

Genetiska kliniken
Hans Ehrencrona

Meddelande om ändrade rutiner för kromosombrottsanalys från 2012-01-01

Genetiska kliniken laboratorium i Lund har under de senaste åren varit det enda laboratorium i Sverige som utför kromosombrottsanalys och cellcykelanalys vid misstanke om kromosombrottsyndrom såsom vid Fanconi anemi. Trots att vi tagit emot prover från hela riket så har endast c:a 20 analyser per år utförts. Då det är i patientens och sjukvårdens intressen att denna analys utförs med högsta möjliga kvalitet så har vi därför beslutat att fr.o.m. 2012-01-01 avveckla kromosombrottsanalysen vid vårt laboratorium då det vid positivt fynd krävs molekyllärologisk analys som vi inte kan erbjuda.

Vi har tagit fram två alternativa laboratorier som utför flera hundra kromosombrottsanalyser per år. Observera att inremitterande måste skicka prover (5-10 ml perifert blod i heparinrör) direkt till dessa laboratorier för att få bästa kvalitet på analysarbetet då analysen kräver färskt blod. Att skicka proverna via Genetiska kliniken medför en onödig tidsåtgång vilket kan försämra analysresultatet, och dessutom innebär det en merkostnad för inremitterande. Vårt pris för brottsanalysen har varit drygt 19 000 kr så ändringen innebär ingen kostnadsökning.

Se bifogade PM från respektive laboratorium; här sammanfattas i korthet alternativen:

1. Amsterdam, VU university medical center. Det cytogenetiska laboratoriet utför kromosombrottsanalys med en angiven svarstid om två veckor till en kostnad av 1493 EUR (c:a 13800 SEK). Fördelen med detta laboratorium är att de även kan gå vidare med den kompletta sekvenseringen av samtliga 13 Fanconiassocierade gener vid positivt fynd, man behöver således inte skicka extra prover för de positiva fallen. Avdelningen har också ett långvarigt forskningsintresse kring Fanconi anemi, och utgör ett "European Fanconi Anaemia Centre", vilket torde borga för kvaliteten i analysen.

2. London, Guy's and St Thomas' Hospital. Det cytogenetiska laboratoriet utför kromosombrottsanalys med en angiven svarstid om 7-10 dagar till en kostnad av 499 GBP (c:a 5400 SEK). Detta laboratorium är således klart billigare än Amsterdam, och potentiellt med snabbare svarstid. De kan dock inte erbjuda komplett molekyllärologisk screening, så vid ev. positivt fynd måste ett nytt blodprov i så fall skickas till Amsterdam för sekvensering.

Lund den 20 december 2011

Ulf Kristoffersson
Verksamhetschef

BILAGA 1:
Cytogenetics laboratory
VU university medical center Amsterdam

**PROTOCOL FOR SENDING BLOOD SAMPLES FOR THE CHROMOSOME
BREAKAGE TEST FOR FANCONI ANEMIA (FA)**

- Please telephone our laboratory to arrange the date and time of sampling and sending the blood. Telephone: +31 20 4440746
- We require 5 to 10 ml of heparin blood (lithium heparin and sodium heparin, also in gel form, are suitable).
The blood sample should be sent to us as soon as possible after taking (please see below for the address of our laboratory).
- Please send the following information together with the blood sample:
Name, date of birth, gender, address, medical details including white cell count, name and telephone number of the referring doctor, and the name and address of the person to whom the invoice should be sent.
- Please note that the FA test cannot be performed directly following a blood transfusion. One needs to wait for 3 to 4 weeks before taking the blood sample.
- The blood should be transported at room temperature. Please put the words “room temperature” on the package. Please also put our telephone number on the package.
- The sample should be sent by a courier service (TNT courier service appears to work well).
- Please fax the airway bill form to us as soon as the courier has picked up the package. Fax number: +31 20 4440744.
- In general, Wednesday appears to be the best day to send us the blood sample. In this way it should arrive here at the latest by Friday. Please note that blood taken more than 48 hours before it reaches us is not usable.
- Chromosome analysis for FA takes about 4 weeks. In urgent cases it can be done within 2 weeks provided you inform us in good time that it is urgent.
- The fee for the test is EURO 1493,--

- Please send the sample to:
Drs. S.L. Bhola
Laboratorium voor Chromosoomdiagnostiek
VU Medisch Centrum
Polikliniek ((PK 0X011)
De Boelelaan 1117
1081 HV Amsterdam
The Netherlands
Tel.no: +31 20 4440746

- For more information you can always contact us by email (Chrom@vumc.nl) . This email is always checked.



BILAGA 2:
Guy's and St Thomas' Hospital NHS Trust
Cytogenetics unit

Guidelines for sample requirements for chromosome breakage studies requests.

The following are a summary of the sample requirements for requests for pre and postnatal diagnosis of chromosome breakage syndromes. Tests are available for Fanconi anaemia, Ataxia telangiectasia, Nijmegen breakage syndrome and Bloom syndrome, and these tests can be discussed in detail by contacting Ian Kesterton by email ian.kesterton@gsts.com or phone 44 (0)20 71881701 or fax 44 (0) 20718 81697 or Anne Bergbaum on 020 71881701; or Dr Zoe Docherty on 020 71881699. All requests for prenatal screening must be discussed with one of these individuals before a test can be offered.

The charge for the test on a blood sample (pre & post natal) is £499:00

Assuming there are no complications we aim to report blood samples within 7-10 days of receipt and fibroblasts (AF, CV & solid tissue samples) within 3-4 weeks. If the result is urgently required a suitable fax number should be sent with the referral so that the report can be faxed to avoid delay in the post.

All samples should be sent at **room temperature** to arrive at this laboratory within 48 hours (ideally 24 hours). The address is Cytogenetics, 5th Floor Tower Wing, Guy's Hospital, Great Maze Pond, London, SE1 9RT.

1. **Fanconi anaemia.**

Screening for Fanconi anaemia can be performed on venous blood (pre and post natal) and fibroblasts (amniotic fluid, chorionic villus or other solid tissue). This laboratory routinely uses Diepoxybutane (DEB) as the DNA stressing agent but tests using Mitomycin C (MMC) can be performed if required; DEB is generally considered to be the agent of choice.

Blood samples:

- For lymphocyte cultures, between 5 and 10 ml of peripheral blood in lithium heparin or sodium heparin is the normal sample requirement, although 1ml is generally sufficient if the blood is in good condition and the patient's white cell count is sufficiently high. For fetal bloods 1-2ml of blood is ideally required; however a test can be performed with as little as 0.5ml as an absolute minimum. If the patient is known to have a very low white cell count it is advisable to discuss this with the breakage section before sending a blood sample.

BILAGA 2:
Guy's and St Thomas' Hospital NHS Trust
Cytogenetics unit

Other tissue samples:

All requests for prenatal diagnosis of Fanconi anaemia must be discussed in advance with the chromosome breakage section.

Where there is a family history of Fanconi anaemia, prenatal diagnosis is only offered to families where clearly raised chromosome breakage has been demonstrated in the proband (preferably by screening the proband in this laboratory, although if this is not possible then a copy of the original cytogenetic results should be obtained from the laboratory that performed the test). Prenatal diagnosis for Fanconi anaemia may also be considered where characteristic features such as radial aplasia are seen on ultra sound.

The limitations applicable to the test must be clearly explained.

Due to the rarity of the syndrome, experience is limited compared to other syndromes and we currently only guarantee a clear cut positive result on chorionic villus samples (CVS) and amniotic fluid (AF) samples, and all negative results should be confirmed on a fetal blood sample. However, most families choose to accept a negative result on CV or AF samples with the limitations that apply, in which case the result should be confirmed postnatally. The only published case of a false negative result for FA was on a CV sample and shown to be due to maternal cell contamination. We can test for this possibility in our prenatal samples by PCR analysis if a sample of maternal blood in lithium heparin is sent with the CV or AF sample; this provides greater confidence in a negative result. To date all results of prenatal tests on CV and AF samples performed by this laboratory have been accurate.

- For AF samples a volume of approximately 15ml should be sent. CV samples should arrive in transport medium and should be sufficiently large to yield 15-20mg of cleaned villi.
- Products of conception should be sent in a dry sterile container.
- Skin biopsies should be 1cm² full depth sent in a dry sterile container.

2. Ataxia telangiectasia and Nijmegen breakage syndrome.

Screening for Ataxia telangiectasia and Nijmegen breakage syndrome can be performed on venous blood (pre and post natal) and fibroblasts (amniotic fluid, chorionic villus or other solid tissue); Gamma ray irradiation is used as the stressing agent.

Blood samples:

- For lymphocyte cultures, between 5 and 10 ml of peripheral blood in lithium heparin is the normal sample requirement; an absolute minimum of 1.5 ml of blood is required. For fetal bloods 1-2ml of blood is ideally required, although a screen can be performed with as little as 0.75ml as an absolute minimum.

Other tissue samples:

The requirements and test limitations for screening on CV, AF and other solid tissue samples are the same as for Fanconi anaemia.

3. Bloom syndrome.

Screening for Bloom syndrome can be performed on venous blood (pre and post natal) and fibroblasts (amniotic fluid, chorionic villus or tissue). The standard sample requirements given for Fanconi anaemia apply for each tissue type.