INFO BROCHURE NIPD

CROUZON SYNDROME WITH ACANTHOSIS NIGRICANS

Non - Invasive Prenatal Diagnosis (NIPD) for Crouzon syndrome with acanthosis nigricans

Craniosynostosis : Craniosynostosis is a condition in which one or more of the fibrous sutures in an infant skull prematurely fuses by turning into bone (ossification), thereby changing the growth pattern of the skull. There are many types of Craniosynostosis : Crouzon syndrome with acanthosis nigricans is a craniosynostosis associated with velvety hyperpigmentation of the skin. Choanal atresia or stenosis is often present and is considered highly suggestive of this disorder. Other commonly reported signs include hydro-cephalus, oral abnormalities (such as cleft palate, dental malocclusion, and cementomas of the jaw), melanocytic nevi and kidney anomalies.

Inheritance : Crouzon syndrome with acanthosis nigricans is an autosomal dominant condition caused by a single c.1172C>A mutation (p.Ala391Glu) in the FGFR3 gene encoding the Fibroblast Growth Factor Receptor 3. The FGFR3 mutation of the affected patient can be absent in the unaffected parents (sporadic cases). In familial cases the affected parent also has a mutation in the FGFR3 gene and there is a 50% risk of any future children inheriting the FGFR3 mutation.

Methods : The c.1172C>A (p.Ala391Glu) mutation in the FGFR3 gene is analysed in DNA isolated from maternal blood (cell free DNA - cfDNA) which also contains fetal DNA. Such **N**on - **I**nvasive **P**renatal **D**iagnosis is referred to as NIPD. In contrast to invasive procedures such as amniocentesis (AC) or chorionic biopsy (CVS) that have an overall risk of miscarriage of 1 %, NIPD is non-invasive and has no risk for the fetus.

Samples : At least 20 ml blood in specific blood tubes provided by GENDIA is required from the mother. The maternal blood can be taken from week 10 of the pregnancy. The sample has to be sent by Express mail to GENDIA's lab in Antwerp, Belgium, and arrive there within 2 days of withdrawal.
All testing must be arranged in advance by emailing to NIPT@GENDIA.net.
It is essential that the laboratory is advised of the pregnancy gestation and that this has been confirmed by ultrasound scan.

Turnaround time : NIPD takes 2 weeks to complete from arrival of the sample in the GENDIA lab.

GENDIA – *Genetic Diagnostic Network*
Emiel Vloorsstraat 9
B-2020 Antwerp
Belgium

Phone : + 32 3 303 08 01
Fax : + 32 3 238 77 70
E-mail : info@gendia.net
Web : www.GENDIA.net

Indications : NIPD for Crouzon syndrome with acanthosis nigricans can be performed when :

1. The father has Crouzon syndrome with acanthosis nigricans with a documented c.1172C>A -(p.Ala391Glu) mutation in the FGFR3 gene.

2. A previous pregnancy has been confirmed to have Crouzon syndrome with acanthosis nigricans with a documented c.1172C>A (p.Ala391Glu) mutation in the FGFR3 gene. In those cases there is a very small risk of recurrence due to germline mosaicism.

The original test lab reports with documented CFTR mutations in both parents must be made available before NIPD can be planned.

Contraindications : NIPD for Crouzon syndrome with acanthosis nigricans can NOT be performed when :

1. When the mother has Crouzon syndrome with acanthosis nigricans no NIPD can be performed as the maternal FGFR3 mutation cannot be differentiated from the fetal mutation in maternal blood.

2. Samples from twin / multiple pregnancies or missed abortion / vanishing twin cannot be accepted for NIPD.

Limitations of NIPD : Samples are analyzed for the c.1172C>A (p.Ala391Glu) mutation in the FGFR3 gene only.

Reliability of NIPD results : The reliability of NIPD is very high (99 %).

Results : NIPD results will be sent to the physician / genetic counseler who ordered the test and who will explain the test results and recommended follow-up steps if necessary.

Follow up steps :

1. In case of a normal NIPD result : when the c.1172C>A (p.Ala391Glu) mutation in the FGFR3 gene is absent from the maternal blood no specific follow up is necessary, unless ultrasound examination of the fetus reveals anomalies and further genetic studies might be indicated.

2. In case of an abnormal NIPD result : when the c.1172C>A (p.Ala391Glu) mutation in the FGFR3 gene is found in the maternal blood, the fetus is affected with Crouzon syndrome with acanthosis nigricans. The physician / genetic counseler will discuss the implications of this finding with the parents.

Price : 1400 Euros.

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