Disease NIPD for Cystic Fibrosis

Contact details

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Samples required

- **Pregnant Women**
  2x 10mls venous blood in plastic EDTA bottles or glass Streck tubes, this should ideally reach the laboratory within 24-48 hours of sampling
- The minimum gestation (by scan) is 9wks for accepting a sample. If earlier than 18wks then 2 blood samples a week apart may be required
- **Testing must be arranged in advance**, through your Local Clinical Genetics Department or Fetal Medicine Unit
- A completed DNA request card and ultrasound report should accompany all samples **with an appropriate telephone number and a secure fax number.**
- **Pregnancy outcome**
  Details of pregnancy outcome will be required for confirmation of laboratory results as part of the ongoing validation of new tests

Patient details

To facilitate accurate testing and reporting please provide patient demographic details (full name, date of birth, address), details of any relevant family history and full contact details for the referring clinician

Introduction

Cystic fibrosis (MIM 219700) is an autosomal recessive condition caused by mutations in the cystic fibrosis conductance regulator (*CFTR*) gene. CF affects epithelia of the respiratory tract, exocrine pancreas, intestine, male genital tract, hepatobiliary system, and exocrine sweat glands, resulting in complex multisystem disease. Pulmonary disease is the major cause of morbidity and mortality in CF. Paternal mutation exclusion by non-invasive prenatal genetic diagnosis (NIPD) is now possible using cell free fetal DNA (cffDNA) in pregnancies at risk of cystic fibrosis for carrier couples where the parental mutations differ and the paternal mutation is one of 11 mutations covered by the panel

Referrals

All referrals should be made via a Clinical Genetics Department or Fetal Medicine Unit. Both parental mutations must have been confirmed by molecular genetic testing. This test is only applicable to couples

1) who are known carriers of **different** CF mutations **AND**
2) the paternal mutation is one of the 11 mutations listed below

c.489+1G>T	c.1519_1521delATC p.(Ile507del)
c.1521_1523delCTT p.(Phe508del)	c.1624G>T p.(Gly542*)
c.1646G>A p.(Ser549Asn)	c.1647T>G p.(Ser549Arg)
c.1652G>A p.(Gly551Asp)	c.1657C>T p.(Arg553*)
c.1679G>C p.(Arg560Thr)	c.3846G>A p.(Trp1282*)
c.3909C>G p.(Asn1303Lys)	

The absence of a paternal mutation indicates that the fetus is at most only a carrier for CF and is therefore predicted to be unaffected. This test is not applicable to couples who carry the same CF mutation, or where the CF mutations have not been characterised. If you wish to refer a case which does not fulfil these criteria please contact Professor Lyn Chitty (l.chitty@ucl.ac.uk) (Clinical) or Fiona McKay (Fiona.McKay@gosh.nhs.uk) (Laboratory).

Service offered

Targeted next generation sequencing (NGS) for 11 mutations in CFTR.

Technical

Maternal EDTA blood is spun as soon as possible after collection, cffDNA is extracted from plasma. Molecular analysis is performed by PCR, followed by NGS (Illumina MiSeq). Amplification of fetal DNA will be confirmed using HLA markers, or *ZFY*-specific sequences.

Target reporting time

Results are normally available within 5 days of sample receipt.