

Cystic Fibrosis: *CFTR* Expanded Mutation Panel

Test Code: MM530

Turnaround time: 2 weeks

CPT Codes: 81220 x1

Condition Description

Cystic fibrosis (CF) is a chronic genetic condition involving multiple organ systems. 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 [1]. 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 2500 live births among Caucasians and is inherited in an autosomal recessive pattern. The carrier frequency is estimated to be approximately 1 in 25 in the Caucasian population, 1 in 24 in the Ashkenazi Jewish population, 1 in 61 in the African American population, 1 in 58 in the Hispanic population and 1 in 94 in the Asian population.

The current recommendation from the American College of Obstetrics and Gynecologists [2, 3] and the American College of Medical Genetics Subcommittee on Cystic Fibrosis [4] is that screening for cystic fibrosis be offered to all patients, regardless of ethnicity, by a minimum panel of 23 common mutations [4].

This test offers an expanded panel of 142 mutations to account for mutations more common in non-Caucasian ethnic groups, as well as rarer mutations across all ethnic groups.

Click [here](#) for a complete list of *CFTR* mutations.

For those providers wishing to order only the ACOG/ACMG recommended 39-mutation panel, see test code CF.

Visit www.ThinkGenetic.com for patient-friendly information on [cystic fibrosis](#).

References:

1. Xu et al. Cystic fibrosis transmembrane conductance regulator is vital to sperm fertilizing capacity and male fertility (2007). *PNAS*. 104(23):9816-21.
2. ACOG Committee Opinion. Update on Carrier Screening for Cystic Fibrosis (2005). *Obstet Gynecol*. 106: 1465-8.
3. ACOG Committee Opinion. Update on Carrier Screening for Cystic Fibrosis (2011). *Obstet Gynecol*. Apr; 117(4): 1029-31.
4. Watson, M. et al. Cystic Fibrosis population carrier screening: 2004 revision of the American College of Medical Genetics mutation panel (2004). *Genet Med*. 6(5):387-91.

Genes

[CFTR](#)

Indications

Testing is indicated for:

- Individuals with a diagnosis of CF, or atypical presentations of CF (chronic pancreatitis, sinusitis).
- Males with congenital bilateral absence of the vas deferens (CBAVD).
- Carrier screening for individuals of Caucasian or Ashkenazi Jewish background.
- 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. This assay detects 142 mutations in the *CFTR* gene, including the 23 mutations recommended by ACMG and ACOG.

Detection

Next Generation Sequencing: Clinical Sensitivity: Unknown. Mutations in the promoter region, some mutations in the introns and other regulatory element mutations cannot be detected by this analysis. Large deletions/duplications will not be detected by this analysis. Results of molecular analysis should be interpreted in the context of the patient's clinical/biochemical phenotype.

Analytical Sensitivity: ~99%.

Specimen Requirements

Submit only 1 of the following specimen types

Type: DNA, Isolated

Specimen Requirements:

Microtainer

8µg

Isolation using the Perkin Elmer™ Chemagen™ Chemagen™ Automated Extraction method or Qiagen™ Puregene kit for DNA extraction is recommended.

Specimen Collection and Shipping:

Refrigerate until time of shipment in 100 ng/µL in TE buffer. Ship sample at room temperature with overnight delivery.

Type: Saliva

Specimen Requirements:

Oragene™ Saliva Collection Kit

Oragene™ Saliva Collection Kit used according to manufacturer instructions. Please contact EGL for a Saliva Collection Kit for patients that cannot provide a blood sample.

Specimen Collection and Shipping:

Please do not refrigerate or freeze saliva sample. Please store and ship at room temperature.

Type: Whole Blood (EDTA)

Specimen Requirements:

EDTA (Purple Top)

Infants and Young Children (2 years of age to 10 years old): 3-5 ml

Older Children & Adults: 5-10 ml

Autopsy: 2-3 ml unclotted cord or cardiac blood

Specimen Collection and Shipping:

Ship sample at room temperature for receipt at EGL within 72 hours of collection. Do not freeze.

Related Tests

- Sequencing and deletion/duplication analysis of the *CFTR* gene is available for individuals who test negative with the common mutation panel, when other mutations are suspected.
- *CFTR* poly T analysis is performed as a reflex test when an R117H mutation is detected or when evaluating males with CBAVD.
- Ashkenazi Jewish Carrier Panel is available to screen for the panel of 19 autosomal recessive conditions common in individuals of Ashkenazi Jewish background.
- Prenatal testing is available to couples who are confirmed carriers of gene mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.
- Cystic fibrosis basic panel (test code CF).