The CBS gene encodes cystathionine beta-synthase (CBS), the only known pyridoxal phosphate-dependent enzyme that contains heme, which catalyzes the first irreversible step of transsulfuration. CBS conjugates homocysteine and serine to form cystathionine, which is subsequently converted into cysteine and alpha-ketobutyrate. CBS gene contains 17 exons and spans about 23.7 kb genomic distance mapped to chromosome 21q22.3. Mutations in CBS gene cause homocystinuria (pyridoxine (vitamin B6) -responsive and nonresponsive types) and hyperhomocysteinemic thrombosis. Classic homocystinuria is an autosomal recessive metabolic disorder of sulfur metabolism. The clinical features usually manifest in the first or second decade of life and include myopia, ectopia lentis, mental retardation, skeletal anomalies resembling Marfan syndrome, and thromboembolic events. Light skin and hair can also be present. Biochemical features include increased urinary homocystine and methionine. CBS mutations demonstrate autosomal recessive inheritance with a broad range of clinical severity both within and between families. Definitive genotype/phenotype correlations have not been described.

The John Welsh Cardiovascular Diagnostic Laboratory offers molecular genetic testing for CBS mutations. Individuals are tested by DNA sequencing of the coding exons of the CBS gene. We strongly recommend initial testing of a clearly affected individual, if available, in order to provide the greatest test sensitivity and clearest interpretation of results for subsequent family members. Genetic counseling is recommended for all individuals.

**METHODOLOGY**

Genomic DNA is analyzed for CBS mutations by DNA sequencing of the coding exons of the CBS gene, as well as the exon/intron junctions and a portion of the 5’ and 3’ untranslated region. Patient DNA is sequenced in both the forward and reverse orientations. If a mutation is identified, additional family members are analyzed only for the familial mutation by automatic fluorescent DNA sequencing.

**SERVICE FEES**

<table>
<thead>
<tr>
<th>Index Case (Male or Female)</th>
<th>Direct and Institutional Billing</th>
<th>CPT Codes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$1,300 per sample</td>
<td>81406</td>
</tr>
<tr>
<td>Additional Family Members</td>
<td>$300 per sample; known familial mutation only</td>
<td>81403</td>
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</tbody>
</table>

**DNA SEQUENCING ANALYSIS**

Approximately 99 percent detection of mutations in the coding exons 3-17 of CBS.

**SPECIMEN REQUIREMENTS**

- **Blood (preferred):** EDTA (purple-top) tubes: Adult: 5 cc  Child: 5 cc  Infant: 2-3 cc
- **Tissue:** Frozen (preferred) or RNAlater
- **Other Body Fluids or Formalin-fixed, Paraffin-embedded Tissue:** Call to inquire

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