Emery-Dreifuss Muscular Dystrophy, X-linked: *EMD* Gene Deletion/Duplication

**Test Code:** EMDDX  
**Turnaround time:** 2 weeks  
**CPT Codes:** 81404 x1

### Condition Description

The clinical diagnosis of Emery-Dreifuss muscular dystrophy (EDMD) is based on the presence of the following triad:

- Joint contractures that begin in early childhood: contractures of the elbow flexors, Achilles tendons (heels), and neck extensors resulting in limitation of neck flexion, followed by limitation of extension of the entire spine
- Slowly progressive wasting and weakness of the humero-peroneal/scapulo-peroneal muscles in the early stages that later extends to the scapular and pelvic girdle muscles
- Cardiac disease with conduction defects and arrhythmias: atrial fibrillation, supraventricular and ventricular arrhythmias, atrio-ventricular and bundle-branch blocks, dilated cardiomyopathy

Age of onset, severity, and progression of muscle and cardiac involvement demonstrate both inter- and intrafamilial variability. Clinical variability ranges from early onset with severe presentation in childhood to late onset with slow progression in adulthood. In general, joint contractures appear during the first two decades, followed by muscle weakness and wasting. Cardiac involvement usually occurs after the second decade.

The two genes known to be associated with EDMD are *EMD*, encoding emerin and causing X-linked EDMD (XL-EDMD), and *LMNA*, encoding lamins A and C and causing autosomal dominant EDMD (AD-EDMD) and autosomal recessive EDMD (AR-EDMD). The diagnosis of X-linked EDMD is based on immunodetection of emerin in various tissues and molecular genetic testing of *EMD*. The diagnosis of AD-EDMD and AR-EDMD is based on clinical findings, family history, and molecular genetic testing of *LMNA*. About 45% of individuals with EDMD who have emerin detected on immunocytochemistry and/or immunoblotting have no mutation identified in *EMD* or *LMNA*, suggesting that these individuals are either misdiagnosed or that other as yet unidentified genes are involved in EDMD.

This testing is for mutations in the *EMD* gene (Xq28) only. For testing of the *LMNA* gene, please see the test description for Limb-Girdle Muscular Dystrophy Type 1B: *LMNA* Full Gene Sequencing (test code SLMNA).

Sequencing of the *EMD* gene detects an *EMD* mutation in more than 99% of individuals with established X-linked inheritance and/or with no emerin detected by immunodetection methods.

For patients with suspected X-linked EDMD, sequence analysis is recommended as the first step in mutation identification. For patients in whom mutations are not identified by full gene sequencing, deletion/duplication analysis is appropriate.

### References:

- GeneReviews: [Emery-Dreifuss Muscular Dystrophy](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5422107/)

### Genes

**EMD**

### Indications

This test is indicated for:

- Confirmation of a clinical diagnosis of X-linked Emery-Dreifuss muscular dystrophy in individuals who have tested negative for sequence analysis
- Carrier testing in adult females with a family history of X-linked Emery-Dreifuss muscular dystrophy who have tested negative for sequence analysis

### Methodology

DNA isolated from peripheral blood is hybridized to a CGH array to detect deletions and duplications. The targeted CGH array has overlapping probes which cover the entire genomic region. 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

Detection is limited to duplications and deletions. The CGH array will not detect point or intronic mutations. Results of molecular analysis must be interpreted in the context of the patient's clinical and/or biochemical phenotype.

### Specimen Requirements

Disclaimer: This information is confidential and subject to change without notice. It may not be reproduced in whole or part unless authorized in writing by an authorized EGL representative.
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™ 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**

Submit copies of diagnostic biochemical test results with the sample, if appropriate. Contact the laboratory if further information is needed.

Sequence analysis is required before deletion/duplication analysis by targeted CGH array. If sequencing is performed outside of EGL Genetics, please submit a copy of the sequencing report with the test requisition.

**Related Tests**

- Sequence analysis of the *EMD* gene is available and is required before deletion/duplication analysis.
- Analysis of the *LMNA* gene is also available for autosomal recessive and autosomal dominant Emery-Dreifuss MD.
- Custom diagnostic mutation analysis (KM) is available to family members if mutations are identified by targeted mutation testing or sequencing analysis.
- Prenatal testing is available for known familial mutations only. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.