In vertebrates, homeobox genes that encode the class of transcription factors are found in clusters named A, B, C, and D on four separate chromosomes. Expression of these proteins is spatially and temporally regulated during embryonic development. HOXA1 (Homeobox A1) gene is part of the A cluster on chromosome 7 and encodes a DNA-binding transcription factor which may regulate gene expression, morphogenesis, and differentiation. The encoded protein may be involved in the placement of hindbrain segments in the proper location along the anterior-posterior axis during development. HOXA1 gene contains two coding exons covering 3.1 Kb genomic sequence and has been mapped to chromosome 7p15.2. The HOXA1 gene is required in vertebrates for the morphogenesis of the digits and external genitals. Autosomal recessive mutations in HOXA1 gene has been linked to both Bosley-Salih-Alorainy syndrome and Athabaskan brainstem dysgenesis syndrome. HOXA1 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 HOXA1 mutations. Individuals are tested by DNA sequencing of the coding exons of the HOXA1 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 CHD.

**METHODOLOGY**

Genomic DNA is analyzed for HOXA1 mutations by DNA sequencing of the coding exons of the HOXA1 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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<tr>
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<th>Direct and Institutional Billing</th>
<th>CPT Codes</th>
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<td>Index Case (Male or Female)</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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</table>

**SENSITIVITY**

DNA Sequencing Analysis: Approximately 99 percent detection of mutations in the coding exons 1-2 of HOXA1.

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

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