EVC2 and EVC are single-pass type I transmembrane proteins constitutively associate with each other in a ring-like pattern near the ciliary transition zone, a protein barrier between the ciliary and plasma membranes. EVC and EVC2 function by transducing extracellular signals to the nucleus via the hedgehog signaling pathway. Human EVC2 gene contains 22 exonsthat have been mapped to chromosome 4p16.2. Mutations in the EVC2 gene can cause Ellis-van Creveld syndrome, which is an autosomal recessive skeletal dysplasia characterized by short limbs, short ribs, postaxial polydactyly, and dysplastic nails and teeth. Congenital cardiac defects, most commonly a defect of primary atrial septation producing a common atrium, occur in 60% of affected individuals. Definitive genotype/phenotype correlations have not been described.

The John Welsh Cardiovascular Diagnostic Laboratory offers molecular genetic testing for EVC2 mutations. Individuals are tested by automatic fluorescent DNA sequencing of the coding exons of the EVC2 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 and Ellis-van Creveld syndrome.

**METHODOLOGY**

Genomic DNA is analyzed for EVC2 mutations by DNA sequencing of the coding exons of the EVC2 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>
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<tr>
<th></th>
<th>Direct and Institutional Billing</th>
<th>CPT Codes</th>
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<tr>
<td>Index Case (Male or Female)</td>
<td>$1,200 per sample</td>
<td>81406</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 exon 1-22 of EVC2.

**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