

## Cystic Fibrosis and CBAVD Testing via *CFTR* Gene Sequencing (Test #150)

**Brief Description of Clinical Features:** Cystic Fibrosis (CF) (OMIM 219700) is a severe disorder with typical onset in infancy. Main features include chronic, debilitating lung infections, pancreatic insufficiency connected to dietary malabsorption; excess Cl<sup>-</sup> in sweat, and absence of the vas deferens. Severity varies widely; genetic and non-genetic modifying factors exist. Average survival in patients is currently ~37 years. Nearly all male patients are infertile. Today, many or even the majority of U.S. CF cases are detected through routine neonatal screening (<http://genes-r-us.uthscsa.edu/>). CF is one of the most common “single gene” disorders with carrier frequencies up to 1/25 in individuals with Northern European ancestry. For more information see Moskowicz et al. GeneReviews 2005 ([www.genetests.org](http://www.genetests.org)) and the Cystic Fibrosis Foundation ([www.cff.org](http://www.cff.org)).

**Genetics:** CF is caused by mutations in the cystic fibrosis conductance regulator (*CFTR*) gene. Inheritance is autosomal recessive. *CFTR* encodes a chloride ion channel in epithelial cells. Over 1300 causative *CFTR* mutations have been reported; most are very rare ([www.genet.sickkids.on.ca/cftr/](http://www.genet.sickkids.on.ca/cftr/)). Missense mutations predominate, but there are also substantial numbers of nonsense, frameshift, and splicing mutations. A relatively small number of larger deletions and other major gene rearrangements have been reported. One major mutation, ΔF508, comprises about 70% of all mutant alleles in Northern Europeans. Correlations between genotyping and phenotype are beginning to be made (Moskowicz et al. 2005; McKone et al. Chest 130:1441-1447, 2006). *CFTR* mutations may also cause congenital bilateral absence of the vas deferens (CBAVD) (OMIM 277180) in the absence of other CF features (Lebo and Grody, Genet Testing 11:32-44, 2007).

**Description of This Particular Test:** This test involves bidirectional sequencing of all 27 exons of the *CFTR* gene. The full coding region of each exon plus ~50 bp of flanking non-coding DNA on either side are sequenced. The test also involves complete analysis of the compound (TG)<sub>n</sub>(T)<sub>n</sub> sequence (5T/TG tract) in intron 8 just before exon 9 (exon 10 in the new exon numbering). The 5T/TG tract affects splicing of exon 9. Our 5T/TG tract analysis involves bidirectional sequencing along with allele length measurement.

**Indications for Test:** Most CF patients and many potential *CFTR* mutation carriers will first receive testing for a collection of ≥23 specific, well characterized mutations (see Amos et al. Am College Med Genet, Technical Standards, 2006, [www.acmg.net](http://www.acmg.net)). PreventionGenetics does not offer such a panel at this time. Patients, however, who carry no more than one of the mutations within the panel, are candidates for our full gene sequencing test. CF patients with Native American, African or Asian ancestry may also be candidates for the full sequencing test, as the standard panel of mutations was designed for Caucasian patients. CBAVD patients are also good candidates for our full sequencing test, especially since the 5T/TG tract has a particularly strong effect on this phenotype. The 5T/TG tract analysis may be ordered alone. We will also sequence any single exon or pair of exons in this gene to confirm mutations previously detected in research or other clinical labs and to test family members of affected individuals.

**Sensitivity of Test:** Our full gene sequencing test is expected to detect >98% of causative mutations (Moskowicz et al. 2005).

**Turn Around Time:** Maximum of 40 days, although many tests are completed in 2-3 weeks.

**Specimen Requirements:** See page 4 of the Requisition Form.

**Prices:** **Sequencing of *CFTR* Exons 1-27, including “5T/TG Tract Analysis”** **\$ 1290**

Please inquiry about price discounts if you would require >5 full sequencing tests per year.

**CPT Codes:**

Sample Ascertainment	83890	\$ 30	DNA Isolation	83891	\$ 40
Amplification x29	83898	\$ 400	Sequencing x29	83904	\$ 610
Separation	83894	\$ 80	Interpretation/Report	83912	\$ 130

**Accreditation Info.** CLIA ID #: 52D1027685 (expires 1/18/13) (CAP#: 7185561, AU ID: 1407125 expires 12/20/12)

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