ABCC6 MUTATION ANALYSIS
JOHN WELSH CARDIOVASCULAR DIAGNOSTIC LABORATORY

ABCC6 (ATP-BINDING CASSETTE, SUBFAMILY C, MEMBER 6) is a member of the multidrug resistance-associated protein (MRP) subfamily of ATP-binding cassette (ABC) transmembrane transporters. Human ABCC6 gene contains 31 exons mapped within chromosome 16p13.11. Mutations in the ABCC6 gene can cause pseudoxanthoma elasticum (PXE), which is an inherited multisystem disorder associated with accumulation of mineralized and fragmented elastic fibers in the skin, vascular walls, and Burch membrane in the eye. Clinically, patients exhibit characteristic lesions of the cardiovascular system with peripheral and coronary arterial occlusive disease as well as gastrointestinal bleedings. Generalized arterial calcification of infancy-2 (GACI2) is an allelic disorder, also caused by homozygous or compound heterozygous mutation in the ABCC6 gene; it has been suggested that GACI and PXE represent 2 ends of a clinical spectrum of ectopic calcification and other organ pathologies rather than 2 distinct disorders. Definitive genotype/phenotype correlations have not been described.

The John Welsh Cardiovascular Diagnostic Laboratory offers molecular genetic testing for ABCC6 mutations. Individuals are tested by automatic fluorescent DNA sequencing of the coding exons of the ABCC6 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, pseudoxanthoma elasticum (PXE) and Generalized arterial calcification of infancy-2 (GACI2).

METHODOLOGY

Genomic DNA is analyzed for ABCC6 mutations by DNA sequencing of the coding exons of the ABCC6 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>$1,200 per sample</td>
<td>81407</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 exon 1-31 of ABCC6.

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