THE UNIVERSITY OF CHICAGO | Genetic Services Laboratories

Aceruloplasminemia testing: Mutation analysis of *CP*

Clinical Features

Aceruloplasminemia [OMIM#604290] is characterized by iron accumulation in the brain and viscera, which leads to retinal degeneration, diabetes mellitus and neurological disease (1). Neurological findings include blepharospasm, grimacing, facial and neck dystonia, tremors, chorea, and ataxia (1). Age of onset ranges from early to late adulthood. Iron accumulation typically occurs in the striatum, thalamus and dentate nucleus of the brain, as well as visceral organs (1). Affected individuals also have low serum copper and iron, and high serum ferritin.

Molecular Genetics

CP [OMIM#117700] encodes for the precursor to ceruloplasmin, which transports copper and also plays an important role in iron mobilization (1). It is thought that ceruloplasmin is important for normal release of cellular iron (2).

Inheritance

Aceruloplasminemia is inherited in autosomal recessive manner. Parents of an affected child are most likely obligate carriers. Recurrence risk for carrier parents is 25%.

Test methods

Comprehensive sequence coverage of the coding regions and splice junctions of the *CP* gene is performed. Targets of interests are captured and amplified using Agilent SureSelect target enrichment system. The constructed genomic DNA library is sequenced using Illumina technology and reads are aligned to the reference sequence. Variants are identified and evaluated using a custom collection of bioinformatic tools and comprehensively interpreted by our team of directors and genetic counselors. All pathogenic and likely pathogenic variants are confirmed by Sanger sequencing. The technical sensitivity of this test is estimated to be >99% for single nucleotide changes and insertions and deletions of less than 20bp.

Our CNV detection algorithm was developed and its performance determined for the sole purpose of identifying deletions and duplications within the coding region of the gene(s) tested. Partial exonic copy number changes and rearrangements of less than 400 bp may not be detected by this methodology. Regions of high homology and repetitive regions may not be analyzed. This methodology will not detect low level mosaicism, balanced translocations, inversions, or point mutations that may be responsible for the clinical phenotype. The sensitivity of our deletion/duplication assay may be reduced when DNA extracted by an outside laboratory is provided.

CP mutation analysis

Sample specifications:	3 to10 cc of blood in a purple top (EDTA) tube
Cost:	$1000
	81405
CPT codes:	81406
Turn-around time:	4 weeks

Note: The sensitivity of our assay may be reduced when DNA is extracted by an outside laboratory.

Results

Results, along with an interpretive report, will be faxed to the referring physician. Additional reports will be provided as requested. All abnormal results will be reported by telephone.

For more information about our testing options, please visit our website at dnatesting.uchicago.edu or contact us at 773-834-0555.

References

1. Miyajima H. Aceruloplasminemia.: GeneReviews [Internet]. Seattle, WA: University of Washington, Seattle., 2003, Aug 12 [Updated 2013, Apr 18].
2. Mukhopadhyay CK, Attieh ZK, Fox PL. Role of ceruloplasmin in cellular iron uptake. Science 1998: 279: 714-717.

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