Overview

Useful For
Diagnostic confirmation of Wilson disease

Genetics Test Information
Ceruloplasmin, serum copper, and urine copper studies are recommended prior to submitting sample. Test includes next-generation sequencing of exons 1 through 21 and for the common Sardinian promoter mutation. Sanger sequencing may be performed to confirm detected variants.

Testing Algorithm
See Wilson Disease Testing Algorithm in Special Instructions.

Special Instructions
- Molecular Genetics: Congenital Inherited Diseases Patient Information
- Informed Consent for Genetic Testing
- Wilson Disease Testing Algorithm
- Informed Consent for Genetic Testing (Spanish)

Method Name
Custom Sequence Capture and Targeted Next-Generation Sequencing (NGS) followed by Polymerase Chain Reaction (PCR) and Sanger Sequencing when appropriate

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.

**Additional Information:** To ensure minimum volume and concentration of DNA is met, the preferred volume of blood must be submitted. Testing may be canceled if DNA requirements are inadequate.

**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: Congenital Inherited Diseases Patient Information** (T521) in Special Instructions

3. If not ordering electronically, complete, print, and send 1 of the following forms with the specimen:
   - Inborn Errors of Metabolism Test Request (T798)
   - Gastroenterology and Hepatology Client Test Request (T728)

**Specimen Minimum Volume**

1 mL

**Reject Due To**

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

**Specimen Stability Information**

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<th>Temperature</th>
<th>Time</th>
<th>Special Container</th>
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**Clinical and Interpretive**

**Clinical Information**

Wilson disease (WD) is an autosomal recessive disorder that results from the body’s inability to excrete excess copper. Typically, the liver releases excess copper into the bile. Individuals with WD lack the necessary enzyme that facilitates clearance of copper from the liver to bile. As a result, copper accumulates first in the liver and gradually in other organs. The brain, kidneys, bones, and corneas can also be affected. WD affects approximately 1 in 30,000 people worldwide, with a carrier frequency of approximately 1 in 90 individuals.

The primary clinical manifestations of WD are hepatic and neurologic. Hepatic disease can be quite variable, ranging from hepatomegaly or other nonspecific symptoms that mimic viral hepatitis to severe liver damage, such as cirrhosis. Neurologic symptoms of WD can include poor fine-motor coordination, ataxia, and dysphagia. Psychiatric
manifestations are reported in approximately 20% of individuals with WD. A characteristic ophthalmologic finding is the Kayser-Fleischer ring. Individuals with WD typically begin to show symptoms of liver dysfunction or neurologic disease in the first or second decade of life. If not treated, WD can cause liver failure, severe brain damage, and even death.

A variety of laboratory tests are recommended in the initial evaluation for WD. In approximately 95% of cases, serum ceruloplasmin is below normal. Additionally, patients with WD show decreased copper in serum, increased copper in urine, and significantly elevated copper on liver biopsy. While liver biopsy is not recommended as a first-tier screening test for WD, it can be useful to help interpret discrepant biochemical or molecular results. The other tests should be performed prior to sequence analysis of the \( \text{ATP7B} \) gene, the gene responsible for WD. More than 300 disease-causing mutations have been identified in the \( \text{ATP7B} \) gene. Most mutations are family-specific with the exception of the H1069Q mutation, which accounts for greater than 50% of identified disease alleles in the Northern European Caucasian population.

See Wilson Disease Testing Algorithm in Special Instructions for additional information.

Reference Values

An interpretive report will be provided.

Interpretation

All detected alterations are evaluated according to American College of Medical Genetics and Genomics (ACMG) recommendations.(1) Variants are classified based on known, predicted, or possible pathogenicity and reported with interpretive comments detailing their potential or known significance.

Cautions

Clinical Correlations:

A small percentage of individuals who are carriers or have a diagnosis of Wilson disease (WD) may have a mutation that is not identified by this method (eg, large genomic deletions, promoter mutations, deep intronic mutations). The absence of a mutation, therefore, does not eliminate the possibility of positive carrier status or the diagnosis of WD. For carrier testing, it is important to first document the presence of an \( \text{ATP7B} \) gene mutation in an affected family member.

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

Technical Limitations:

In some cases, DNA variants of undetermined significance may be identified.

Due to the limitations of next-generation sequencing, small deletions and insertions may not be detected by this test. If a diagnosis is still suspected, contact a molecular genetic counselor in the Genomics Laboratory at 800-533-1710 for more information regarding follow-up testing options.

Rare polymorphisms exist that could lead to false-negative or false-positive results. If results obtained do not match the clinical findings, additional testing should be considered.

Evaluation Tools:

Multiple in-silico evaluation tools were used to assist in the interpretation of these results. These tools are updated regularly; therefore changes to these algorithms may result in different predictions for a given alteration. Additionally, the predictability of these tools for the determination of pathogenicity is currently unvalidated.
Unless reported or predicted to cause disease, alterations that do not result in an amino acid substitution are not reported.

Reclassification of Variants-Policy:

All detected alterations are evaluated according to American College of Medical Genetics and Genomics (ACMG) recommendations. Variants are classified based on known, predicted, or possible pathogenicity and reported with interpretive comments detailing their potential or known significance. At this time, it is not standard practice for the laboratory to systematically review likely pathogenic alterations or variants of uncertain significance that are detected and reported. The laboratory encourages health care providers to contact the laboratory at any time to learn how the status of a particular variant may have changed over time.

Supportive Data

Ninety-six normal Caucasian specimens were screened for the presence of benign polymorphisms in the ATP7B gene. Selected exons from 21 of these specimens were confirmed by direct sequencing to have at least a single polymorphism. One normal specimen was found to be a carrier of an ATP7B mutation (IVS11-2A>G). Five Wilson disease patients with known ATP7B mutations were sequenced with 100% concordance.

Clinical Reference


Performance

Method Description

Next-generation sequencing is used to test for the presence of a mutation in all coding exons and intron/exon boundaries, as well as a portion of the 5â€™ untranslated region (UTR), of the ATP7B gene. Sanger sequencing is used to confirm alterations detected by next-generation sequencing when appropriate. (Unpublished Mayo method)

PDF Report

No

Day(s) and Time(s) Test Performed

Performed weekly; Varies

Analytic Time

14 days
Test Definition: WDZ
Wilson Disease Full Gene Analysis

Maximum Laboratory Time
20 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
81406

LOINC® Information

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