Disease NIPD for Crouzon syndrome with acanthosis nigricans (CAN)

Contact details

Regional Genetics Service
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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

Crouzon syndrome is an autosomal dominant disorder characterised by craniosynostosis causing secondary alterations of the facial bones and facial structure. Crouzon syndrome with acanthosis nigricans (CAN) (MIM 612247) presents with congenital craniofacial abnormalities consistent with classic Crouzon syndrome plus velvety hyperpigmentation of the skin and is caused by a single missense mutation in FGFR3 (c.1172C>A p.(Ala391Glu)). Choanal atresia or stenosis is often present (41%), and is considered highly suggestive of CAN. Other commonly reported signs include hydrocephalus (43%), oral abnormalities such as cleft palate, dental malocclusion, and cementomas of the jaw (34%), and melanocytic nevi (25%). Kidney involvement has also been reported. Some of these specific features are rare in patients with classic Crouzon syndrome.

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

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) (Clinical) or Fiona McKay (Fiona.McKay@gosh.nhs.uk) (Laboratory)

- Paternal Crouzon syndrome with acanthosis nigricans (CAN) syndrome **OR**
- a previous pregnancy has been confirmed to have Crouzon syndrome with acanthosis nigricans (CAN), thus there is a very small risk of recurrence due to germline mosaicism

Service offered

Targeted next generation sequencing (NGS) for FGFR3 c.1172C>A p.(Ala391Glu).

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.