

Cardiovascular Diseases Genetic Testing Program

EMD Sequencing

The *EMD* gene encodes emerin, an inner nuclear membrane protein. Emerin is found in many cell types including skeletal and cardiac muscle. The exact function of emerin in these cells has not been identified, although protein function is thought to include stabilization of the nuclear envelope, nuclear assembly, and gene expression (1). Mutations in the *EMD* gene have been identified in individuals with Emery-Dreifuss muscular dystrophy (EDMD). EDMD is characterized by early onset of contractures, humeroperoneal muscle wasting and weakness and cardiac conduction defects, most often heart block (1, 2). *EMD* has also been recognized as a non-syndromic cause of atrial fibrillation and sinus node dysfunction (3).

The *EMD* gene contains 6 exons and is located at chromosome Xq28. Mutations in *EMD* account for approximately 60% of cases of X-linked EDMD (4, 5). *EMD* mutations are inherited in an X-linked recessive manner with variable expressivity. Affected males are expected to develop arrhythmias and contractures by the third decade (1). Female carriers of *EMD* mutations are typically asymptomatic but may also be affected.

Indication

EMD sequencing is utilized to confirm a clinical diagnosis of Emery-Dreifuss muscular dystrophy and as carrier testing in females with a family history of X-linked EDMD. It may also be considered in cases of non-syndromic atrial fibrillation and/or sinus node dysfunction that appear to follow X-linked inheritance. Other genes have been identified to cause EDMD with autosomal dominant, autosomal recessive and X-linked inheritance patterns, and should be considered if this individual meets clinical criteria for EDMD and sequencing of *EMD* reveals no mutation. We recommend testing the most clearly affected individual in the family whenever possible.

Molecular Genetics Laboratory

Shipping Instructions

Please enclose a test requisition form with sample. All information must be complete before sample can be processed. Samples may be shipped at room temperature by overnight Federal Express to arrive Monday through Friday.

Ship to:

Molecular Genetics Lab
Cincinnati Children's Hospital
3333 Burnet Ave. NRB 1042
Cincinnati, OH 45229

Phone: 513-636-4474
Fax: 513-636-4373

Methodology:

All coding exons as well as the exon/intron boundaries and a portion of untranslated regions of the gene(s) are amplified by PCR. Genomic DNA sequences from both forward and reverse directions are obtained by automatic fluorescent detection using an *ABI PRISM® 3730 DNA Analyzer*. Sequence variants different from National Center for Biotechnology Information GenBank references are further evaluated for genetic significance. If a mutation is identified, known familial mutation analysis will be available for additional family members.

Sensitivity & Accuracy:

Greater than 98.5% of the mutations in exons 1-6 of *EMD* are detectable by sequence based methods. Sequencing does not detect deletions or duplications in carrier females but may detect these changes in affected males. Mutations in *EMD* account for approximately 61% of X-linked Emery-Dreifuss muscular dystrophy.

References:

1. Morris, G.E. and Manilal, S. (1999) Heart to heart: from nuclear proteins to Emery-Dreifuss muscular dystrophy. *Human Molecular Genetics*. 8:1847-1851.
2. Boriani, G., Gallina, M., Merlini, L., et al. (2003) Clinical Relevance of Atrial/Fibrillation/Flutter, Stroke, Pacemaker Implant, and Heart Failure in Emery-Dreifuss Muscular Dystrophy: A Long-Term Longitudinal Study. *Stroke*. 34:901-908.
3. Karst, M.L., Herron, K.J., Olson, T.M. (2007) X-linked Nonsyndromic Sinus Node Dysfunction and Atrial Fibrillation Caused by *Emerin* Mutation. *Journal of Cardiovascular Electrophysiology*. 19: 510- 515.
4. Gueneau, L., Bertrand, A.T., Jais, J., et al. (2009) Mutations of the *FHL1* Gene Cause Emery-Dreifuss Muscular Dystrophy. *The American Journal of Human Genetics*. 85:338-353.
5. Bonne, G., Leturcq, F., Yaou, R.B. (2010) Emery-Dreifuss Muscular Dystrophy. *GeneReviews*. Retrieved September 21, 2010.

Specimen:

Peripheral blood in EDTA tube

Adult: 3-5mL

Child: 3-5mL

Infant: 1-3mL

For other specimen types, please contact us at 513-636-4474

Turnaround Time:

Full Mutation Analysis 2-4 weeks

Known Mutation Analysis 1-2 weeks

CPT Codes:

Full Gene Sequencing 81405

Additional Family Members 81403