Mutations in the presenilin proteins (PSEN1 and PSEN2) or in the amyloid precursor protein (APP) result in increased production of the longer form of amyloid-beta, the main component of amyloid deposits. PSEN1 encodes presenilin 1, one member of the presenilins that are postulated to regulate APP processing through their effects on gamma-secretase, an enzyme that cleaves APP. PSEN1 gene contains 10 coding exons and spans 87.3 kb genomic distance which has been mapped to chromosome 14q24.3. Diseases associated with PSEN1 mutations include PSEN1-related dilated cardiomyopathy and frontotemporal dementia. PSEN1 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 PSEN1 mutations. Individuals are tested by DNA sequencing of the coding exons of the PSEN1 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 PSEN1-related dilated cardiomyopathy and frontotemporal dementia.

**METHODOLOGY**

Genomic DNA is analyzed for PSEN1 mutations by DNA sequencing of the coding exons of the PSEN1 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>Description</th>
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<td>Additional Family Members</td>
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**SENSITIVITY**

DNA Sequencing Analysis: Approximately 99 percent detection of mutations in the coding exons 3-12 of PSEN1.

**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