FANCA MUTATION ANALYSIS
JOHN WELSH CARDIOVASCULAR DIAGNOSTIC LABORATORY

FANCA (Fanconi anemia, complementation group A) protein is a part of a nuclear multiprotein core complex which triggers activating monoubiquitination of the FANCD2 protein during S phase of the growth cycle and after exposure to DNA crosslinking agents. Human FANCA gene contains 43 exons mapped to chromosome 16q24.3. Mutations in the FANCA gene can cause Fanconi anemia, which is a genetically heterogeneous recessive disorder characterized by cytogenetic instability, hypersensitivity to DNA crosslinking agents, increased chromosomal breakage, and defective DNA repair. Clinical manifestations include pre- and postnatal growth retardation; malformations of the kidneys, heart, and skeleton, a typical facial appearance with small head, eyes, and mouth, hearing loss and reduced fertility, cutaneous abnormalities, bone marrow failure and susceptibility to acute myeloid leukemia. Definitive genotype/phenotype correlations have not been described.

The John Welsh Cardiovascular Diagnostic Laboratory offers molecular genetic testing for FANCA mutations. Individuals are tested by automatic fluorescent DNA sequencing of the coding exons of the FANCA 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.

Molecular confirmation of the diagnosis of CHD and Fanconi anemia (FA).

Genomic DNA is analyzed for FANCA mutations by DNA sequencing of the coding exons of the FANCA 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.

DNA Sequencing Analysis: Approximately 99 percent detection of mutations in the coding exons 1-43 of FANCA.

**Direct and Institutional Billing**

<table>
<thead>
<tr>
<th>Index Case (Male or Female)</th>
<th>$1,500 per sample</th>
<th>81407</th>
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<tbody>
<tr>
<td>Additional Family Members</td>
<td>$300 per sample;</td>
<td>81403</td>
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<td>known familial mutation only</td>
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**Sensitivity**

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

John Welsh Cardiovascular Diagnostic Laboratory • Section of Cardiology • Department of Pediatrics
Baylor College of Medicine • 1102 Bates Avenue, Suite 480.02 • Houston, TX 77030
PHONE: (832) 824-4155 • FAX: (832) 825-5159 • E-MAIL: yuxinf@bcm.edu
Web Site: www.bcm.edu/pediatrics/welsh