FBN2 gene, mapped to chromosome 5q23-q31, is composed of 65 coding exons. The FBN2 encoded 2,889-amino acid protein contains an N-terminal signal peptide, followed by a proline-rich region, three tandem N-terminal EGF-like repeats and 41 calcium-binding EGF-like repeats interspersed with another EGF-like repeat, a glycine-rich region, seven TGF-binding protein repeats and two Fib motifs. FBN2 also has two potential cell attachment sequences, multiple N-glycosylation sites and two C-terminal polylysine stretches. The structures of FBN2 and FBN1 are highly similar, with the most significant difference being the glycine-rich sequence near the N terminus of FBN2, where FBN1 has a proline-rich sequence. Northern blot analysis detected a 10- to 11-kb FBN2 transcript. Western blot analysis detected FBN2 at an apparent molecular mass of 350 kD. Mutations in FBN2 have been described in patients with congenital contractural arachnodactyly, which is a rare, autosomal dominant connective tissue disorder characterized by contractures, arachnodactyly, scoliosis and crumpled ears. It shares overlapping features with Marfan syndrome, which is caused by mutations in the gene encoding fibrillin-1. Although definitive genotype/phenotype correlations have not been identified, however, FBN2 mutations have been noted to demonstrate broad variable expressivity.

The John Welsh Cardiovascular Diagnostic Laboratory offers molecular genetic testing for FBN2 mutations. Individuals are tested by DNA sequencing of all 65 exons of the FBN2 gene. Genetic counseling is recommended for all individuals in order to identify additional at-risk family members and to discuss reproductive issues.

**REASONS FOR REFERRAL**

Molecular confirmation of the diagnosis of congenital contractural arachnodactyly and congenital heart defects.

**METHODOLOGY**

Genomic DNA is analyzed for FBN2 mutations by DNA sequencing of all 65 exons of the FBN2 gene, as well as the exon/intron junctions and a portion of the 5’ and 3’ untranslated regions. 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(s) by automatic fluorescent DNA sequencing.

**SERVICE FEES**

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<th>Direct and Institutional Billing</th>
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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 exons 1-65 of FBN2.

**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