

INFORMED CONSENT FOR ARRAY CGH TESTING

Background

The aim of genetic testing is to detect or exclude the presence of, or predisposition for, genetic disease by directly or indirectly analysing the genetic constitution (chromosomes, genes).

The human genetic constitution is present in the nucleus of every cell in the body. It consists of 23 pairs of chromosomes, one of which is the sex chromosomes: XX in women and XY in men. Sperm and egg cells are special however, and contain only one copy of each chromosome which allow the pairs to reform after fertilisation. Genes, which consist of DNA, are the basic units of heredity. They are lined up in a strand to form the chromosomes, with each nucleus containing around 21 000 genes. Within the cell, but outside the nucleus, a few genes are located in the mitochondrial structures and show a variable number of copies. The complete set of genes present (the genome) form the blueprint for the structure and function of the body by coding for the synthesis of proteins.

There are basically two levels where genetic changes occur:

- **Chromosomal changes**

Changes in the number or structure of chromosomes are detected under the microscope and described in the karyotype. In cases where changes are too small to be detected by this method (so-called submicroscopic aberrations) a high resolution chromosome analysis (array CGH) can be offered which is able to detect some of these changes.

- **Molecular changes**

Small changes at the level of single or several genes called "gene or DNA mutations" are studied by molecular methods. The choice of test depends on the specific disease. They are not always informative and sometimes no result can be obtained. Molecular genetic testing is always related to a specific disease question. Screening (non-directed search for changes) of the genome cannot be offered.

Implications

Genetic tests may provide information of a highly personal nature and require your consent. They can determine whether a person is a carrier of a mutation which may be inherited and associated with disease in their offspring. Genetic tests may show that a person is affected by a specific genetic disease or at an increased risk of being affected by it in the future. They may also reveal an increased risk for other family members or for the child of an ongoing pregnancy.

In order to be aware of the aims, consequences and limitations of genetic testing, adequate genetic counselling by a trained professional is required by law.

Genetic counselling

Genetic testing, like any other diagnostic procedure, is voluntary and requires formal consent.

You should take the time to ask any questions you might have to help you make an independent personal decision. It may be advisable to reconsider your decision and ask for a second appointment.

Below you will find some aspects that should be discussed in language easily understandable by you before you decide for or against a genetic test.

- The **major medical facts** including the diagnosis, the prognosis and ways of prevention and treatment of the disorder tested.
- The **genetic facts** involved including risks for other family members.
- The probability that the test will give a correct result or prediction, or indeterminate or unexpected findings.
- The risk of receiving an **unfavourable test** result and the **possible consequences** for yourself and your family.
In case of a prenatal diagnosis, this may include the risk of facing a decision about termination of pregnancy. The decision about termination is totally independent of the decision to perform the test.
- **Alternatives** to genetic testing.
- Your right to **refuse** the test.
- Potential benefits and disadvantages, including **questions of privacy protection** dealing with insurances, banks or employers.
- Your care will **not be jeopardized** whatever decision you and your family make.
- Possible use of your tissue sample after testing: retention for reanalysis upon request/ DNA banking (storage)/ use for medical research/destroyed.
- Information about the **costs** and whether covered by health insurance or not.

Procedure

Genetic tests require a small amount of blood to be taken from a vein (about 3 ml). There is no need for this to be on an empty stomach. Genetic material can also be extracted from other sources (e.g. skin, muscle, amniotic fluid).

Legal framework

Federal law on human genetic analyses (LAGH – GUMG).

Cost

Tests included on the list of analyses are covered by the obligatory health insurance. Patients requiring a confirmation of coverage in advance should request this directly from their insurer. Unless otherwise agreed, the bill will be sent directly to the patient. For tests not included on the list of analyses, we recommend that a commitment to provide cover is requested by the referring physician.

Pre-natal array CGH - a method to detect very small chromosomal changes (chromosome aberrations)

Usually after an amniocentesis or chorion biopsy, a conventional chromosome analysis is performed. Trisomy (e.g. Down Syndrome) and the loss or gain of large segments of chromosome material can be reliably detected using this method. These aberrations are the most frequent cause of fetal anomalies involving multiple organ systems recognisable on ultrasound scan.

However, in some cases no chromosome aberration can be detected despite an abnormal ultrasound. This may be because the change is too small to be detected by conventional chromosome analysis. These so-called submicroscopic aberrations may, however be detected using array CGH. The DNA chips used are very high resolution and cover all chromosomes, allowing detection of small losses and gains of chromosome material with a high level of accuracy. These may include well-described, but lesser known abnormalities. A causative chromosome aberration is found by using array CGH in 10-15% of pregnancies with fetal abnormalities.

Indication - when is it useful to perform a pre-natal array CGH analysis?

Array CGH increases the diagnostic possibilities in pre-natal diagnosis and is indicated in cases with fetal abnormality in ultrasound scan (e.g. cardiac anomalies in conjunction with growth retardation, multiple organ abnormalities, suspicion of chromosome microdeletion or microduplication syndromes).

Very small changes in only one gene e.g. point mutations cannot be detected using array CGH testing.

Small chromosome changes are also found in healthy individuals

All human beings are carriers of very small chromosomal differences that have little effect on their health or mental capabilities. When a previously undescribed and unclear change is found prenatally using array CGH, it is recommended that both parents are tested to determine whether the change has newly occurred in the fetus or if it has been inherited from one of the parents. In some cases, even after testing the parents, it may not be possible prenatally to predict the relevance of the results for the child. Array CGH testing should only be carried out when **clearly indicated**.

Rarely, results of an array CGH analysis on a child can be an indirect indication of the carrier status for genetic disease of one of the parents. Carrier status usually has no effect on the health of the individual. It does, however, mean an increase in the risk of having further affected children. If, due to the trio analysis (both parents and child), questions arise concerning paternity or consanguinity, they will not be taken further.

If the amount or quality of DNA after sampling is insufficient, it may not be possible to carry out array CGH testing.

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Consent for array CGH analysis

I confirm that I have received genetic counselling and that enough time for questions and reflection has been provided. My physician has informed me that this consultation conforms with the federal law on human genetic analyses (GUMG). With this signature I agree to the following investigation/analysis

Disease / Diagnosis:.....

Genetic analysis: Array CGH testing

Copies of the results should be sent to the following : (address required)

.....
.....

I wish to be informed...

- of the results of the genetic testing for the reasons above Yes No
- of any incidental findings of clinical relevance without reference to the above Yes No

I agree to ...

- the storage of test material for use in quality control or for any future testing (in my interest and only at my request) Yes No

Comments:

.....
Place, Date Signature (Patient / (parent / legal representative where applicable))

Referring physician

I hereby confirm that I have counselled this patient in accordance with the federal law on human genetic analyses (GUMG)

.....
Place, Date Signatur and stamp (referring physician)