Hannover Medical School

Department of Human Genetics
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Study Information

"Predicting the clinical outcome of non-muscle actinopathies"

Purpose of this research
You have been / your child has been diagnosed with a genetic change (mutation) in either the *ACTB* or *ACTG1* gene. Clinically, a non-muscular actinopathy (NMA) is present. This may be Baraitser-Winter cerebrofrontofacial syndrome (BWCFF), an *ACTB*-associated developmental disorder, an *ACTG1*-associated hearing loss or ocular coloboma or another *ACTB*- or *ACTG1*-associated disorder. Any disease in the NMA spectrum is very rare. So far, only a few patients have been described worldwide. The exact disease mechanism is still unknown and no specific therapeutic approaches have yet been developed. It is not yet clear why some *ACTB* or *ACTG1* mutations lead to multiple symptoms of BWCFF and others do not.
Our aim is to learn more about the nature of *ACTB*- or *ACTG1*-based diseases by applying cellular, molecular-biological, biochemical and biophysical experiments. We will investigate the consequences of the genetic change for different processes in the patient's cells. Our long-term goal is to develop specific therapeutic strategies.
An additional aim of our research is to further characterize the clinical course of BWCFF and non-BWCFF conditions associated with *ACTB or ACTG1*-mutations. This will allow us to detect late complications and set up corresponding preventative measures.

Before consenting to participate in the study, the following information must be taken into account:

Eligibility criteria
The inclusion criterion for this study is the confirmation of a genetic change in one of the two genes *ACTB* or *ACTG1*.

It is up to you to decide whether or not you (or your child) participate in this study. Your decision will not affect your/your child's future medical care. If you/your child decide to join the study you will still be able to withdraw at any time during the research without giving any reason.

Procedure of the study

The tests usually require two blood samples (5-10 ml) and a single skin biopsy (diameter of 3 mm) of the affected person as well as a blood sample of both parents. Blood samples of both parents are necessary for better evaluation of the child's results.
The blood sample will be taken in conjunction with another blood sample that needs to be taken anyway. **Your / your child's consent is the most important prerequisite for the sample collection.**

The following clinical data is documented as part of the study: Family history, information on the course of pregnancy and birth, birth measurements, course of the first months of life, in particular neurological complications and surgical interventions, course of development (achievement of milestones, available results of developmental diagnostics, IQ test), other previous medical findings, available cMRI images, epilepsy history (if applicable), available laboratory findings.
We will also take photographs of you / your child, which will be stored on secure servers at the Department of Human Genetics at the MHH. If you are not coming to the genetics clinic in person, we will ask you to send us some private photographs. In some cases, it will be necessary for the photographs to be used in the publication of the study results. The facial images are recognizable and their publication poses a confidentiality risk.

We will contact you at regular intervals to monitor the clinical progress.

You can contact us in any way you wish (in person during our consultation hours, by telephone, video conference or by post).

Handling the samples and results

The blood samples taken are labeled pseudonymously and stored at the Department of Human Genetics at the MHH. Excess test material is stored for the purpose of verifying our results and for later analyses to characterize the NMA disease within this study. The samples are stored for at least 10 years and in principle indefinitely.
This study involves characterizing the cell cultures created from your / your child's donated material with regard to changes in their biological, molecular biological, biochemical and biophysical properties due to the presence of mutations. The research data collected will be correlated with the clinical findings with the aim of developing therapeutic approaches for these rare hereditary diseases. The results are published in renowned journals and presented anonymously at specialist conferences.
If, in the course of this study, there are changes in the activity or function of the actin proteins in your / your child's cells that cannot be correlated with the other data collected, we will sequence the actin genes again to verify the mutation. We would like to point out that we will not collect any additional health-relevant findings in this context and that no genome-wide sequencing will be carried out with the samples.
We do not assume that the results obtained within the research framework will have any direct consequences for study participants in terms of diagnosis and treatment. However, if this should be the case, these results will be communicated to the patients and their families as part of genetic counseling.
We will be happy to explain the overall results of the study on request.

Financial benefits and insurance

Participation in the study is free of charge for you. You will not receive any payment for providing the blood samples. You are not entitled to any remuneration, royalties or any other participation in financial benefits and profits that may be obtained on the basis of the research with your blood samples or the blood and tissue samples of your child.
We would like to point out that there is no travel insurance.

Data protection

Within this study, we will collect personal data (name, date of birth, contact address) that will be stored electronically in a pseudonymized form at a different location than the clinical information. This means

that the personal data will be replaced by a computer-generated, 5-digit number identification (pseudonym) that does not contain any features that would allow unauthorized persons to identify the study participant. All samples and other materials of the enrolled patients will be processed in this pseudonymized form.
In contrast to anonymization, pseudonymized samples could in principle be followed back to the patient, i.e. to combine person and data, but this is not possible without the knowledge of a specific allocation key and without access authorization to the correspondingly secured servers of the Department of Human Genetics, MHH. Therefore, only a small group of persons has access to the stored data. These persons have been instructed in accordance with the Federal Data Protection Act and have been obligated to maintain secrecy and data confidentiality. The data is secured against unauthorized access. The reason why the data are used in a pseudonymized and not anonymized form in this study is, that in research studies of this kind it may be necessary to consult with the patient, e.g. to ask for certain details about the disease or to be able to correctly assign material that is not collected at the time of inclusion in the study but is sent later (or before) by the family doctor to the respective person. Informing the attending physicians about the study results requires your explicit consent.
Experimental data will be handled confidentially in accordance with the general data protection regulations (GDPR; further information on the EU data protection rules: https://ec.europa.eu/info/law/law-topic/data-protection/eu-data-protection-rules_en) and all national regulations.

Experimental data will be stored locally in the Department of Human Genetics of MHH in a long-term archive which are secured by regular backups and password-protected access. The raw data is archived for at least ten years. This data can be reused for potential follow-up projects.
Publication in a professional journal is made anonymously, without naming personal data and without the possibility of tracing personal data for outsiders. Please note that if the facial images are published, the possibility of the person being recognized cannot be ruled out.

Benefits of the study
You will be informed in detail about BWCFF syndrome and other non-muscular actinopathies.

The *ACTB* and *ACTG1* genes are expressed in every cell in the body. They are two proteins that are essential for many cell functions. Although the role of these two proteins in several biological processes, from embryonic development to neuronal degradation and cancer metastasis, is under debate, there is still insufficient information on the functions of individual actin forms in mammalian cells (including human cells).
The study of the patient's own cells with different mutations in the actin genes offers a unique opportunity to understand the processes controlled by actin.
Our preliminary work suggests that there is a strong correlation between the changes in individual cells and the severity of the disease. If the correlation is proven, we will provide a tool for a more accurate prognosis. Additionally, we expect to establish the first assessment of the disease course in adult patients, with special interest in the potentially increased risk for hematological malignancies. We will also establish detailed clinical guidelines that can be offered to all study participants.

There is also the opportunity to get to know other families who have children with the same illness. Please let us know if you are interested in making contact.

If necessary, additional reports are prepared for submission to the health insurance companies if questions arise regarding the assumption of costs for the care measures.

Potential risks
Sample collection: The tests usually require a single blood sample (5-10 ml) and a single skin biopsy (diameter of 3 mm) of the affected person as well as a blood sample of both parents. Blood draw can leave a small bruise. There is also a very small chance of infection or a nerve injury where the needle pokes the skin. The skin biopsy causes a small scar.

Withdrawal of consent

If you wish to terminate your participation in the study, please inform us of your decision. The notification can be made by telephone, post or email. Please do not hesitate to contact us if you have further questions or require more information.

Contact

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You are hereby informed of your rights under the General Data Protection Regulation (GDPR) (Article 12 et seq. GDPR):

Legal basis:
The legal basis for the processing of your personal data in medical studies is your voluntary written consent in accordance with the GDPR and the Declaration of Helsinki (declaration of the World Medical Association on ethical principles for medical research involving human subjects) and the guideline for good clinical practice.

You have the following rights with regard to your data (Article 13 et seq. GDPR):

Right to information:
You have the right to information about the personal data concerning you that is stored in the collected, processed or, if necessary, transmitted to third parties in anonymized or pseudonymized form (provision of a free copy) (Article 15 GDPR).

Right to rectification:
You have the right to have inaccurate personal data concerning you rectified (Articles 16 and 19 GDPR).

Right to erasure:
You have the right to erasure of personal data concerning you, e.g. if this data is no longer necessary for the purpose for which it was collected (Articles 17 and 19 GDPR).

Right to restriction of processing:
Under certain circumstances, you have the right to request that processing be restricted. This means that the data may only be stored, not processed. You must request this. To do so, please contact your examiner or the data protection officer of the test center (Articles 18 and 19 GDPR).
In the event of rectification, erasure or restriction of processing, all those who have received your anonymized/pseudonymized data will also be notified (Article 17 (2) and Article 19 GDPR).

Right to data portability:
You have the right to receive the personal data concerning you that you have provided to those responsible for the study. This means that you can request that this data be transmitted either to you or, if technically possible, to another body designated by you (Article 20 GDPR).

Right of objection:
You have the right to object at any time to specific decisions or measures concerning the processing of personal data relating to you (Article 21 GDPR). Such processing will then generally no longer take place.

Consent to the processing of personal data and the right to withdraw this consent:
The processing of your personal data is only lawful with your consent (Article 6 GDPR). You have the right to withdraw your consent to the processing of personal data at any time. However, the data collected up to this point may be processed by the bodies named in the patient information and consent form for the respective study (Article 7 (3) GDPR).

Notification of personal data breaches ("data breaches"):
If a personal data breach is likely to result in a high risk to your personal rights and freedoms, you will be notified immediately (Article 34 GDPR).

If you would like to exercise one of these rights, please contact your auditor or the data protection officer at your test center.
You also have the right to lodge a complaint with the supervisory authority/authorities if you believe that the processing of personal data concerning you is in breach of the GDPR (see contact details).

CONTACTS DATA PROTECTION

Data Protection Officer of the MHH
Hannover Medical School
OE 0007
Data Protection Officer
Carl-Neuberg-Straße 1, 30625 Hannover
Email: Datenschutz@mh-hannover.de

If you wish to exercise your right to information in accordance with Art. 15 GDPR as a patient of the MHH, please contact PatientendatenanfragenDSGVO@mh-hannover.de

Data protection supervisory authority:
State Commissioner for Data Protection of Lower Saxony (LfD)
Prinzenstraße 5, 30159 Hannover
P.O. Box 221, 30002 Hannover
Email: poststelle@lfd.niedersachsen.de