

## Disease NIPD for Apert syndrome

### 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

Apert syndrome (MIM 101200) is a congenital disorder characterized primarily by craniosynostosis, midface hypoplasia, and syndactyly of the hands and feet with a tendency to fusion of bony structures. Most cases are sporadic, but autosomal dominant inheritance has been reported. Apert syndrome can be very severe and is easily distinguishable from other craniosynostosis syndromes. Two mutations in FGFR2 exon 8, c.755C>G (p.Ser252Trp) and c.758C>G (p.Pro253Arg), account for over 98% of reported cases.

Non-invasive prenatal genetic diagnosis (NIPD) is now possible using cell free fetal DNA (cffDNA) in pregnancies at risk of Apert syndrome.

### Referrals

All referrals should be made via a Clinical Genetics Department or Fetal Medicine Unit and will be accepted in either of the categories given below. If you wish to refer a case which does not fulfil these criteria please contact Professor Lyn Chitty ([l.chitty@ucl.ac.uk](mailto:l.chitty@ucl.ac.uk)) (Clinical) or Fiona McKay ([Fiona.McKay@gosh.nhs.uk](mailto:Fiona.McKay@gosh.nhs.uk)) (Laboratory)

1. At risk pregnancy
  - Paternal Apert syndrome **OR**
  - a previous pregnancy has been confirmed to have Apert syndrome, thus there is a very small risk of recurrence due to germline mosaicism
2. Abnormal ultrasound findings
  - Acrocephaly **AND**
  - Symmetrical syndactyly

### Service offered

Targeted next generation sequencing (NGS) for p.Ser252Trp (c.755C>G), p.Pro253Arg (c.758C>G) and c.755\_756delinsTT (p.Ser252Phe) mutations in FGFR2

### 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.