Assay Summary

Lamin A/C (LMNA) Gene Mutation Analysis

Emery-Dreifuss Muscular Dystrophy (Autosomal), Limb-Girdle Muscular Dystrophy (Type 1B), Dilated Cardiomyopathy, Charcot-Marie-Tooth Neuropathy Type 2, Familial Partial Lipodystrophy, Dunnigan Type, Hutchinson-Gilford Progeria Syndrome, Atypical Werner Syndrome, Mandibuloacral Dysplasia

Synopsis

Germline mutations in the LMNA gene encoding lamins A and C have been found in patients with Emery-Dreifuss muscular dystrophy (autosomal dominant, autosomal recessive, and sporadic forms of the disease), in limb-girdle muscular dystrophy (Type 1B), in Charcot-Marie-Tooth disorder type 2, and in Dunnigan type familial partial lipodystrophy. Mutations in the LMNA gene have also been detected in patients with Hutchinson-Gilford progeria syndrome, atypical Werner syndrome, and mandibuloacral dysplasia. Mutations in this gene also have been reported to cause familial dilated cardiomyopathy, a genetically heterogeneous disease caused by perhaps as many as eleven different genes, only a few of which have been identified. Identification of lamin A/C gene mutations in patients with any of these diseases may permit identification of carriers as well as individuals who are at high risk for dilated cardiomyopathy in these families.

Indications for testing

Patients with non-X-linked Emery-Dreifuss muscular dystrophy, limb-girdle muscular dystrophy (Type 1B), an inherited form of dilated cardiomyopathy, or other diseases listed above may consider, with genetic counseling, lamin A/C (LMNA) gene sequence analysis. If a mutation is identified in the patient, other at-risk family members may be tested for carrier status.

Methodology

Coding exons and associated intron junctions are captured and enriched using custom Agilent SureSelect technology. Next-generation sequencing is performed on Illumina MiSeq. Additional Sanger sequencing is performed for any regions with insufficient depth of coverage or for verification of suspect variant calls. Targeted testing for known familial mutation is performed by Sanger sequencing.

Limitations

The mutation analysis will not detect mutations located in regions of the LMNA gene that are not analyzed (non-coding exon regions, intron regions other than the splice junctions, and upstream and downstream regions). The method also will not detect gross genetic alterations including most duplications, inversions, or deletions. Some sequence alterations that may be detected (such as those causing missense or synonymous changes) will be of unknown clinical significance. Interpretation of test results should be in the context of the patient’s ethnicity, clinical and family histories, and other laboratory test results.
**Specimen Requirements**

Blood samples: 2 tubes with a total of 6 ccs in ACD (yellow top) or EDTA (lavender top) tubes. Keep at ambient temperature and ship by overnight courier. Samples must be received in our laboratory within 72 hours of draw.

**Note:**

i) for infants, a minimum of 3 ccs is sufficient.

ii) we accept DNA; at least 10 micrograms is required.

**Test Request Form (TRF)**

A completed CMDL TRF is required for each specimen. Please submit the completed TRF with the specimen. Complete testing and billing information must be provided before the specimen is processed.

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<th>Order Codes</th>
<th>CPT Codes</th>
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<tbody>
<tr>
<td>LMNA-SEQ</td>
<td>81406, G0452</td>
<td>3 wks</td>
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<td>(Lamin A/C (LMNA) gene, full gene sequencing by NGS)</td>
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<td>LMNA-CAS</td>
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<td>(Lamin A/C (LMNA) gene, targeted mutation analysis, known mutation)</td>
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**References**


NOTE: This test is performed pursuant to a license agreement with Roche Molecular Systems, Inc.