

## UCLA ORPHAN DISEASE TESTING CENTER

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### Cystic Fibrosis Full Gene DNA Sequencing Assay

**Sample type:** Blood

**Clinical Significance:**

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 and analysis of sweat chloride.

In contrast to many other recessive disorders, the carriers of CF mutations have no biochemical or physiological alterations by which they can be identified. Before the identification of the gene that underlies CF, couples learned that they were both carriers upon the birth of an affected child. Analysis of the Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) gene, which is located on the long arm of chromosome 7, allows for identification of familial mutations in an affected patient, assessing carrier risk for an individual planning a pregnancy or relatives of affected patients, prenatal diagnosis, diagnosis in a symptomatic newborn, 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. To date, over 1000 different mutations in the CFTR gene have been described, although fewer than 35 occur with appreciable frequency. In 1997, a NIH consensus panel recommended that all individuals considering a pregnancy be offered testing for CFTR mutations to determine carrier status. The American College of Medical Genetics has published a minimum mutation panel recommended for general population carrier screening (Grody et al., 2001). As for any DNA-based test, CF mutation analysis must always be followed by appropriate counseling so that the patient fully understands the residual risk associated with a negative result.

## **Methodology:**

The ACMG mutation panel will detect approximately 97% of mutations in Ashkenazi Jews, 88% of mutations in non-Hispanic Caucasians, and lower percentages in other ethnic groups. Accordingly, some CF patients may have one or both of their mutations not detected if only the panel is used. Therefore, we have developed a full gene sequencing assay for the CFTR gene which includes all exons, intron/exon borders, and specific intronic regions that is capable of detecting >95% of all known CF mutations according to the Cystic Fibrosis Mutation Database as of 2009. Large deletions are not detected by this analysis.

**Turnaround Time:** 4 weeks

## **References:**

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