NRAS encodes a membrane protein that shuttles between the Golgi apparatus and the plasma membrane. This shuttling is regulated through palmitoylation and depalmitoylation by the ZDHHC9-GOLGA7 complex. The encoded protein has intrinsic GTPase activity, and is activated by a guanine nucleotide-exchange factor and inactivated by a GTPase activating protein. NRAS gene contains 4 coding exons and spans a genomic distance of about 12.43 kb which has been mapped to chromosome 1p13.2. Mutations in NRAS gene have been associated cardiomyopathy and Noonan syndrome 6. NRAS 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 NRAS mutations. Individuals are tested by DNA sequencing of the coding exons of the NRAS 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 Noonan syndrome 6

**METHODODOLOGY**
Genomic DNA is analyzed for NRAS mutations by DNA sequencing of the coding exons of the NRAS 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>
<th>CPT Codes</th>
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<tr>
<td>Index Case (Male or Female)</td>
<td>$500 per sample</td>
<td>81404</td>
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<tr>
<td>Additional Family Members</td>
<td>$300 per sample; known familial mutation only</td>
<td>81403</td>
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**SENSITIVITY**
DNA Sequencing Analysis: Approximately 99 percent detection of mutations in the coding exons 2-5 of NRAS.

**SPECIMEN REQUIREMENTS**

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