**TERT MUTATION ANALYSIS**

**JOHN WELSH CARDIOVASCULAR DIAGNOSTIC LABORATORY**

*TERT* gene encodes telomerase reverse transcriptase, a vital component of telomerase. Telomerase is a specialized, ribonucleoprotein polymerase that functions to maintain telomeres by adding the telomere repeat TTAGGG to the ends of chromosomes to compensate for the small amounts of terminal sequences that are lost during DNA replication. Mapped to chromosome 5p15.33, *TERT* gene spans a genomic distance of approximately 35-37 kb and is composed of 16 exons. While alternatively-spliced variants of *TERT* encode various isoforms of telomerase, mutations in this gene have been associated with 8%-15% of families with idiopathic pulmonary fibrosis (IPF), and germline mutations in *TERT* are seen in 1%-3% of simplex cases of idiopathic pulmonary fibrosis (IPF). It is thought that mutations in *TERT* impair the ability of telomerase to repair telomeres after cell division, leading to the presence of short, dysfunctional telomeres that halt the progression of cell proliferation. As a result of this impaired process, cell death and organ failure occur. *TERT* mutations appear to demonstrate autosomal dominant inheritance with reduced penetrance. Definitive genotype/phenotype correlations have not yet been described.

The John Welsh Cardiovascular Diagnostic Laboratory offers molecular genetic testing for *TERT* mutations. Individuals are tested by DNA sequencing of the coding exons of the *TERT* 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 idiopathic pulmonary fibrosis (IPF) or familial pulmonary fibrosis (FPF).

**METHODOLOGY**

Genomic DNA is analyzed for *TERT* mutations by DNA sequencing of the coding exons of the *TERT* 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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<tr>
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<th><strong>Direct and Institutional Billing</strong></th>
<th><strong>CPT Codes</strong></th>
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<tbody>
<tr>
<td>Index Case (Male or Female)</td>
<td>$1,000 per sample</td>
<td>81406</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 1-16 of *TERT*.

**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