ZNF469 (Zinc Finger Protein 469) gene, located on chromosome 16q24, encodes a zinc-finger protein. Previous studies suggest that it may function as a transcription factor or extra-nuclear regulator factor for the synthesis or organization of collagen fibers, although the protein function has not been completely elucidated. Mutations in ZNF469 gene cause brittle cornea syndrome, an autosomal recessive generalized connective tissue disorder characterized by extreme thinning and fragility of the cornea that may rupture in the absence of significant trauma leading to blindness. ZNF469 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 ZNF469 mutations. Individuals are tested by DNA sequencing of the coding exons of the ZNF469 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 brittle cornea syndrome.

**METHODOLOGY**

Genomic DNA is analyzed for ZNF469 mutations by DNA sequencing of the coding exons of the ZNF469 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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<th>Direct and Institutional Billing</th>
<th>CPT Codes</th>
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<td>Index Case (Male or Female)</td>
<td>$900 per sample</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 exons of ZNF469.

**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