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**Cystic Fibrosis Mutation Analysis**

**↑CPT**

83890; 83900; 83901 (x14); 83909; 83912; 84311

Poly T tract reflex test includes these additional CPT codes: 83900; 83901 (x14); 83909; 83912

**↑Synonyms**

Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) Gene

**↑Test Includes**

Identification of common mutations in the CFTR gene. **Note:**Carrier screening on healthy children will generally not be performed.

**↑Laboratory**

Molecular Pathology

**↑Availability**

Monday - Friday, 0600-1700

**↑Turnaround Time**

3-14 days

**↑Special Instructions**

Do not centrifuge specimen

**↑Specimen**

Whole blood

**↑ Volume**

4 mL

**↑ Minimum Volume**

1 mL

**↑ Container**

Lavender top (EDTA) tube

**↑ Storage Instructions**

All specimens should be sent to the laboratory immediately after collection, preferably by overnight delivery. Specimens should be kept at room temperature or refrigerated but not frozen.

**↑ Causes for Rejection**

Clotted blood; repeatedly thawed and frozen specimen (yields low quality DNA); specimen inadequately identified; specimen from healthy child

**↑ Reference Range**

No mutations detected

**↑ Use**

Identification of common mutations in an affected patient, assessing carrier risk for an individual planning a pregnancy or relatives of affected patients, prenatal diagnosis, identification of mutations in an infertile male with a diagnosis of congenital bilateral absence of the vas deferens, work-up for male infertility, prenatal diagnosis of a fetus with echogenic bowel and population carrier screening.

**↑ Limitations**

This test detects the 23 mutations recommended by the 2004 American College of Medical Genetics (ACMG) guidelines for use in CF population carrier screening. Coverage also includes 9 additional mutations as part of an expanded core panel to support genetic diversity of multiethnic populations. It will not detect the hundreds of other possible mutations in the CFTR gene. For follow up testing of affected individuals whose familial mutations are not known or who have no mutations or only one mutation found using this panel, extended mutation panels are available in other laboratories and

complete DNA sequencing of the gene is available in the UCLA Orphan Disease Testing Center.

## Methodology

A multiplex polymerase chain reaction (PCR) is performed to amplify the genomic DNA sample with 16 pairs of PCR primers and DNA polymerase. Next, the oligonucleotide ligation assay (OLA) is performed on the CFTR amplicons. Allele-specific OLA probes hybridize to the respective normal, mutant, and variant alleles and become ligated with fluorescent-labeled common probes upon successful annealing by the ligase enzyme. The OLA probes are varied in length due to the addition of inert mobility modifiers. The ligated, fluorescent-labeled DNA fragments are separated by capillary electrophoresis and detection is based on size and fluorescent label. The ACMG-recommended mutations detected by this method are: G85E, R117H, 621+1G>T, 711+G>T, R334W, R347P, A455E, delta1507, deltaF508, 1717-1G>A, G542X, G551D, R553X, R560T, 1898+1G>A, 2184delA, 2789+5G>A, 3120+1G>A, R1162X, 3659delC, 3849+10kbC>T, W1282X, and N1303K. The 9 additional mutations detected are: S549N, S549R, V520F, 3876delA, 394delTT, 2183AA>G, R347H, 1078delT, and 3905insT. The polymorphisms detected (via reflex testing after detection of homozygosity for del1507 or delF508) are: I506V, I507V, F508C. The poly-T tract of intron 8, 5T/7T/9T, is intended as a reflex test for individuals who have the R117H mutation in order to determine the likely phenotypic effect (CF vs. congenital bilateral absence of the vas deferens).

## Additional Information

Cystic fibrosis (CF) is the most common lethal autosomal recessive disorder among Caucasians of northern European ancestry and the most common genetic cause of infant mortality. CF is found less frequently in other racial and ethnic groups. The heterozygote (carrier) frequency among Caucasians in the United States is approximately 1 in 29. CF is characterized by one or more clinical features that vary in severity, including a progressive decline of pulmonary function secondary to chronic lung infections, exocrine pancreatic insufficiency and elevated chloride concentration in sweat. Almost all males with CF are sterile due to congenital bilateral absence of the vas deferens. Affected newborns may present with meconium ileus. These clinical manifestations of CF are the result of abnormally viscous mucous secretions from glands and duct epithelia, leading to infection. The basic defect causing this disease remains unknown. Diagnosis of CF is based on carefully defined clinical criteria, analysis of sweat chloride concentration, and mutation analysis. In 2001, the American College of Medical Genetics and the American College of Obstetricians and Gynecologists established a standard of care that all pregnant couples and those planning a pregnancy be offered carrier screening for the 25 most common CFTR mutations, and the panel was revised in 2004 to a total of 23 mutations after the removal of two variants (1078delT and I148T). The test described here is suitable for that purpose. For individuals who are negative for mutations by targeted mutation testing, DNA sequence analysis of the entire CFTR gene coding region is available

(offered as Cystic Fibrosis Full Gene Sequencing) in the Orphan Disease Testing Center. Genetic consultation with the laboratory directors is available.

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