

# Cystic Fibrosis: DNA Analysis

## Indications for Molecular Testing

- Cystic Fibrosis diagnosis (abnormal mucus clearance from respiratory tract with frequent infections, pancreatic insufficiency, abnormal salt transport, meconium ileus, infertility in males)
- Family history of cystic fibrosis
- Carrier detection

## Molecular Detection of Cystic Fibrosis Mutations

**AIM:** Direct detection of point mutations and small deletions in the *CFTR* gene on chromosome 7. The assay consists of multiplex PCR followed by allele specific assay for 25 different mutations in 14 different regions of the *CFTR* gene with comparison to positive control specimens. The heterozygote (carrier) frequency is listed below for several ethnic populations. Genotype-phenotype considerations are important as some mutations associated with mild disease are dominant to alleles usually associated with more severe symptoms, in the compound heterozygous individual. This test represents the ACMG/ACOG recommended allele screening. Mutations screened include:  $\Delta F508$ ,  $\Delta I507$ , R117H, 621+1 G>T, R334W, R347P, A455E, 1717-1 G >A, G542X, G551D, R553X, R560T, R1162X, 3659delC, N1303K, W1282X, 1078 del T, 2789+5 G>A, 3849+10kb C>T, G85E, 711+1 G>T, 3120+1 G>A, 1898+1 G>A, 2184 del A.

### *Cystic Fibrosis Carrier Rate by Racial and Ethnic Group, before and after Screening*

Racial or ethnic group	Detection Rate	Estimated Carrier Risk	
		Before test	After Negative test
Ashkenazi Jewish	97%	1/29	~ 1/930
European Caucasian	80%	1/29	~ 1/140
Hispanic American	57%	1/46	~ 1/105
African American	69%	1/65	~ 1/207
Asian American	Not Available	1/90	Not Available

## Interpretation of DNA analysis

Results are interpreted in the context of family history and autosomal recessive inheritance pattern of cystic fibrosis. Both asymptomatic carrier detection and diagnosis of affected individuals are available. The child of two carriers has a one in four chance of being affected due to inheritance of a mutant *CFTR* allele from each parent. The test utilizes allele specific oligonucleotides that distinguish wild type and mutant alleles. An individual with normal *CFTR* genes will have a pattern of hybridization for the wild type sequence. A heterozygous carrier will have signal from both wild type and mutant alleles. An individual with cystic fibrosis will not have signal from the wildtype allele (homozygous affected) or will have two different mutant allele signals (compound heterozygote) plus the corresponding wild type alleles. Due to significant allelic heterogeneity, rare *CFTR* mutant alleles (<0.1% of patients) may not be detected in our screening panel and further testing may be recommended.

## Specimen Requirements

Peripheral blood samples (3-5ml) collected in purple-topped (EDTA) tubes shipped to the address below. Blood spot cards or buccal swabs may also be used for specimen collection; call the lab (314 454-8685) for details on collection device and shipment. Send specimens with request form to the following address:

**Molecular Diagnostic Laboratory**  
**Barnes-Jewish Hospital North, Room 2445**  
**MailStop 90-28-372**  
**216 South Kingshighway**  
**St. Louis MO 63110**

Clinical information must be provided with specimen referral in order to correctly interpret test results.

## Current Pricing

Contact Lab Customer Service for current pricing 314-362-1470.  
CPT codes: 83907, 83890, 83900, 83896, 83912.

Ref: Trends in Genetics 8: 392-398, 1992. Tsui, LC.  
Human Mutation 4: 167-177, 1994. The Cystic Fibrosis Genetic Analysis Consortium.