Cystic Fibrosis (CF) – OMIM 219700

Background

Cystic Fibrosis (CF) is one of the UK's most common life-threatening inherited diseases; it affects over 8,000 people in the UK. The gene responsible for CF, *CFTR* (OMIM 602421) is involved in controlling the movement of salt around the body. CF affects the internal organs, especially the lungs and digestive system, by clogging them with thick sticky mucus making it difficult to breathe and digest food. This can lead to infections and inflammation in the airways and gut. Another common symptom in males is infertility. Severity of the disease varies widely from mild to severe. CF is autosomal recessive; an individual needs two altered copies of the *CFTR* gene to be affected. Over two million people in the UK (about 1 in 25) are carriers of CF, and if two carriers have a child, there is a one in four chance of that child being affected.

Recommended Clinical Referral Criteria

- Gut Echogenicity (EGB) on ultrasound scan of foetus (initially test parents)
- Meconium Ileus in newborn; failure to thrive in newborn and infant
- High Immuno Reactive Trypsinogen (IRT) found during newborn screening
- Pulmonary and/or digestive problems with positive sweat test in infant/child/adult
- Infertility in males due to Congenital Bilateral Absence of the Vas Deferens (CBAVD)
- Known family history (with or without confirmation of familial pathogenic variants)

Molecular Analysis

Pathogenic variant screen:

Level 1: In-house real-time PCR assay for 8 common pathogenic variants* in the CFTR gene (90% clinical sensitivity)**

Level 2: Analysis of 50 common European pathogenic variants in the CFTR gene using the Elucigene CF-EU2v1 kit (96.6% clinical sensitivity)**https://www.yourgene-health.com/reproductive-health/cystic-fibrosis/cystic-fibrosis-analysis

** Clinical sensitivity is based on the incidence of these CFTR pathogenic variants in the Welsh population – **it is important to note that the pathogenic variant frequencies vary between different ethnic populations.**

For patients clinically diagnosed with CF, approximately 1% (CF8) and 0.1% (CF50 CF EU2) would appear normal, i.e. no pathogenic variants would be detected. Patients with a strong clinical suspicion of CF or a positive sweat test can be forwarded to a specialist laboratory for a full gene screen.

Family follow-up: Testing for known familial pathogenic variants in *CFTR* gene

*CF8 pathogenic variants: c.254G>A, p.(Gly85Glu); c.489+1G>T; c.1521_1523del, p.(Phe508del); c.1624G>T, p.(Gly542Ter); c.1652G>A, p.(Gly551Asp); c.1657C>T, p.(Arg553Ter); c.1766+1G>A; c.3848G>T, p.(Arg1283Met). CFTR gene reference sequence is NM_000492.3 (LRG_663t1),

Test (Price available on request)	TAT(calendar days)
Known pathogenic variant testing on a fetal sample **or** CF8 screen in fetal sample when EGB detected on ultrasound	3
Parental screening for 8 common pathogenic variants after detection of EGB on fetal ultrasound	14
Diagnostic testing for 8 common pathogenic variants in Newborns with suspected CF (delayed meconium or failure to thrive)	14
Prenatal carrier status	14
Confirmation of a newborn screening (NBS) result	14
Diagnostic test for 8 common *CFTR* pathogenic variants (CF8) or 50 common *CFTR* pathogenic variants (CF50) in a patient with suspected CF or CFTR-related disease	42
Population screening for partner of a patient affected with CF or a carrier of CF	42
Known pathogenic variant testing for a patient with a family history of CF	42

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Sample Requirements
Blood – 5ml in EDTA (1ml neonates/infants);
Please contact lab prior to sending a prenatal sample.
Please label samples with three identifiers and date of collection.
All samples must be accompanied by request form
Consent for testing & DNA storage is assumed when request for test received

Links
Orphanet
https://www.orpha.net/consor/cgi-bin/index.php
OMIM
https://omim.org/
Genetic Test Registry
https://www.ncbi.nlm.nih.gov/gtr/
Support
Cystic Fibrosis Trust
https://www.cysticfibrosis.org.uk/