MAYO CLINIC LABORATORIES

Test Definition: DMDZ

DMD Gene, Full Gene Analysis, Varies

Overview

Useful For

Establishing a molecular diagnosis for patients with Duchenne muscular dystrophy and Becker muscular dystrophy

Identifying variants within *DMD* known to be associated with Duchenne muscular dystrophy or Becker muscular dystrophy, allowing for predictive testing of at-risk family members

Genetics Test Information

This test utilizes next-generation sequencing to detect single nucleotide and copy number variants in one gene associated with Duchenne muscular dystrophy and Becker muscular dystrophy: *DMD*. See Method Description for additional details.

Identification of a disease-causing variant may assist with diagnosis, prognosis, clinical management, recurrence risk assessment, familial screening, and genetic counseling for Duchenne muscular dystrophy and Becker muscular dystrophy.

Testing Algorithm

For more information see Neuromuscular Myopathy Testing Algorithm

Special Instructions

- Informed Consent for Genetic Testing
- Molecular Genetics: Neurology Patient Information
- Neuromuscular Myopathy Testing Algorithm
- Informed Consent for Genetic Testing (Spanish)

Method Name

Sequence Capture and Targeted Next-Generation Sequencing followed by Polymerase Chain Reaction (PCR) and Sanger Sequencing

NY State Available

Yes

Specimen

Specimen Type

Varies

Ordering Guidance

Targeted testing for familial variants (also called site-specific or known mutations testing) is available for variants identified in the *DMD* gene. See FMTT / Familial Variant, Targeted Testing, Varies. To obtain more information about this

testing option, call 800-533-1710.

Testing for the *DMD* gene as a customized panel is available. For more information see CGPH / Custom Gene Panel, Hereditary, Next-Generation Sequencing, Varies.

Shipping Instructions

Specimen preferred to arrive within 96 hours of collection.

Specimen Required

Patient Preparation: A previous bone marrow transplant from an allogenic donor will interfere with testing. Call 800-533-1710 for instructions for testing patients who have received a bone marrow transplant.
Specimen Type: Whole blood
Container/Tube: Lavender top (EDTA) or yellow top (ACD)
Acceptable: Any anticoagulant
Specimen Volume: 3 mL
Collection Instructions:
1. Invert several times to mix blood.
2. Send whole blood specimen in original tube. **Do not aliquot.**
Specimen Stability Information: Ambient (preferred)/Refrigerated

Forms

1. **New York Clients-Informed consent is required.**
Document on the request form or electronic order that a copy is on file.
The following documents are available:
-Informed Consent for Genetic Testing (T576)
-Informed Consent for Genetic Testing (Spanish) (T826)
2. Molecular Genetics: Neurology Patient Information
3. If not ordering electronically, complete, print, and send a Neurology Specialty Testing Client Test Request (T732) with the specimen.

Specimen Minimum Volume

1 mL

Reject Due To

All specimens will be evaluated at Mayo Clinic Laboratories for test suitability.

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Varies	Varies		

Clinical & Interpretive

Clinical Information

Duchenne muscular dystrophy (DMD) is an X-linked recessive disorder characterized initially by proximal muscle

weakness beginning before age 5 years. Affected individuals typically have pseudohypertrophy of the calf muscles and exhibit toe-walking, waddling gait, and the Gower sign (climbing up the legs when rising from a seated position on the floor). Not only is skeletal muscle affected in DMD but also the smooth muscle of the gastrointestinal tract and possibly bladder as well as cardiac muscle.

Initial symptoms are followed by dramatic progression of weakness leading to loss of ambulation by age 11 or 12 years. Death is often caused by cardiac failure or by respiratory failure before age 30 years unless ventilator support is provided.

The allelic Becker muscular dystrophy (BMD) has a similar presentation, although age of onset is later, and the clinical course is much milder. Cardiac involvement can be the only sign and patients are often ambulatory into their thirties.

DMD and BMD are caused by mutations in the *DMD* gene, which encodes for dystrophin. Approximately 50% to 65% of patients have intragenic deletions and approximately 5% to 10% have intragenic duplications. Less frequently, DMD and BMD result from nondeletion and nonduplication mutations.

Approximately one-third of sporadic cases of DMD/BMD occur due to new variants. In sporadic cases, it is possible for the mother of an affected individual to have germline mosaicism. This means that the germ cells may contain a variant even if the variant is not detected in peripheral blood. In cases of germline mosaicism, which occurs with a frequency of up to 15%, further offspring are at risk of inheriting a dystrophin variant.

Reference Values

An interpretive report will be provided.

Interpretation

All detected variants are evaluated according to American College of Medical Genetics and Genomics recommendations.(1) Variants are classified based on known, predicted, or possible pathogenicity and reported with interpretive comments detailing their potential or known significance.

Cautions

Clinical Correlations:
Test results should be interpreted in the context of clinical findings, family history, and other laboratory data. Misinterpretation of results may occur if the information provided is inaccurate or incomplete.

If testing was performed because of a clinically significant family history, it is often useful to first test an affected family member. Detection of a reportable variant in an affected family member would allow for more informative testing of at-risk individuals.

To discuss the availability of additional testing options or for assistance in the interpretation of these results, contact the Mayo Clinic Laboratories genetic counselors at 800-533-1710.

Technical Limitations:
Next-generation sequencing may not detect all types of genomic variants. In rare cases, false-negative or false-positive results may occur. The depth of coverage may be variable for some target regions; assay performance below the minimum acceptable criteria or for failed regions will be noted. Given these limitations, negative results do not rule out the diagnosis of a genetic disorder. If a specific clinical disorder is suspected, evaluation by alternative methods can be

considered.

There may be regions of genes that cannot be effectively evaluated by sequencing or deletion and duplication analysis as a result of technical limitations of the assay, including regions of homology, high guanine-cytosine (GC) content, and repetitive sequences. Confirmation of select reportable variants will be performed by alternate methodologies based on internal laboratory criteria.

This test is validated to detect 95% of deletions up to 75 base pairs (bp) and insertions up to 47 bp. Deletions-insertions (delins) of 40 or more bp, including mobile element insertions, may be less reliably detected than smaller delins.

Deletion/Duplication Analysis:
This analysis targets single and multi-exon deletions/duplications; however, in some instances single exon resolution cannot be achieved due to isolated reduction in sequence coverage or inherent genomic complexity. Balanced structural rearrangements (such as translocations and inversions) may not be detected.

This test is not designed to detect low levels of mosaicism or to differentiate between somatic and germline variants. If there is a possibility that any detected variant is somatic, additional testing may be necessary to clarify the significance of results.

For detailed information regarding gene specific performance and technical limitations, see Method Description or contact a laboratory genetic counselor.

If the patient has had an allogeneic hematopoietic stem cell transplant or a recent blood transfusion, results may be inaccurate due to the presence of donor DNA. Call Mayo Clinic Laboratories for instructions for testing patients who have received a bone marrow transplant.

Reclassification of Variants:
At this time, it is not standard practice for the laboratory to systematically review previously classified variants on a regular basis. The laboratory encourages healthcare providers to contact the laboratory at any time to learn how the classification of a particular variant may have changed over time. Due to broadening genetic knowledge, it is possible that the laboratory may discover new information of relevance to the patient. Should that occur, the laboratory may issue an amended report.

Variant Evaluation:
Evaluation and categorization of variants are performed using published American College of Medical Genetics and Genomics and the Association for Molecular Pathology recommendations as a guideline.(1) Other gene-specific guidelines may also be considered. Variants are classified based on known, predicted, or possible pathogenicity and reported with interpretive comments detailing their potential or known significance. Variants classified as benign or likely benign are not reported.

Multiple in silico evaluation tools may be used to assist in the interpretation of these results. The accuracy of predictions made by in silico evaluation tools is highly dependent upon the data available for a given gene, and periodic updates to these tools may cause predictions to change over time. Results from in silico evaluation tools should be interpreted with caution and professional clinical judgment.

Rarely, incidental or secondary findings may implicate another predisposition or presence of active disease. These findings will be carefully reviewed to determine whether they will be reported.

Clinical Reference

1. Richards S, Aziz N, Bale S, et al: Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. Genet Med. 2015 May;17(5):405-424
2. Aartsma-Rus A, Ginjaar IB, Bushby K: The importance of genetic diagnosis for Duchenne muscular dystrophy. J Med Genet. 2016 Mar;53(3):145-151

Performance

Method Description

Next-generation sequencing (NGS) and/or Sanger sequencing are performed to test for the presence of variants in coding regions, and intron/exon boundaries of the gene analyzed, as well as some other regions that have known disease-causing variants. The human genome reference GRCh37/hg19 build was used for sequence read alignment. At least 99% of the bases are covered at a read depth over 30X. Sensitivity is estimated at above 99% for single nucleotide variants, above 94% for deletion-insertions (delins) less than 40 base pairs (bp), above 95% for deletions up to 75 bp and insertions up to 47 bp. NGS and/or a polymerase chain reaction-based quantitative method is performed to test for the presence of deletions and duplications in the gene analyzed.

There may be regions of genes that cannot be effectively evaluated by sequencing or deletion and duplication analysis as a result of technical limitations of the assay, including regions of homology, high guanine-cytosine (GC) content, and repetitive sequences.(Unpublished Mayo method)

The reference transcript for *DMD* gene is NM_004006.2. Reference transcript numbers may be updated due to transcript re-versioning. Always refer to the final patient report for gene transcript information referenced at the time of testing.

Confirmation of select reportable variants may be performed by alternate methodologies based on internal laboratory criteria.

PDF Report

Supplemental

Day(s) Performed

Varies

Report Available

28 to 42 days

Specimen Retention Time

Whole blood: 2 weeks (if available); Extracted DNA: 3 months

Performing Laboratory Location
Rochester

Fees & Codes

Fees

- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact Customer Service.

Test Classification

This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. It has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information

81408

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
DMDZ	DMD Gene, Full Gene Analysis	22075-6

Result ID	Test Result Name	Result LOINC® Value
617533	Test Description	62364-5
617534	Specimen	31208-2
617535	Source	31208-2
617536	Result Summary	50397-9
617537	Result	82939-0
617538	Interpretation	69047-9
618177	Additional Results	82939-0
617539	Resources	99622-3
617540	Additional Information	48767-8
617541	Method	85069-3
617542	Genes Analyzed	48018-6
617543	Disclaimer	62364-5
617544	Released By	18771-6