COL4A1 MUTATION ANALYSIS
JOHN WELSH CARDIOVASCULAR DIAGNOSTIC LABORATORY

COL4A1 (COLLAGEN OF BASEMENT MEMBRANE, ALPHA-1 CHAIN) encodes the alpha-1 subunit of type IV collagen. Type IV collagen is the major structural component of glomerular basement membranes, inhibits angiogenesis and tumor formation. The C-terminal half is found to possess the anti-angiogenic activity, specifically inhibits endothelial cell proliferation, migration and tube formation. Human COL4A1 gene contains 52 exons mapped within chromosome 13q34. Mutations in this gene are found in patients with Hereditary Angiopathy with Nephropathy, Aneurysms and muscle Cramps (HANAC). HANAC is a autosomal dominant hematuria associated with extrarenal manifestations. All affected patients had leukoencephalopathy, cerebral aneurysms, Raynaud phenomenon, cardiac arrhythmia, and bilateral large kidney cysts. Definitive genotype/phenotype correlations have not been described.

The John Welsh Cardiovascular Diagnostic Laboratory offers molecular genetic testing for COL4A1 mutations. Individuals are tested by automatic fluorescent DNA sequencing of the coding exons of the COL4A1 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 valvar and vascular disorders, Hereditary Angiopathy with Nephropathy, Aneurysms and muscle Cramps (HANAC).

METHODOLOGY

Genomic DNA is analyzed for COL4A1 mutations by DNA sequencing of the coding exons of the COL4A1 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>
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<tbody>
<tr>
<td>$1,600 per sample</td>
<td>81408</td>
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| Additional Family Members  | $300 per sample; known familial mutation only | 81403 |

SENSITIVITY


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