Cystic Fibrosis: *CFTR* Gene Sequencing

**Test Code:** JK  
**Turnaround time:** 4 weeks  
**CPT Codes:** 81223 x1

### Condition Description

Cystic fibrosis (CF) is a chronic genetic condition involving multiple organ systems [1]. Classical CF primarily involves the respiratory and digestive systems, and may have a range of clinical severity. Pulmonary symptoms often include lower airway inflammation, chronic cough, chronic sinusitis, and recurrent infections. Digestive symptoms often include meconium ileus, pancreatic insufficiency resulting in malabsorption and/or failure to thrive, diabetes mellitus, and hepatobiliary disease. Congenital bilateral absence of the vas deferens (CBAVD) is seen in men without pulmonary or digestive symptoms of CF, and results in azoospermia [2]. CBAVD is a significant cause of male infertility.

CF is caused by mutations in the cystic fibrosis transmembrane conductance regulator (*CFTR*) gene. Individuals with mutations in the *CFTR* gene may also present with milder or atypical symptoms such as pancreatitis or chronic sinusitis.

The incidence of CF is approximately 1 in 3200 live births among Caucasians and is inherited in an autosomal recessive pattern. The carrier frequency is estimated to be approximately 1 in 22-28 in the Caucasian population, 1 in 29 in the Ashkenazi Jewish population, 1 in 60-65 in the African American population, 1 in 46 in the Hispanic population and 1 in 90 in the Asian population.

Initial evaluation and screening of patients for *CFTR* mutations is accomplished through a panel of 23 common mutations as recommended by the American College of Medical Genetics Subcommittee on Cystic Fibrosis [3] and the American College of Obstetrics and Gynecologists [4]. The detection rate of this panel depends on the patient's ethnicity.

When the common mutation panel is negative and mutations to the *CFTR* gene are suspected, sequencing of the entire gene is recommended to detect rare mutations. For patients with mutations not identified by full gene sequencing, a separate deletion/duplication assay is available using a targeted CGH array (JL).

Click here for the GeneReviews summary on this condition.


References:
6. Chevalier-Porst (2005) Identification and Characterization of Three Large Deletions and a Deletion/Polymorphism in the *CFTR* Gene. Hum Mut Mutation in Brief #806 Online
7. http://www.genet.sickkids.on.ca/

### Genes

**CFTR**

### Indications

Testing is indicated for:
- Patients suspected to have a mutation to the *CFTR* gene and who tested negative using the common mutation panel.
- Family members of an affected individual at risk to be carriers of CF.

### Methodology

**Next Generation Sequencing:** In-solution hybridization of all coding exons is performed on the patient's genomic DNA. Although some deep intronic regions may also be analyzed, this assay is not meant to interrogate most promoter regions, deep intronic regions, or other regulatory elements, and does not detect single or multi-exon deletions or duplications. Direct sequencing of the captured regions is performed using next generation sequencing. The patient's gene sequences are then compared to a standard reference sequence. Potentially causative variants and areas of low coverage are Sanger-sequenced. Sequence variations are classified as pathogenic, likely pathogenic, benign, likely benign, or variants of unknown significance. Variants of unknown significance may require further studies of the patient and/or family members.

### Detection

The detection rates for this assay, as with the common mutation panel, varies in different racial/ethnic groups.

- **Clinical Sensitivity:** 97 - 98% [5, 6, 7].
- **Analytical Sensitivity:** ~99%

Results of molecular analysis must be interpreted in the context of the patient's clinical phenotype.
**Specimen Requirements**

Submit only 1 of the following specimen types

* Preferred specimen type: Whole Blood

**Type: Whole Blood**

Specimen Requirements:

In EDTA (purple top) or ACD (yellow top) tube:
- Infants (2 years): 3-5 ml
- Older Children & Adults: 5-10 ml

Specimen Collection and Shipping: Refrigerate until time of shipment. Ship sample within 5 days of collection at room temperature with overnight delivery.

**Type: Saliva**

Specimen Requirements:

Oragene™ Saliva Collection kit (available through EGL) used according to manufacturer instructions.

Specimen Collection and Shipping: Store sample at room temperature. Ship sample within 5 days of collection at room temperature with overnight delivery.

**Special Instructions**

Completion of the cystic fibrosis common mutation panel should be completed PRIOR to CFTR gene sequence analysis.

Submit copies of diagnostic biochemical test results (i.e. sweat test results) with the sample, if appropriate. Contact the laboratory if further information is needed.

Sequence analysis is required before deletion/duplication analysis by targeted CGH array. If sequencing is performed outside of Emory Genetics Laboratory, please submit a copy of the sequencing report with the test requisition.

**Related Tests**

- CF common mutation panel (CF).
- Ashkenazi Jewish Carrier Panel is available to screen for the panel of 9 autosomal recessive conditions common in individuals of Ashkenazi Jewish background.
- **Custom diagnostic mutation analysis (KM)** is available to family members if mutations are identified by sequencing.
- A deletion/duplication assay is available separately for individuals where mutations are not identified by sequence analysis. Refer to the test requisition or contact the laboratory for more information.
- Prenatal testing is available for known familial mutations only. Please call the Laboratory Genetic Counselor before collecting a fetal sample.