MAP2K2 encodes a member of the dual specificity protein kinase family, which acts as a mitogen-activated protein (MAP) kinase kinase. This kinase is known to play a critical role in mitogen growth factor signal transduction. It phosphorylates and thus activates MAPK1/ERK2 and MAPK2/ERK3. The activation of this kinase itself is dependent on the Ser/Thr phosphorylation by MAP kinase kinase kinases. MAP2K2 gene contains 11 coding exons and spans 33.8 kb genomic distance which has been mapped to chromosome 19p13.3. Mutations in this gene cause cardiomyopathy and cardiofaciocutaneous syndrome (CFC syndrome), a disease characterized by heart defects, mental retardation, and distinctive facial features similar to those found in Noonan syndrome. MAP2K2 mutations demonstrate autosomal dominant 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 MAP2K2 mutations. Individuals are tested by DNA sequencing of the coding exons of the MAP2K2 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.

**REASONS FOR REFERRAL**
Molecular confirmation of the diagnosis of cardiomyopathy and cardiofaciocutaneous syndrome (CFC syndrome).

**METHODOLOGY**
Genomic DNA is analyzed for MAP2K2 mutations by DNA sequencing of the coding exons of the MAP2K2 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></th>
<th>Direct and Institutional Billing</th>
<th>CPT Codes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Index Case (Male or Female)</strong></td>
<td>$900 per sample</td>
<td>81406</td>
</tr>
<tr>
<td><strong>Additional Family Members</strong></td>
<td>$300 per sample; known familial mutation only</td>
<td>81403</td>
</tr>
</tbody>
</table>

**SENSITIVITY**
DNA Sequencing Analysis: Approximately 99 percent detection of mutations in the coding exons 1-11 of MAP2K2.

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