PTRF (Polymerase I And Transcript Release Factor) gene encodes protein cavin, an essential factor in the biogenesis of caveolae, which are 50- to 100-nm invaginations of cell-surface membranes putatively involved in numerous processes, including signal transduction and membrane and lipid trafficking. This protein also regulates rRNA transcription by promoting the dissociation of transcription complexes and the reinitiation of polymerase I on nascent rRNA transcripts. PTRF gene contains two coding exons and spans 21.07 kb genomic distance on chromosome 17q21.2. Mutations in this gene cause congenital generalized lipodystrophy 4, a disorder characterized by the association of congenital generalized lipodystrophy with muscular dystrophy and cardiac anomalies. PTRF 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 PTRF mutations. Individuals are tested by DNA sequencing of the coding exons of the PTRF 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 congenital generalized lipodystrophy 4.

METHODOLOGY
Genomic DNA is analyzed for PTRF mutations by DNA sequencing of the coding exons of the PTRF 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>$500 per sample</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 1-2 of PTRF.

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