PREVENTION GENETICS
DISEASE PREVENTION THROUGH GENETIC TESTING

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Wilson Disease/Hepatolenticular Degeneration *via* *ATP7B* Gene Sequencing -- Test # 460

Brief Description of Clinical Features: Wilson disease (WD, OMIM 277900), also called hepatolenticular degeneration, is a disorder of copper metabolism. WD results from the toxic accumulation of copper mainly in the liver, brain, kidneys and eyes. WD is characterized by an extensive clinical variability between individuals with regards to age of onset, severity, and clinical presentation. The hallmarks of WD include a gold-brown ring (Kaiser-Fleischer ring) around the edge of the iris and in the rim of the cornea, reduced serum levels of ceruloplasmin and elevated urinary copper excretion. Depending on which organ systems are affected, symptoms may also include jaundice, enlargement of the liver or spleen, fatigue, seizures, slurred speech, difficulty swallowing, tremor, dystonia, personality changes, depression and psychosis. Age of onset varies between three and seventy years of age. WD occurs worldwide, with an estimated incidence between 1:30,000 and 1:100,000 (Ala et al. Lancet 369:397-408, 2007; de Bie et al. J Med Genet 44:673-688, 2007). It is however most common in the Sardinian population. See Cox and Roberts, GeneReviews, 2006 at www.genetests.org and the Wilson Disease Association at http://www.wilsondisease.org/.

Genetics: WD is inherited with an autosomal recessive manner and results from mutations in the *ATP7B* gene (Bull et al. Nat Genet 5:327-337, 1993; Tanzi et al. Nat Genet 5:344-350, 1993). Over 500 mutations have been detected in patients with WD, most of which are missense/nonsense, small insertions/deletions and splicing. Gross insertions, deletions and complex rearrangements are rare. Although most WD-causing mutations are found only in single families, three mutations are prevalent. These are the H1069Q substitution in European and North American populations, the R778L substitution in Southeast Asia (Ferenci Hum Genet 120:151-159,2006), and a 15-bp deletion in the gene promoter in the Sardinian population (Loudianos et al. Hum Mutat 14:294-303, 1999).

Description of This Particular Test: The *ATP7B* gene encodes an ATPase which participates in the transport of copper ions across membranes. This test involves bidirectional DNA sequencing of all 21 exons and splice sites of the *ATP7A* gene. The full coding sequence of each exon plus ~ 50 bp of flanking DNA on either side are sequenced. We will sequence any single or double exons in family members of patients with known mutation or to confirm previous results.

Reference Sequences: Genomic: **NC_000013.9** mRNA and Protein: **CCDS 41892.1**

Indications for Test: Patients with WD, their siblings and children, and symptomatic relatives are candidates for this test.

Sensitivity of Test: This Test detects mutations in about 98% of individuals with WD (Cox and Roberts, GeneReviews, 2006 at www.genetests.org).

Turn Around Time: Maximum of 40 calendar days.

Specimen Requirements: See page 4 of the Requisition Form.

Price: **Sequencing of all coding exons of the *ATP7B* gene: $990**

CPT Codes:

Sample Ascertainment x1	83890	$ 30	DNA Isolation x1	83891	$ 40
Amplification x21	83898	$ 310	Sequencing x21	83904	$ 460
Separation x1	83894	$ 70	Interpretation/Report x1	83912	$ 80

Accreditation: CLIA ID #: 52D1027685 (expires 1/18/13) (CAP#: 7185561, AU ID: 1407125 expires 12/20/12)

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