

Cystic Fibrosis DNA Screen

Background

Cystic fibrosis is an autosomal recessive disease caused by a defect in a gene called *CFTR* (cystic fibrosis transmembrane conductance regulator). This assay tests for the most common mutations in the *CFTR* gene, and includes all mutations in the panel recommended by the American College of Medical Genetics for general population carrier testing for cystic fibrosis (ref. 2, 3, 6). The mutation detection rate is ~89% (ref 4) in the overall population tested by this laboratory, which is mostly European. The mutation detection rate can be higher or lower than this for specific ethnic groups. Mutations included in this screen are:

A455E, deltaF508, deltaI507, G542X, G551D, G85E, N1303K, R1162X, R117H, R334W, R347P, R553X, R560T, W1282X, 1717-1G->A, 1898+1G->A, 2184delA, 2789+5G->A, 3120+1G->A, 3659delC, 3849+10kbC->T, 621+1G->T, and 711+1G->T.

Reflex testing for I506V, I507V, F508C, and 5T/7T/9T variants may also be performed in selected cases as recommended by the ACMG (ref. 2, 3,6).

Indications for Testing

- Carrier testing in an individual with or without family history of CF, or in spouse of CF carrier
- Evaluate suspected CF
- Establish mutation status of CF-affected individual or obligate carrier
- Evaluate male infertility due to congenital bilateral absence of vas deferens
- Follow up prenatal ultrasound findings that are suspicious for CF
- Evaluate idiopathic chronic pancreatitis

Genetic Counseling

Genetic counseling can be useful to patients and families considering genetic testing. The laboratory can provide referrals to genetics clinics in the patient's locale or a listing can be found at www.genetests.org

Ordering

1. Obtain blood sample.
If prenatal, call Genetics Lab with information on fetal sample and when it will be obtained.
2. Fill out a Clinical Lab Request - Genetics for each patient.
(available at <http://depts.washington.edu/labweb/dept/div/genetics/geninfo.html>).
-Request: "Cystic Fibrosis"
3. Provide items needed for test interpretation and risk calculation:
Clinical diagnosis
Ethnic background
Pedigree (if appropriate)
4. Call Laboratory Medicine Community Services (206) 598-6066 to arrange the best method of shipment.

Sample Requirements and Specimen Handling

Whole blood - EDTA (purple top) - adults - 5 mL, children - 1-3 mL.
Samples should be received within 72 hours of collection.
Samples may be refrigerated until shipped.
For prenatal diagnosis specimens, consult laboratory.
Heparin (green top) tubes are not acceptable.

Test Frequency and Reporting

Test results usually within 1-2 weeks of specimen receipt. A written interpretative report is issued.

References

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2. Grody WW, Cutting GR, Klinger KW, et al. Laboratory standards and guidelines for population-based cystic fibrosis carrier screening. *Genetics in Medicine* 3:149-154, 2001. Also available at <http://www.acmg.net/resources/policy-list.asp>
3. Richards CS, Bradley LA, Amos J, et al. Standards and guidelines for CFTR mutation testing. *Genetics in Medicine* 4:379-391, 2002.
4. Watson MS, Cutting GR, Desnick RJ, et al. Cystic fibrosis population carrier screening: 2004 revision of American College of Medical Genetics mutation panel. *Genetics in Medicine* 6:387-391, 2004. Also available at <http://www.acmg.net/resources/policy-list.asp>
5. Palomaki GE, Haddow JE, Bradley LA, FitzSimmons SC. Updated assessment of cystic fibrosis mutation frequencies in non-Hispanic Caucasians. *Genetics in Medicine* 4:90-94, 2002.
6. Watson MS, Desnick RJ, Grody WW, et al. Cystic fibrosis carrier screening: Issues in implementation. *Genetics in Medicine* 4:407-409, 2002.
7. Rowe SM, Miller S, Sorscher EJ. Cystic fibrosis. *N Engl J Med* 352:1992-2001, 2005.