PPP1R17 MUTATION ANALYSIS
JOHN WELSH CARDIOVASCULAR
DIAGNOSTIC LABORATORY

G-substrate (GSBS), an endogenous substrate for cGMP-dependent protein kinase, exists almost exclusively in cerebellar Purkinje cells, where it functions as a protein phosphatase inhibitor and is possibly involved in the induction of long-term depression. The human G-substrate contains 2 putative phosphorylation sites (Thr68 and Thr119) and the amino acid sequence was found identical to rabbit G-substrate. It is encoded by PPP1R17 (protein phosphatase 1, regulatory subunit 17) gene, which contains 4 exons spanning around 21.7kb genomic distance and has been mapped to chromosome 7p15. The G-substrate mRNA was expressed almost exclusively in the cerebellum as a single transcript, however, two transcript variants encoding different isoforms have been identified. Diseases associated with PPP1R17 include hypercholesterolemia. Definitive genotype/phenotype correlations have not been described.

The John Welsh Cardiovascular Diagnostic Laboratory offers molecular genetic testing for PPP1R17 mutations. Individuals are tested by DNA sequencing of the coding exons of the PPP1R17 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 association of hypercholesterolemia.

METHODOLOGY
Genomic DNA is analyzed for PPP1R17 mutations by DNA sequencing of the coding exons of the PPP1R17 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>$500 per sample</td>
<td>81404</td>
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<tr>
<td>Additional Family Members</td>
<td>$300 per sample; Known familial mutation only</td>
<td>81403</td>
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SENsitIvity
DNA Sequencing Analysis: Approximately 99 percent detection of mutations in the coding exons 1-4 of PPP1R17.

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