MAP2K1 encodes a member of the dual specificity protein kinase family, which acts as a mitogen-activated protein (MAP) kinase kinase. This protein kinase lies upstream of MAP kinases and stimulates the enzymatic activity of MAP kinases upon wide variety of extra- and intracellular signals. As an essential component of MAP kinase signal transduction pathway, MAP2K1 is involved in many cellular processes such as proliferation, differentiation, transcription regulation and development. MAP2K1 gene contains 11 exons and spans 105.5 kb genomic distance which was mapped to chromosome 15q22.31. Diseases associated with MAP2K1 gene mutation include cardiomyopathy, cardiofaciocutaneous syndrome 3 (CFC3), Noonan syndrome (NS) and MAP2K1-related cardiofaciocutaneous syndrome. MAP2K1 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 MAP2K1 mutations. Individuals are tested by DNA sequencing of the coding exons of the MAP2K1 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, cardiofaciocutaneous syndrome 3, Noonan syndrome (NS) and MAP2K1-related cardiofaciocutaneous syndrome.

**METHODOLOGY**

Genomic DNA is analyzed for MAP2K1 mutations by DNA sequencing of the coding exons of the MAP2K1 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**

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<th>Direct and Institutional Billing</th>
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<td>Index Case (Male or Female)</td>
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<tr>
<td>Additional Family Members</td>
<td>$300 per sample; known familial mutation only</td>
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**SENSITIVITY**

DNA Sequencing Analysis: Approximately 99 percent detection of mutations in the coding exons 1-11 of MAP2K1.

**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