Patient Information for Adolescents (12-17 years)

on the scientific study

Identifying the Causes of Rare Diseases Using Genome-Wide Sequencing

Klinikum rechts der Isar
Public Law Institution

Institute of Human Genetics

Prof. Dr. Julia Höfele
Provisional Head of Institute

Office: Iris Weisenstein
sekretariat.ihg@mri.tum.de
Trogerstraße 32
D-81675 München
Tel. +49 89 4140 6381
Fax: +49 89 4140 6382
www.mri.tum.de/humangenetik

Dear Patient!

Thank you for your interest in our study and for reading this information sheet.

We would like to invite you to take part in a study that will help us to find out more about where **rare diseases** come from, how to recognise them better and how they can best be treated.

As part of your treatment, data about your health will be collected and body materials (tissues or samples of body fluids) may be taken during a blood sample or an operation. The body materials are called "biosamples".

Now we are asking you to donate your patient data and certain biosamples for research on the congenital causes of rare diseases. Please consider carefully if you take part in our study. Please also discuss your thoughts with your parents.

Your consent is voluntary. If you refuse or wish to withdraw your consent at a later date, this will not result in any disadvantages for you or your parents.

Within the framework of this research project, we adhere to the requirements of the German Genetic Diagnostics Act (GenDG).

On the following pages, we will explain our study in more detail so that you can then decide for or against participation. If you would like to know more about the study, you can ask us questions at any time.

Rare Diseases

A disease is considered rare if it affects **no more than 5 in 10,000** people. Most rare diseases are hereditary, so they often manifest at birth or in early childhood. However, some of these diseases only manifest in later childhood or adulthood.

Changes (so-called genetic variants, formerly mutations) have already been found in many different genetic make-ups (the so-called genes, i.e. the "blueprint" that nearly every cell in a human being carries) that can cause rare diseases. However, many disease-causing genes are still unknown.

In order to better predict the course of a disease and then perhaps treat it more effectively, we need to understand the genetic (i.e. hereditary) causes of diseases more precisely. With our study, we want to gain new knowledge for the future diagnosis and treatment of rare diseases.

Aim of the Study

We want to study the entire genetic material (the genome) of young people or adults with the disease and their families in order to find out which hereditary (or genetic) changes lead to certain rare diseases. However, the primary aim of this study is not to diagnose yourself. Your data and biosamples will *be made available to medical researchers* to help them make progress in identifying and treating rare diseases. However, **your data and biosamples will never be sold**!

Study Procedure

In order to systematically investigate the changes in the genetic material (or the genes), we ask adults and children who have a rare disease, as well as their possibly unaffected relatives/family members, to donate blood samples for medical research. The significance of genetic examinations is increased if your parents and/or other relatives can also be examined.

The aim of the research project is to examine the entire genetic material (the genome) of the biosample donors - i.e. children, adolescents, and adults - for disease-causing changes that could be associated with the respective disease. The significance of changes in the genetic material can then be confirmed by examining other biosamples provided by you, e.g. by examining messenger molecules of the genetic material (RNA messenger molecules) or proteins and metabolic products which can be isolated from blood, but also from tissues.

In order to assess whether a change found in the genetic material causes the disease or not, it is usually necessary to examine the genetic material of the parents and the genetic material of other family members.

What are we asking you?

- Your treating physician will talk to you in detail about this study. After sufficient time for reflection, we ask you for your written consent to participate in our study. You can confirm this with your signature. In addition, your parents must give their written consent to your participation in the study.
- With the help of various data from you, i.e. also from previous and current examination findings (e.g. ultrasound examinations, ECG, X-ray or magnetic resonance imaging examinations) and laboratory results (e.g. from blood, urine, possibly nerve fluid or tissue samples), the current state of health is described as accurately as possible. Selected patient data are entered in **encrypted form** into the study database of the Klinikum rechts der Isar. Encrypted means that neither your name nor your initials nor your date of birth are used for encryption, but only **a letter-number code**, the so-called pseudonym (see also under "Who has access to your data and biosamples and how are they protected?").
- Blood will be taken from all study participants in order to examine the hereditary substance (genetic analysis) and - depending on the clinical picture - also to carry out further laboratory tests.
- Your attending physician will decide together with you which biosamples from you may still be required:

- Fingernail sample
- Urine sample (spontaneous urine)
- 24-hour urine sample
- Saliva
- Skin biopsy (tissue sample from the skin only for patients of whom a skin sample is taken anyway as part of the medical diagnosis or treatment, no additional sample is taken)
- Muscle tissue (only if a muscle sample is taken anyway as part of the medical diagnosis or treatment, no additional sample is taken)
- Cerebrospinal/nerve fluid (in patients only as an additional sample up to a maximum of 5 ml during a routine puncture that is being performed anyway)

- In addition, we ask you to allow us to use biosamples such as small tissue parts and/or body fluids that have already been taken from you for diagnosis or therapy and are no longer needed (residual materials) for our study. These may be blood, saliva, nerve fluid or tissue taken during an operation or biopsy.
- The same rules and principles as described above for your patient data are applied to the handling of the biosamples, their pseudonymisation (encryption) and the analysis results obtained from the biosamples.

Risks

Identification of your person: Whenever data is collected, stored and transmitted in the context of research projects using patient data, there is a potential risk of traceability to your person by obtaining of additional information, e.g. from the internet (public databases) or social networks (e.g. Facebook). This is especially the case if you yourself publish information on your hereditary constitution (i.e. genetic data) and other health data, e.g. for genealogical research via the internet.

Blood sampling: The risks for patients are usually very low and do **not** increase the usual risks of a routine blood withdrawal (haematoma, local infection, very rarely damage to skin nerves). The total amount of additional blood collected for this study is - depending on the decision of your attending physician - up to a maximum of 25 ml (corresponding to about two tablespoons).

Risks associated with obtaining other biosamples that may be required:

Urine sample/saliva sample: The donation of a urine sample or a saliva sample is not associated with any additional risks.

Tissue sample: The procedure is performed under local anaesthesia only in the context of treatment if the collection of a tissue sample (skin, muscle) **is planned anyway**. The tissue sample is taken under local anaesthetic, so you will not feel any pain. *You will be informed separately about the risks associated with the tissue biopsy that is necessary for treatment or diagnosis.* As a rule, taking small skin samples is free of complications. However, despite all the care taken, complications can occur, e.g. a bruise (a haematoma) can appear around the incision site. In rare cases, there may also be soft tissue damage and nerve damage in the collection area, localised inflammation and/or blood poisoning. Permanent damage to nerves with subsequent sensory disturbance or even paralysis is even rarer.

Nerve fluid: Spinal fluid (liquor, cerebrospinal fluid) can - depending on the decision of your treating physician - only be taken as an additional sample of a maximum of 5 ml during a puncture that **is planned anyway** as part of the medical treatment/diagnosis. This additional collection does not cause you any additional risk. *You will be informed separately about the other risks involved in the routine puncture necessary for treatment or diagnosis.*

What are the benefits and consequences of participating in the study for you personally?

Since it usually takes a long time to improve the detection and treatment of rare diseases, you will probably not benefit directly from the scientific use of your data and biosamples - at least we cannot promise that.

However, in individual cases it is possible that we obtain knowledge that could also influence your specific treatment. If we find such indications of the possible genetic cause of your disease, we would like to inform you and your parents about it. Your parents can choose in the consent form whether they/you want to receive such information or not.

In rare cases, a research result might indicate that, in addition to the disease under investigation, an additional serious, previously possibly unrecognised disease probably exists in a study participant or will occur in the future, which could be treated or whose outbreak could even be prevented. This is what we then call "additional findings". If the researchers notice something that could be important for your health, we will inform your parents if they agree.

Who has access to your data and biosamples and how are they protected?

Your biosamples and data are not stored with your personal data (name, date of birth, address), but are encrypted with a letter/number code. Your data can only be assigned to your person by your attending physicians.

Your biosamples and medical data may be shared with institutions that are working with us in this study. They may also be shared with researchers who are not involved in this study. Your parents have received more information about this. The researchers who work with your biosamples only know the letter/number code, nothing else. Even if the results of the research are published - e.g. in scientific journals or in the internet - your name will never be mentioned.

Your patient data and biosamples shall be stored at least **until the day you turn 19 years. However, on the day you reach the age of majority, you can decide yourself about the further use of your donated biosamples and data**. For this purpose, the study personnel will contact you and your parents. If you do not report back (within one year), your biosamples will be destroyed and the allocation key will also be destroyed, so that it is no longer possible to allocate your data to your person, even via the primary study investigator.

Recontacting and communicating of results

We may want to contact you and your parents again, e.g. to inform about important results of this study or important additional findings (see further above under "What are the benefits and consequences of participating in the study for you") or also to ask for further information and/or biosamples from you. If you or your parents do not agree with this, you should check the appropriate box in your parent's (or guardian's) consent form.

All study and research results that we share with you/your parents in the context of a new consultation are only preliminary and <u>do not represent</u> valid genetic findings. In coordination with you and your parents, your caring doctors can arrange for a renewed quality-checked human genetic analysis on the basis of the German Genetic Diagnostics Act (GenDG). We will be happy to help you arrange this.

What does your right of withdrawal mean?

Your consent is voluntary!

You can withdraw your consent to the further collection and scientific use of your patient data and the biosamples you donated at any time without providing reasons and without disadvantages for you or your parents.

In the case of a withdrawal, the biosamples you have provided for medical research will be destroyed and your patient data stored according to this consent will be deleted. If deletion is not possible or not possible with acceptable technical effort, your data will be anonymised by deleting the identification code assigned to the data.

For a withdrawal, please contact your treating physician:

name:_____phone:_____

or contact the study office of the Klinikum rechts der Isar of the Technical University of Munich, tel: 089-4140-6381, who will then forward your request to the physician you named.

Further information on data protection

You can request information from the Klinikum rechts der Isar of the Technical University of Munich about the data stored of you within the scope of the legal requirements. If incorrect personal data is processed, you have the right to request correction. You and your parents can also request the deletion of personal data or the restriction of processing or data transfer.

If you have any questions about the progress of the study and the processing of your data, you are welcome to contact the study management at the Institute of Human Genetics (contact via: sekretariat.ihg@mri.tum.de, phone: +49 89 4140 6381).

The data controller within the meaning of the GDPR is **Klinikum rechts der Isar der Technischen Universität München**, Anstalt des öffentlichen Rechts, Ismaninger Straße 22, 81675 München, Tel.: +49 89-4140-0 or e-mail: vorstand@mri.tum.de. The Klinikum rechts der Isar of the Technical University of Munich has appointed a data protection officer, whom you can contact with any concerns about your patient data or with a report about data protection irregularities. The contact details are as following: **Klinikum rechts der Isar der Technischen Universität München, Stabsstelle Datenschutz, Ismaninger Straße 22, 81675 München, phone: +49 89-4140-0 or E-Mail: datenschutz@mri.tum.de.**

You and your parents also have a right of complaint with any data protection supervisory authority. You can find a list of the supervisory authorities in Germany at:

https://www.bfdi.bund.de/DE/Infothek/Anschriften_Links/anschriften_links-node.html

The data supervisory authority responsible for the Klinikum rechts der Isar of the Technical University of Munich is:

der Bayerische Landesbeauftragte für den Datenschutz,
Postfach 22 12 19, 80502 München, E-Mail: poststelle@datenschutz-bayern.de

If you and your parents have any questions about the research project or what it means for you, please do not hesitate to contact us at any time.