The official name of HRAS gene is “Harvey rat sarcoma viral oncogene homolog.” The HRAS gene provides instructions for making a protein called H-Ras that is involved primarily in regulating cell division. Through a process known as signal transduction, the H-Ras protein relays signals from outside the cell to the cell's nucleus. These signals instruct the cell to grow or divide. The H-Ras protein is a GTPase, which means it converts a molecule called GTP into another molecule called GDP. The human gene HRAS encodes 5 exons. It is located at 11p15.5. At least 15 mutations in the HRAS gene have been identified in people with Costello syndrome, a rare condition that affects many parts of the body and increases the risk of developing cancerous and noncancerous tumors. This disease also comprises cardiovascular abnormalities, such as typically pulmonic stenosis, hypertrophic cardiomyopathy, and/or atrial tachycardia. The mutations change single protein building blocks (amino acids) in a critical region of the H-Ras protein. Definitive genotype/phenotype correlations have not been described.

The John Welsh Cardiovascular Diagnostic Laboratory offers molecular genetic testing for HRAS mutations. Individuals are tested by DNA sequencing of the coding exons of the HRAS 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 Costello syndrome, Atrial tachycardia and HCM.

**METHODOLOGY**

Genomic DNA is analyzed for HRAS mutations by DNA sequencing of the coding exons of the HRAS 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>$500 per sample</td>
<td>81404</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>

**SENSITIVITY**

DNA Sequencing Analysis: Approximately 99 percent detection of mutations in the coding exons 2-5 of HRAS.

**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 or Formalin-fixed, Paraffin-embedded Tissue: Call to inquire