



INFORMATION FOR PATIENTS

Informed choice in diagnostic genetic testing

The purpose of genetic testing is the detection or exclusion of genetic changes that may underlie a given genetic disorder or represent a risk factor for a disorder. This information sheet lists a few aspects that should be considered prior to a genetic test. Furthermore, information is provided regarding different methods used for the genetic investigations and their application.

Before undertaking a genetic investigation

Genetic testing is performed on a voluntary basis and requires your formal consent since the analyses may provide sensitive data. A consultation with a specialist is recommended in order to discuss the options, pros and cons, consequences and limits of the specific genetic test. You should make sure that you have sufficient time for decision making and that you clarify all questions you may have. For your assistance we have listed several points which should be discussed in the context of a genetic counselling session and which should provide you with the necessary information to make a personal, informed decision whether or not you are willing to perform the genetic test.

- Clinical utility of the genetic test for diagnosis, prognosis, prevention and therapy regarding the disorder to be tested.
- The results of genetic testing may have implications for further family members.
- Meaning of a genetic test result, its clinical validity as well as the possibility of false negative, false positive or inconclusive results as well as incidental findings.
- Probability of an unfavourable result with all the consequences and decision making that may arise (including a possible disclosure of the results to health insurance companies).
- Alternatives to a genetic test.
- Your right to refuse the genetic tests.
- Your decision concerning the use of the biological sample after testing: e.g. storage for possible future analyses, archiving, use of the sample for medical research purposes, or disposal of the sample.
- Information regarding costs of the analyses, and whether or not the costs would be covered by the health insurance.

Procedure

A small amount of venous blood is usually sufficient for genetic analyses. Fasting prior to sampling is not necessary. At times the analyses are performed using other tissues (for example skin and muscle biopsies, or amniotic fluid for prenatal analyses).

Legal framework

In Switzerland the analyses are performed according to the law on genetic testing on humans (GUMG, SR 810.12)

Possible application fields for genetic testing

Genetic investigations provide important information in many medical fields. The applications can be roughly subdivided into the following groups:

Diagnostic genetic testing aims at establishing or confirming a genetic diagnosis for an affected patient. A clear diagnosis is often possible, with the benefit of enabling appropriate medical care.

Presymptomatic and predictive testing aims at determining whether a healthy individual is at risk or is carrier of a specific genetic disorder.

Prenatal analyses aim at the detection, exclusion or confirmation of genetic defects in a fetus. Prenatal analyses include non-invasive analyses (e.g. non-invasive prenatal test: NIPT performed on maternal peripheral blood) and invasive procedures (e.g. amniotic fluid sampling).

Screenings in families aim at determining whether family members (with or without symptoms) may be carriers of the genetic defects detected in a close relative and whether they may be at risk of passing the genetic defect to the next generation.

Somatic genetic testing aims at detecting genetic changes in specific tissues, for example in tumor tissues. The primary aim is to gain information for therapies and prognosis of a tumor. It is possible that these analyses reveal not only somatic changes but also inherited changes that may represent familial genetic risk factors for cancer.

Background and methods

The human genetic material (which consists of DNA) is located mostly in the nucleus of every cell in the body and with a small amount outside the nucleus in so-called mitochondria. The nuclear genetic material is subdivided into 23 pairs of chromosomes, one pair of which are the sex chromosomes (XX in women, XY in men). Approximately 20'000 genes are located on the chromosomes. A small number of genes are situated on the mitochondrial DNA. All genes together build the genetic blueprint for the structure and metabolism of the body. Changes in the genetic blueprint can lead to disorders: n.b. genetic changes involving small as well as large parts of the genome may lead to severe disorders. Some changes will clearly lead to a disorder whilst other changes may only represent a risk factor for a disorder. Genetic changes are usually analysed at two levels:

At the level of chromosomes: Changes in the number or structure of the chromosomes (chromosomal abnormalities). Large chromosome abnormalities are usually detected by microscopic analysis of the chromosomes. Changes involving small parts of a chromosome are detectable with high resolution molecular chromosome analyses.

At the gene level: Changes at the DNA-sequence level of single genes (gene mutations). Gene mutations may be detected with a range of different molecular methods. The genetic test may be restricted to the analysis of a single gene, to several genes or can be extended to the entire genome (high throughput sequencing). The interpretation of results obtained from the analysis of the entire genome is extremely complex. The simultaneous analysis of a number of genes increases the risk of detecting genetic changes in genes not directly associated with a patient's disorder (i.e. incidental findings) or genes with as yet unclear association with a disorder.

Information regarding high-throughput sequencing

High-throughput sequencing is a method that allows simultaneous examination of multiple genes, the whole exome, or even the whole genome. This method is currently in clinical use for the diagnosis of single-gene defects only. This kind of testing has an increased risk of unexpected or incidental findings i.e. of identifying genetic changes that have no relation to the initial query.

There are a number of different outcomes possible after high-throughput sequencing and you need to decide beforehand, which results you wish to be informed about:

- 1) **Results** that relate directly to the clinical disease pattern i.e. known disease-causing mutations (as already described in the medical literature in association with a given disease) or variants which very probably cause disease and are therefore **compatible with the clinical findings**.
- 2) **Results of unclear significance** whose relationship with the clinical findings is not known. These are so-called “variants of unknown significance” (VUS) for which the predictive programs give differing or contradictory results. Further testing of family members can shed light on the relevance of these variants. As our knowledge of genetics is expanding rapidly, it is expected that the relevance of some of these results will become clearer at some point in the future.
- 3) **Unexpected results**, which are completely unrelated to the initial query and clinical findings. Such results may give information about risks for further disease. Symptoms may already be apparent, or may only develop at a later date. This information, as all genetic results, can have consequences for family members and future offspring.

The possibilities are as follows:

- a) A genetic change with known clinical relevance and associated with a known genetic disease. There are methods of early detection and treatment, and therapeutic methods that can affect the progress of the disease.
- b) A genetic change that causes the predisposition for a genetic disease for which there are currently no possibilities for prevention or therapy.
- c) Detection of carrier status for an autosomal-recessive inherited disease that can occur in family members or offspring.
- d) A variant of unclear significance.
- e) A known benign variant with no effect.

You may withdraw your consent fully, or partially at any time and without stating the reason. You will, however, be billed for services carried out up until the point when consent is withdrawn and the sample will be disposed of.

Due to their complexity, the results of high-throughput sequencing may only be conveyed through the referring clinician and only with your written consent. All raw data will be stored confidentially and conforming to the law.

Patient Database

Registration of the name, surname, date of birth, primary diagnosis and the identified genetic variant in the database of the organization RETINA SUISSE, which combines all patients suffering from degenerative diseases of the retina, permits RETINA SUISSE to inform patients specifically and individually about future newly developed therapy options.

Variant Database

Registration of the genetic variants in an anonymous form in a public but non-commercial database in the Leiden Open Variation Database format (LOVD) allows improvements in molecular diagnostics for other patients and helps to improve the knowledge on disease mechanisms. This registration is made according to the rules for data protection defined by the respective federal law.

Costs

The obligatory health insurance covers all tests that are included on the analysis list. A request for coverage of the costs by the health insurance will be made by the clinic. For genetic analyses covered by the health insurance the costs of the analyses will be taken over by the insurance except for the patient's contribution and liability. Unless otherwise agreed, the patient will receive all bills directly.

Universitätsklinik für Kinderheilkunde

Abteilung Humangenetik, 3010 Bern
Leitung: Prof. Dr. phil. nat. Sabina Gallati
Tel. +41 31 632 94 46
Fax +41 31 632 94 84

INFORMED CONSENT BEFORE GENETIC TESTING

I confirm that I have received genetic counselling and that I have had a sufficient amount of time for questions and reflection. I have been informed by my physician that the advice I received conforms to federal law on human genetic testing (GUMG).

With this signature I give my permission for the following investigations:

Disorder:

Genetic analysis/es:

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

.....
.....

I wish the testing to be carried out...

- even if it is not under obligatory cover and in the absence of a confirmation of coverage YES NO
(If necessary I will cover the costs up to CHF myself)

Incidental findings: Should the analysis/es reveal results not directly related to the testing requested (so called "incidental findings"), I wish to be informed as follows:

- disorder for which preventive and/or therapeutic measures are available YES NO
- disorder for which no preventive / therapeutic measures are yet available YES NO
- State of healthy carrier of a recessive disorder which could concern the following generation or other family members YES NO

Should these questions remain unanswered it will be assumed that the patient does NOT want to be informed about incidental findings.

Storage and use of the remaining biological material and data for further analyses

- I agree that the remaining biological material and data will be stored for possible further analyses. YES NO
In case of a negative answer the remaining biological sample will be destroyed after the analysis!
- I agree that my biological sample and data are used anonymously for quality testing YES NO
- I agree that my biological sample and data coded with a pseudonym are used for scientific purposes. YES NO
This includes analyses exclusively to clarify the question asked above as well as the publication of anonymized data in scientific journals.
- I agree to have my data registered in the registry of the patient organisation RETINA SUISSE YES NO
(Name, Surname, date of birth, primary diagnosis and genetic variants)
- I agree to have my data registered in an public, non-commercial database (LOVD format) YES NO

Signature: Place and date:
(Patient or parent/legal guardian)

Referring physician:

I declare that I've informed the above mentioned person/s, according to the law on genetic testing on humans (GUMG), about the planned genetic tests and their limits as well as providing answers to the patient's questions.

Surname: Name:

Signature: Place and date: Stamp :