Wilson Disease (ATP7B) Sequencing

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Wilson disease (WD) is a rare inherited genetic disorder caused by pathogenic variants in the *ATP7B* gene, resulting in excessive amounts of copper accumulating in the body, particularly in the liver, brain, and eyes. Signs and symptoms most often appear during the teens but may appear as early as age 6 or as late as the mid-40s. Liver disease is typically the initial feature of Wilson disease in affected children and young adults. Nervous system or psychiatric problems are often the initial features in individuals diagnosed in adulthood, and commonly occur in young adults. For additional details on diagnostic testing for WD, refer to the ARUP Consult Wilson Disease topic and the Wilson Disease Testing Algorithm.

Featured ARUP Testing

Wilson Disease (ATP7B) Sequencing 3004411

Method: Massively Parallel Sequencing

Preferred test for genetic confirmation of Wilson disease or determination of carrier status

If a familial sequence variant has been previously identified, targeted sequencing for that variant may be appropriate; refer to the Laboratory Test Directory for additional information.

Disease Overview

Symptoms

- Neurologic: clumsiness, tremors, difficulty walking, speech problems
- Psychiatric: impaired thinking, depression, anxiety, mood swings
- Other: Kayser-Fleischer ring, abnormalities in eye movement

Diagnostic Issues

- Affected individuals occasionally have normal biochemical test results
- Up to 20% of WD carriers have equivocal biochemical findings

Genetics

Gene

ATP7B

Inheritance

Autosomal recessive

Penetrance

Age dependent, may be reduced

Test Interpretation

Clinical Sensitivity

98%[1]

Analytic Sensitivity

For massively parallel sequencing:

Variant Class	Analytic Sensitivity (PPA) Estimate[a] (%)	Analytic Sensitivity (PPA) 95% Credibility Region[a] (%)
SNVs	>99	96.9-99.4
Deletions 1-10 bp	93.8	84.3-98.2
Deletions 11-44 bp	>99	87.8-100
Insertions 1-10 bp	94.8	86.8-98.5
Insertions 11-23 bp	>99	62.1-100

[a]Gene included on this test is a subset of a larger methods-based validation from which the PPA values are derived.

bp, base pairs; PPA, positive percent agreement; SNVs, single nucleotide variants

Results

Results as Reported in Patient Chart	Variant(s) Detected	Clinical Significance
Positive	Two pathogenic ATP7B gene variants detected on opposite chromosomes	Consistent with a diagnosis of WD
Negative	No pathogenic ATP7B variants detected	Significantly reduces the likelihood of being affected with or a carrier of WD
See note	One pathogenic ATP7B gene variant detected	Individual is at least a carrier of WD and may be affected with WD if an undetected variant is present on the opposite chromosome
	Variants of uncertain clinical significance may be identified	Uncertain

Limitations

- Diagnostic errors can occur due to rare sequence variations
- Not determined or evaluated:
  - Regulatory region variants, including the Sardinian founder variant, c.-436_-422del15
  - Deep intronic variants
  - Large deletions/duplications
  - Variants in genes other than *ATP7B*

References

1. Stättermayer A, Zoller HM, Weiss KH, et al. Patients with Wilson disease without detectable ATP7B mutations. Abstract 464. Boston, MA: 65th Annual Meeting of the American Association for the Study of Liver Diseases. 2014.

Related Information

Wilson Disease
Wilson Disease Testing Algorithm