



EmArray *Dystrophin* CGH ©2007

Emory Genetics Laboratory now offers EmArray *Dystrophin*, a new line of tests consisting of a high resolution array CGH and a resequencing array to detect mutations in the *dystrophin* gene. The use of array permits detection of **deletions, duplications and point mutations as well as previously unidentified deep intronic mutations** and **can be used for testing in females and prenatal analysis.**

Emory Genetics Laboratory, Parent Project Muscular Dystrophy, leading researchers, and DMD clinicians are working together to offer improved testing and develop a mutation and clinical data collection system based on the CETT Program model of collaboration.

Current *dystrophin* diagnostic testing typically screens for the most common deletions and duplications. **Methods currently used have inherent drawbacks:** Multiplex PCR, southern blot analysis and point mutation detection is very laborious and costly. Southern blot analysis is difficult to interpret and is prone to errors. Moreover, traditional detection of deletions and duplications does not provide precise identification of the underlying mutation and the size and breakpoints remain unknown. Use of these combined methodologies will fail to identify a mutation in ~10-12% of individuals tested. In addition, female carrier testing with these approaches is *limited when a related affected male is not available.*

What is EmArray *Dystrophin* CGH?

EmArray *Dystrophin* is a CGH array with overlapping probes covering the entire 2.2MB of the *dystrophin* gene to detect deletions and duplications. Deletions and duplications can be detected in males and females. This test is indicated for individuals suspected to carry a *dystrophin* 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.

Why use EmArray *dystrophin*?

Diagnostic testing using EmArray *Dystrophin* provides confirmation of clinical diagnosis, characterization of the *dystrophin* gene mutation, and enables carrier testing for female family members and prenatal testing. Additional advantages include:

- **Equal sensitivity and detection for males and females**
- **Deletions and duplication mapped to the exact nucleotide breakpoint**
- **Enhanced detection of duplications that may be missed by other methods**
- **Rapid turn-around time**
- **Improved access to carrier and prenatal testing**

The combined detection of both methods is estimated to be 99%, thereby providing the most comprehensive and robust analysis of the *dystrophin* gene.

Duchenne and Becker Muscular Dystrophy

Duchenne and Becker muscular dystrophies (DMD/BMD) are a spectrum of neuromuscular diseases caused by gene mutations in the *dystrophin* gene, located on the X chromosome. Becker and Duchenne are both characterized by progressive muscle wasting and proximal muscle weakness but differ in severity and age of onset. Individuals with Duchenne muscular dystrophy often have muscle weakness that is progressive from early childhood. Calf pseudohypertrophy is common. Dilated cardiomyopathy may develop in adolescence and may become life threatening. Some individuals with Duchenne have mild mental retardation. Becker muscular dystrophy generally presents at a later age and progresses at a slower rate. Individuals with Becker muscular dystrophy may develop dilated cardiomyopathy that may be life-threatening. Women who are carriers of a *dystrophin* mutation may show observable symptoms including: histological abnormalities in skeletal muscle (70%), elevated serum creatine kinase activity (45-70%), clinical symptoms such as muscle weakness (5-10%), and are at risk for dilated cardiomyopathy.

The incidence of DMD is approximately 1 in 3500 newborn males and the incidence of BMD is approximately 1 in 18,000 newborn males. Two thirds of these cases are inherited, while one third of DMD/BMD cases result from new mutations, where the mother is not a carrier for the *dystrophin* mutation. Large rearrangements in the *dystrophin* gene are found in about two thirds of DMD patients, with approximately 60% carrying deletions of one or more exon, 5-10% carrying duplications or one or more exon. The remaining cases are caused by point mutations or smaller deletions/duplications in the *dystrophin* gene.

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 *dystrophin* mutation

Related tests:

The *Dystrophin* Resequencing Array is available to test for promoter, intronic and point mutations. A cDNA sequencing assay is also available for functional characterization of novel variants in the *dystrophin* gene (Please call Emory Genetics Laboratories for more information)

Methodology:

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 *dystrophin* gene. Deletions and duplications will subsequently confirmed using multiplex PCR (males) and MLPA (females).

Clinical Sensitivity:

Deletion and duplication mutations account for approximately 65% of mutations to the *dystrophin* 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 the EmArray *Dystrophin* Resequencing Array).

Reference Range:

Ratio of <0.8 for deletion; ratio of >1.2 for duplication.

Turnaround Time

One week

Specimen Requirements

Collect whole blood

- Children under 2 years: Collect 3-5 ml blood in a purple top (EDTA) or yellow top (ACD) tube.
- Older children and adults: Collect 5-10 ml blood in a purple top (EDTA) or yellow top (ACD) tube.

Refrigerate sample until shipment. Send the sample at room temperature using overnight delivery within 7 days of collection.

CPT codes:

83890, 83892 (x2), 83894, 83896 (x10), 83897, 88384, 88385, 88386

Contact Emory Genetics Laboratory with your questions by calling (404)778-8500.