Duchenne/Becker Muscular Dystrophy: DMD Gene Deletion/Duplication

Test Code: EG  
Turnaround time: 2 weeks  
CPT Codes: 81161 x1

Condition Description

EGL Genetics (EGL) offers a line of tests that together provide the highest detection of DMD mutations available. Testing includes EmArray DMD -- a high resolution array CGH to detect deletions and duplications (test code EG) and full gene sequence analysis (test code EE). EGL’s comprehensive DMD testing can provide confirmation of a clinical diagnosis, characterization of the DMD gene mutation, and carrier testing for female family members and prenatal testing. The combined EmArray DMD and DMD full gene sequence analysis detects ~98-99% of mutations in both males and females, thereby providing the most comprehensive and robust analysis of the DMD gene.

Deletion/Duplication by EmArray DMD

Testing begins with EmArray DMD (test code EG), a targeted CGH array which consists of overlapping probes covering the entire 2.2MB of the DMD gene. Deletion and duplication mutations account for 65% of mutations in the DMD gene, and EmArray DMD testing will detect deletions and duplications in both males and females. This testing is indicated for individuals suspected to carry a DMD gene mutation who have not yet had testing or for individuals with previous deletion/duplication test results that do not clearly identify the breakpoints and size of the deletion or duplication. EmArray DMD testing can also be performed for female carrier testing even when an affected male is not available for testing.

Methods other than CGH array that have been used to test for DMD deletions and duplications have inherent drawbacks. These methods include multiplex PCR, Southern blotting, and MLPA. Drawbacks of these methods include difficulties in detecting small deletions, difficulties in detecting most duplications, difficulties in detecting female carriers, and the inability to determine precise boundaries of deletions and duplications. Use of these other methodologies will fail to identify a mutation in ~5-10% of individuals tested (Prior and Bridgeman, 2005). EmArray DMD testing can be performed when an individual has had previous negative deletion/duplication results by one of these other methods.

Full Gene Sequence Analysis

If no deletion or duplication is identified by EmArray DMD, testing can continue with full gene sequence analysis (test code EE). The remaining 35% of mutations in the DMD gene are point mutations and small deletions and duplications that can be detected by direct sequencing. Sequence analysis interrogates the 14kb coding region, 1.4kb of intronic sequence flanking the exon/intron boundaries, 8 DMD promoters, and 5 cryptic deep intronic mutations. This test is indicated for individuals suspected to carry a DMD mutation in whom previous testing did not identify a deletion or duplication. Rarely, novel missense changes or changes in introns other than at standard splice consensus sites are discovered. Testing of additional family members may be necessary for further interpretation in these cases. EGL follows the ACMG recommendations for interpretation and reporting of sequence variations (Richards et al., 2008).

Advantages of Using EGL’s Comprehensive DMD Testing

- Equal sensitivity and detection for males and females
- Deletions and duplications mapped to the exact nucleotide breakpoint using CGH array
- Enhanced detection of duplications that may be missed by other methods
- Rapid turn-around time
- Improved access to carrier and prenatal testing
- Carrier risk adjustment using Bayesian analysis is provided if appropriate family history information is provided

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EGL Genetics, Parent Project Muscular Dystrophy (PPMD), leading researchers, and Duchenne muscular dystrophy (DMD) clinicians are working together to offer improved testing for DMD and to develop a mutation and clinical data collection system based on the CETT Program model of collaboration.


References:


Genes

DMD

Indications

This test is indicated for:

- Males with a clinical diagnosis or symptoms of Duchenne or Becker muscular dystrophy
- Females who are at risk to be a carrier or have a family history of Duchenne or Becker muscular dystrophy
- Individuals with previous deletion/duplication test results that do not clearly identify the breakpoints and size of the deletion or duplication
- Prenatal testing is available to females who carry an identified DMD mutation

Methodology

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DNA isolated from peripheral blood is hybridized to a CGH array to detect deletions and duplications. The targeted CGH array has 385,000+ overlapping probes which covers the entire 2.2MB of the \textit{DMD} gene.

Please note that a "backbone" of probes across the entire genome are included on the array for analytical and quality control purposes. Rarely, off-target copy number variants causative of disease may be identified that may or may not be related to the patient's phenotype. Only known pathogenic off-target copy number variants will be reported. Off-target copy number variants of unknown clinical significance will not be reported.

**Detection**

**Clinical Sensitivity:** Deletion and duplication mutations account for approximately 65% of mutations to the \textit{DMD} gene in Duchenne muscular dystrophy and 85% of mutations in Becker muscular dystrophy, and are detectable by the CGH array. Detection is limited to duplications and deletions. Array CGH will not detect point mutations or intronic mutations (refer to \textit{DMD} full gene sequencing).

**Reference Range**

Ratio of 1.2 for duplication.

**Specimen Requirements**

Submit only 1 of the following specimen types

* Preferred specimen type: Whole Blood

**Type: Whole Blood**

Specimen Requirements:

In EDTA (purple top) tube:

- Infants (2 years): 3-5 ml
- Older Children & Adults: 5-10 ml

Specimen Collection and Shipping: Refrigerate until time of shipment. Ship sample within 5 days of collection at room temperature with overnight delivery.

**Type: Saliva**

Specimen Requirements:

Oragene\textsuperscript{TM} Saliva Collection kit (available through EGL) used according to manufacturer instructions.

Specimen Collection and Shipping: Store sample at room temperature. Ship sample within 5 days of collection at room temperature with overnight delivery.

**Special Instructions**

Click here for the Dystrophin Clinical Information Form to send with the sample.

**Related Tests**

- Full gene sequence analysis of the \textit{DMD} gene is available to test for point mutations and mutations in the \textit{DMD} promoter and intronic regions.