VCP MUTATION ANALYSIS

JOHN WELSH CARDIOVASCULAR
DIAGNOSTIC LABORATORY

VCP gene encodes the valosin-containing protein, a ubiquitously expressed multifunctional protein belonging to the AAA+ (ATPase associated with various activities) protein family. It has been implicated in multiple cellular functions ranging from organelle biogenesis to ubiquitin-dependent protein degradation. VCP gene contains 17 coding exons and spans 17.2 kb genomic distance which was mapped to chromosome 9p13.3. Mutations in this gene cause arrhythmia and inclusion body myopathy with early-onset Paget disease with or without frontotemporal dementia 1 (IBMPFD1). VCP mutations demonstrate autosomal dominant 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 VCP mutations. Individuals are tested by automatic fluorescent DNA sequencing of the coding exons of the VCP 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 arrhythmia and inclusion body myopathy with early-onset Paget disease with or without frontotemporal dementia 1 (IBMPFD1).

METHODOLOGY

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

<table>
<thead>
<tr>
<th>Direct and Institutional Billing</th>
<th>CPT Codes</th>
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<tbody>
<tr>
<td>Index Case (Male or Female)</td>
<td>$1,100 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 1-17 of VCP.

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 Tissues: | Call to inquire |

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