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 \textit{EMD}, encoding emerin and causing X-linked EDMD (XL-EDMD), and \textit{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 \textit{EMD}. The diagnosis of AD-EDMD and AR-EDMD is based on clinical findings, family history, and molecular genetic testing of \textit{LMNA}. About 45% of individuals with EDMD who have emerin detected on immunocytochemistry and/or immunoblotting have no mutation identified in \textit{EMD} or \textit{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 \textit{EMD} gene (Xq28) only. For testing of the \textit{LMNA} gene, please see the test description for Limb-Girdle Muscular Dystrophy Type 1B: \textit{LMNA} Full Gene Sequencing (test code SLMNA).

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

References:
- GeneReviews: Emery-Dreifuss Muscular Dystrophy
- OMIM #310300 Emery-Dreifuss Muscular Dystrophy 1

Genes

\textbf{EMD}

Indications

This test is indicated for:

- Confirmation of a clinical diagnosis of X-linked Emery-Dreifuss muscular dystrophy
- Carrier testing in adult females with a family history of X-linked Emery-Dreifuss muscular dystrophy

Methodology

PCR amplification of 6 exons contained in the \textit{EMD} gene is performed on the patient's genomic DNA. Direct sequencing of amplification products is performed in both forward and reverse directions, using automated fluorescence deoxy sequencing methods. The patient's gene sequences are then compared to a normal reference sequence. Sequence variations are classified as mutations, benign variants unrelated to disease, or variations of unknown clinical significance. Variants of unknown clinical significance may require further studies of the patient and/or family members. This assay does not interrogate the promoter region, deep intronic regions, or other regulatory elements, and does not detect large deletions.

Detection

Clinical Sensitivity: Sequencing of the \textit{EMD} gene detects an \textit{EMD} mutation in more than 99% of individuals with established X-linked inheritance and/or with no emerin detected by immunodetection methods. Mutations in the promoter region, some mutations in the introns and other regulatory element mutations cannot be detected by this analysis. Large deletions will not be detected by this analysis. Results of molecular analysis should be interpreted in the context of the patient's biochemical phenotype.

Analytical Sensitivity: \(\sim 99\%\)

Specimen Requirements
Submit only 1 of the following specimen types

* Preferred specimen type: Whole Blood

**Type: Whole Blood**

Specimen Requirements:

In EDTA (purple top) or ACD (yellow 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.

**Related Tests**

- Sequence 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.