The dystrophin gene is the largest gene found in nature, measuring 2.4 Mb. It is located at Xp21.2-p21.1 and encodes a 3,685-amino acid protein product with 4 distinct domains and shares many features with spectrin and alpha-actinin. Dystrophin is a rod-like cytoskeletal protein at the inner surface of muscle fibers. It is part of the dystrophin-glycoprotein complex (DGC), which bridges the inner cytoskeleton (F-actin) and the extra-cellular matrix. Diseases associated with DMD include Duchenne muscular dystrophy, Becker muscular dystrophy and DMD-associated dilated cardiomyopathy. DMD is a recessive, fatal, X-linked disorder. BMD is a milder allelic form. In general, DMD patients carry mutations that cause premature translation termination (nonsense or frame shift mutations), while in BMD patients dystrophin is reduced either in molecular weight (derived from in-frame deletions) or in expression level. Definitive genotype/phenotype correlations for DMD-associated cardiomyopathy have not been described.

The John Welsh Cardiovascular Diagnostic Laboratory offers molecular genetic testing for DMD mutations. Individuals are tested by DNA sequencing of the coding exons of the DMD 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 Duchenne muscular dystrophy, Becker muscular dystrophy and DMD-associated dilated cardiomyopathy.

METHODOLOGY

Genomic DNA is analyzed for DMD mutations by DNA sequencing of the coding exons of the DMD 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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<tr>
<td>Index Case (Male or Female)</td>
<td>$2,500 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 1-79 of DMD.

SPECIMEN REQUIREMENTS

Blood (preferred): EDTA (purple-top) tubes: Adult: 5 cc Child: 5 cc Infant: 2-3 cc
Tissue: Frozen (preferred) or RNAlater
Other Body Fluids or Formalin-Fixed, Paraffin-Embedded Tissue: Call to inquire