Overview

Useful For
Molecular confirmation of clinically suspected cases of c9FTD/ALS, frontotemporal dementia (FTD), or amyotrophic lateral sclerosis (ALS)

Presymptomatic testing for individuals with a family history of c9FTD/ALS and a documented expansion in the C9orf72 gene

Testing Algorithm
See Inherited Motor Neuron Disease Testing Algorithm in Special Instructions.

Special Instructions
- Informed Consent for Genetic Testing
- Molecular Genetics: Neurology Patient Information
- Inherited Motor Neuron Disease Testing Algorithm
- Informed Consent for Genetic Testing (Spanish)

Method Name
Polymerase Chain Reaction (PCR)

NY State Available
Yes

Specimen

Specimen Type
Varies

Shipping Instructions
Specimen preferred to arrive within 96 hours of collection.

Specimen Required
Patient Preparation: A previous bone marrow transplant from an allogenic donor will interfere with testing. Call 800-533-1710 for instructions for testing patients who have received a bone marrow transplant.

Specimen Type: Whole blood

Container/Tube:
Preferred: Lavender top (EDTA) or yellow top (ACD)

Acceptable: Any anticoagulant

Specimen Volume: 3 mL

Collection Instructions:
1. Invert several times to mix blood.
2. Send specimen in original tube.

**Forms**

1. **New York Clients-Informed consent is required.** Document on the request form or electronic order that a copy is on file. The following documents are available in Special Instructions:

   - *Informed Consent for Genetic Testing* (T576)
   - *Informed Consent for Genetic Testing (Spanish)* (T826)

2. **Molecular Genetics: Neurology Patient Information** in Special Instructions

3. If not ordering electronically, complete, print, and send a *Neurology Specialty Testing Client Test Request* (T732) with the specimen.

**Specimen Minimum Volume**

1 mL

**Reject Due To**

All specimens will be evaluated at Mayo Clinic Laboratories for test suitability.

**Specimen Stability Information**

<table>
<thead>
<tr>
<th>Specimen Type</th>
<th>Temperature</th>
<th>Time</th>
<th>Special Container</th>
</tr>
</thead>
<tbody>
<tr>
<td>Varieties</td>
<td>Ambient (preferred)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Frozen</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Refrigerated</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Clinical and Interpretive**

**Clinical Information**

Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disease affecting the upper and lower motor neurons. The disease is characterized by progressive spasticity, muscle wasting and paralysis, typically leading to death from respiratory failure.

Frontotemporal dementia (FTD) is a dementia syndrome that predominantly involves the frontal and temporal lobes of the brain. Clinical presentation is variable and includes progressive changes in behavior and personality and language disturbances. Affected individuals may also exhibit extrapyramidal signs.

ALS and FTD are now thought to represent an overlapping spectrum of disease. Recent literature has found that approximately 40% of familial ALS, 25% of familial FTD, and 90% of familial ALS/FTD cases have a large hexanucleotide repeat (GGGGCC) expansion in a noncoding region of *C9orf72*. At lower frequency, *C9orf72* hexanucleotide repeat expansions have also been observed in individuals with sporadic ALS, FTD, and ALS/FTD. The vast majority of individuals affected with a *C9orf72*-related disorder (c9ALS, c9FTD, or c9ALS/FTD) have hexanucleotide repeat expansions in the hundreds to thousands, while unaffected individuals have repeat sizes less than 20. The significance of repeat sizes between 20 and 100 repeats is currently unclear as both healthy controls and individuals with ALS and/or FTD phenotypes have been reported with repeat sizes in this range.
Reference Values
Normal alleles (reference): <20 GGGGCC repeats
Indeterminate alleles: 20-100 GGGGCC repeats
Pathogenic alleles: >100* GGGGCC repeats

*The exact cutoff for pathogenicity is currently undefined. Although additional studies are needed to confirm if 100 repeats is the cutoff for pathogenicity, most individuals affected with a C9orf72-related disorder have C9orf72 hexanucleotide repeat expansions with hundreds to thousands of repeats.

An interpretive report will be provided.

Interpretation
An interpretive report will be provided.

Cautions
For predictive testing, it is important to first document the presence of the hexanucleotide repeat expansion in the C9orf72 gene in an affected family member to confirm that the repeat expansion is the underlying mechanism of disease in the family.

We strongly recommend that patients undergoing predictive testing receive genetic counseling both prior to testing and after results are available.

Predictive testing of an asymptomatic child is not recommended.

Test results should be interpreted in the context of clinical findings, family history, and other laboratory data. Errors in our interpretation of results may occur if information given is inaccurate or incomplete.

Due to somatic mosaicism, repeat size identified in the peripheral blood specimen may not reflect the repeat size in untested tissues (e.g., central nervous system). In addition, a negative result does not rule out the presence of a mutation in the mosaic state that may be present but below the limit of detection of this assay (approximately 5%).

Rare sequence variants immediately downstream of the C9orf72 repeat region may interfere with genotype results but are not expected to affect repeat-primed peaks.

Rare undocumented polymorphisms in PCR primer binding regions may lead to false negative results.

This test does not assess methylation status of the C9orf72 gene.

Clinical Reference
Test Definition: C9ORF
C9orf72, Molecular Analysis


Performance

Method Description

PDF Report
No

Day(s) and Time(s) Test Performed
Tuesday; 10 a.m.

Analytic Time
5 days
Maximum Laboratory Time
11 days

Specimen Retention Time
Whole Blood: 2 weeks (if available); Extracted DNA: 3 months

Performing Laboratory Location
Rochester

Fees and Codes

Fees
- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their Regional Manager. For assistance, contact Customer Service.

Test Classification
This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the U.S. Food and Drug Administration.

CPT Code Information
81479

LOINC® Information

<table>
<thead>
<tr>
<th>Test ID</th>
<th>Test Order Name</th>
<th>Order LOINC Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>C9ORF</td>
<td>C9orf72, Molecular Analysis</td>
<td>81846-8</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Result ID</th>
<th>Test Result Name</th>
<th>Result LOINC Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>52852</td>
<td>Result Summary</td>
<td>50397-9</td>
</tr>
<tr>
<td>52853</td>
<td>Result</td>
<td>77635-1</td>
</tr>
<tr>
<td>52854</td>
<td>Interpretation</td>
<td>69047-9</td>
</tr>
<tr>
<td>52855</td>
<td>Reason for Referral</td>
<td>42349-1</td>
</tr>
<tr>
<td>52856</td>
<td>Specimen</td>
<td>31208-2</td>
</tr>
<tr>
<td>55158</td>
<td>Method</td>
<td>49549-9</td>
</tr>
<tr>
<td>52857</td>
<td>Source</td>
<td>31208-2</td>
</tr>
<tr>
<td>52858</td>
<td>Released By</td>
<td>18771-6</td>
</tr>
</tbody>
</table>