the presenting feature (Towbin 1998). Females who are heterozygous for a DMD causative mutation are at risk for dilated cardiomyopathy and 70% have slightly elevated CK (Schade van Westrum et al. 2011). Carriers may also present with a myopathy resembling limb-girdle muscular dystrophy (Moser and Emery 1974).

The dystrophinopathies are inherited as X-linked recessive disorders caused by DMD gene located at Xp21 which encodes dystrophin. Heterozygous female carriers are at increased risk for dilated cardiomyopathy. Approximately two-thirds of the mutations in DMD patients are deletions of one or more exons in the DMD gene. The occurrence of deletions is slightly higher in BMD patients. Duplications are found in approximately 10% of DMD patients and 20% of BMD patients. In general, in-frame deletions, which preserve partial functional dystrophin protein, are correlated with a milder (BMD) clinical phenotype (Monaco et al. 1988; Aartsma-Rus et al. 2006).

**Limitations:** DMD base pair substitutions, small deletions/duplications, deep intronic, and regulatory region mutations will not be detected. Breakpoints for large deletions/duplications will not be determined. Diagnostic errors can occur due to rare sequence variation.

#### Disclaimer

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- Test results should be interpreted in the context of clinical findings, family history, and other laboratory data. Errors in our interpretation of results may occur if information given is inaccurate or incomplete.
- This test doesn't detect SNPs in the DMD gene.
- Although all precautions are taken while conducting these tests, there is a standard error rate of approximate 1% in all genetic tests and this should be taken into consideration before any clinical decision.
- It is presumed that the specimen used to perform the test belongs to the patient specified above, such verification having been carried out at the collection level of sample.
- Diagnostic errors can occur due to rare sequence variations. Regulatory region mutations, large gene deletions/duplications and some deep intronic mutations will not be detected.

### References

- Katharina J Hoff (2009): The effect of sequencing errors on metagenomic gene prediction. *BMC Genomics*, 10:520.
- Hoffman, E. P. et al. Characterization of dystrophin in muscle-biopsy specimens from patients with Duchenne's or Becker's muscular dystrophy. *N. Engl. J. Med.* (1988). doi:10.1056/NEJM198805263182104
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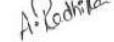
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9. Sun MX, Jing M, Hua Y, Wang JB, Wang SQ, Chen LL, Ju L, Liu YS. A female patient carrying a novel DMD mutation with non-random X-chromosome inactivation from a DMD family. BMC Med Genomics. 2024 Feb 1;17(1):46. doi: 10.1186/s12920-024-01794-x. PMID: 38303044; PMCID: PMC10832127.

**\*\*\* End Of Report \*\*\***

**Suggested clinical correlation & follow up**

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