Homocystinuria: *CBS* Gene Deletion/Duplication

**Test Code:** EZ  
**Turnaround time:** 2 weeks  
**CPT Codes:** 81228 x1

### Condition Description

Homocystinuria is an autosomal recessive disorder resulting from a deficiency of the enzyme cystathionine beta-synthase (*CBS*). Laboratory findings include markedly increased concentrations of plasma homocystine, total homocysteine, and methionine; increased concentration of urine homocystine; and reduced cystathionine beta-synthase (*CBS*) enzyme activity.

The disease presents with findings that can range from multiple organ disease beginning in infancy or early childhood to only thromboembolism expressed in early to middle adult years. The major findings in classic homocystinuria include developmental delay and mental retardation, ectopia lentis and/or severe myopia, skeletal abnormalities, vascular abnormalities such as thromboembolism, and clinical similarities to Marfan syndrome. Expressivity is variable for all of the clinical signs. Two phenotypic variants are recognized, B6-responsive homocystinuria and B6-non-responsive homocystinuria. B6-responsive homocystinuria is typically, but not always, milder than the non-responsive variant. The mean IQ of affected individuals with B6-responsiveness is 79 versus 57 for those who are B6 non responsive. Thromboembolism is the major cause of early death and morbidity. Other features that may occur include seizures, psychiatric problems, extrapyramidal signs such as dystonia, hypopigmentation, pancreatitis, malar flush, and livedo reticularis.

Homocystinuria is caused by mutations in the *CBS* gene (21q22.3). Sequencing of the *CBS* gene is recommended after a biochemical diagnosis of homocystinuria, and provides a complementary method to confirm the presence of mutations in a proband, identify carriers among the proband’s relatives, and provide prenatal diagnosis in families with known mutations.

### References:

- GeneReviews Clinical Summary

### Genes

**CBS**

### Indications

This test is indicated for:

- Confirmation of a clinical/biochemical diagnosis of homocystinuria
- Carrier testing in adults with a family history of homocystinuria

### Methodology

DNA isolated from peripheral blood is hybridized to a CGH array to detect deletions and duplications. The targeted CGH array has overlapping probes which cover the entire genomic region. Please note that a “backbone” of probes across the entire genome are included on the array for analytical and quality control purposes. Rarely, off-target copy number variants causative of disease may be identified that may or may not be related to the patient’s phenotype. Only known pathogenic off-target copy number variants will be reported. Off-target copy number variants of unknown clinical significance will not be reported.

### Detection

Detection is limited to duplications and deletions. Array CGH will not detect point mutations or intronic mutations. Results of molecular analysis must be interpreted in the context of the patient’s clinical and/or biochemical phenotype.

### Specimen Requirements

Submit only 1 of the following specimen types

* Preferred specimen type: Whole Blood

**Type: Whole Blood**

Specimen Requirements:

In EDTA (purple top) or ACD (yellow top) tube:

- Infants (2 years): 3-5 ml
- Older Children & Adults: 5-10 ml

Specimen Collection and Shipping: Refrigerate until time of shipment. Ship sample within 5 days of collection at room temperature with overnight delivery.

**Type: Saliva**
Specimen Requirements:

Oragene™ Saliva Collection kit (available through EGL) used according to manufacturer instructions.

Specimen Collection and Shipping: Store sample at room temperature. Ship sample within 5 days of collection at room temperature with overnight delivery.

### Special Instructions

Submit copies of diagnostic biochemical test results with the sample. Contact the laboratory if further information is needed. Sequence analysis is required before deletion/duplication analysis by targeted CGH array. If sequencing is performed outside of EGL Genetics, please submit a copy of the sequencing report with the test requisition.

### Related Tests

- Plasma Amino Acid Analysis (AA) and Urine Amino Acid Analysis (UA) are used in the diagnosis of a patient with homocystinuria.
- Custom Diagnostic Mutation Analysis (KM) is available to family members if mutations are identified by sequencing.
- Prenatal testing is available for known familial mutations only. Please call the Laboratory Genetic Counselor before collecting a fetal sample.