Krebsprädispositionssyndrom-Register 01

Registerleitung:
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Prof. Dr. med. Stefan Pfister

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Information for adolescents 12-17 years of age

ADDRess as a part of

Cancer-Predisposition-Syndrome-Registry-01

Dear _____,

In conversation with your parents and your physician, you have just noticed that you and your parents are being asked to participate in a scientific project. These forms will inform you about the project. You can read them think about it and discuss it with your parents and your physician whether you would like to participate.

You have a very rare kind of disease. It is still very unknown in children and teenagers. That is why a number of physicians have joined forces to research this disease. This is only possible through a very large network of physicians because it is not easy to find out anything about rare diseases.

You already agree to participate in the Cancer-Predisposition-Syndrome-Registry-01.

In a further project we want to investigate, how we can improve the treatment of rare diseases like yours. We want to learn how cancer develops, which will eventually lead to milder and more successful therapies.

In this project we want to take blood, bone marrow, a small piece of skin and a cheek swab from all participating children and adolescents. If you already have a blood or bone marrow sample taken, the blood, bone marrow and skin samples required for this project can be taken at the same time, so that we have to prick you as rarely as possible. The samples taken are either first collected at the Children's Oncology Department of Hannover Medical School or directly passed on to various researchers and scientists, where the special examinations are carried out.

Your samples and your medical history will be treated confidentially and in accordance with the data protection process. This means that only we can see your name in connection with your medical history and we will not tell your story in connection with your name or address. If we share our experiences in the treatment of your illness with other physicians (e.g. in a publication), your name and address will be deleted, i.e. it is not possible to see that you are meant.

We would be very happy if you would like to help us and other patients with this disease and we could analyse your samples. If you do not want to participate or if you want to withdraw your consent, this is not a problem. Your medical treatment will be continued normally and for your best.

As soon as you are of legal age, we will contact you again to ask if you would like to continue participating in the study.

You can ask your physicians if you do not understand something. They will gladly help you.

Thank you very much.

Your physician's team

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Informed Consent for patients 12-17 years of age

ADDRess as a part of

Cancer-Predisposition-Syndrome-Registry-01

Surname, first name of the patient _____ Date of birth _____

Treating hospital _____

I agree that information about my illness as well as blood, bone marrow, skin and cheek mucosa as described in the information form, may be passed on to the ADDRess project as a part of CPS-R01 so that research can be conducted on my illness. The aim of the research is to learn more about the disease in the long term. With the knowledge gained in this way, it should be possible to treat those affected better in the future.

The study was explained to me personally and I read the information form. I had the opportunity to ask questions. I know that my participation is voluntary and that I can withdraw my consent at any time without giving reasons and without any disadvantages. I understand that I will be contacted again as soon as I am 18 years old so that I can then decide whether I want to continue participating in the study.

CONFIRMATION OF THE PARTICIPANT

Surname, first name of the patient

Place, date

Signature of the patient

CONFIRMATION OF THE ATTENDING PHYSICIAN

I have discussed the CPS-Registry-01 and the accompanying research including the patient information and the declaration of consent with the patient. All questions were answered comprehensively. I explained to the participant that participation is voluntary. I have obtained the patient's consent.

Name of physician

Place, date

Signature of physician

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Information for parents/guardians

ADDRess as a part of

Cancer-Predisposition-Syndrome-Registry-01

Dear Parents/Guardians,
The physician of your child has informed you that your child has been diagnosed with a cancer predisposition syndrome (CPS). One main feature of this genetic condition is an increased cancer risk.

You have already agreed to your child's participation in the cancer predisposition syndrome register 01.

In order to improve medical and psychosocial care, cancer monitoring, diagnosis and treatment for people with DNA repair disorders, patient representatives, physicians from various disciplines and researchers have joined forces to form the "ADDRess" consortium. ADDRess stands for "Abnormal DNA Damage Response" and consists of 9 subprojects. In these subprojects several scientists throughout Germany are working and researching on this research project and pursue the following aims:

- We want to create an infrastructure that facilitates the exchange of information, the coordination of consultation and the processing of medical patient data for both: patients and healthcare professionals. (Subproject 1, Hannover)
- We want to analyse the molecular mechanisms of diseases with DNA repair defects. (Subproject 2, Würzburg)
- We want to promote psychosocial support by using an evidence-based approach. (Subproject 3, Heidelberg)

- We want to improve cancer monitoring through imaging, pathology and genetic analyses. (Subproject 4, Heidelberg)
- We want to work out cancer-treatment strategies and improve the diagnosis of cancer studying genetic features of patients with DNA repair defects. (Subproject 5-8, Düsseldorf, Hannover, Heidelberg)
- We want to create preclinical models to search for new therapies for patients with DNA-repair-defect-associated cancer that can be tested in early clinical trials. (Subproject 9, Heidelberg)

Brief Overview

Current state of knowledge: Disorders with abnormal DNA damage response (DADDR) are rare genetic diseases with limited DNA repair. The patients share one common feature in shape of an increased cancer risk. The treatment remains complicated due to the genetic disorder. Patients who are treated with analogue radiation or chemotherapy strategies may suffer from an increased level of side effects and intolerances, secondary malignancies and poor treatment outcome, just like cancer-patients without underlying DNA repair defects. Mortality may also be increased. The development of treatment strategies is therefore urgently needed.

Study design: We collect and analyse biospecimen such as blood, bone marrow, tumor specimens, skin and cheek mucosa from individuals with DNA repair defects, in order to improve the medical and psychosocial care, as well as surveillance strategies, diagnosis and treatment of patients with underlying DNA repair disorders.

Procedures and processes: At the time that blood draws are normally completed for your medical care, blood samples will be taken and stored for research purposes. An additional blood sample may be necessary in individual cases. If possible, about 45ml of blood should be taken. Bone marrow will only be collected as part of a diagnostic or routine bone marrow puncture. Skin biopsies will be performed as part of a bone marrow collection if possible. In some exceptional cases it is possible that an additional skin sample collection may be necessary if an adequate skin sample could not be collected during the diagnostic bone marrow puncture. A tumor specimen is collected for research purposes only when a biopsy or tumor resection is performed as part of the patient's medical care. The size of the collected tumor specimen cannot be predicted as it depends on the size of the removed tumor sample. It is assured that research samples will be collected only if there is sufficient tumor material for diagnostic and therapeutic decisions for the patient. Therefore, the collection of tumor specimen for our registry does not impose additional risks. The cheek swab is additionally performed with a cotton swab to obtain DNA. The findings will be transferred to the CPS register and the other subprojects. Since this is a long-term investigation that addresses the course of a condition over several years, the study has no defined duration.

The Risks and Benefits of Participation

Expected individual benefit:
Donating your child's biospecimen and medical data will not necessarily lead to a direct benefit to your child. Our analysis serves primarily as scientific research and is not intended as actionable conclusions for your child's health. Nevertheless, the research may lead to findings that may be of importance to your child's health. In the situation, when an analysis reveals evidence of a severe previously unknown

condition, that can potentially be treated or prevented, we may want to contact you in order to give you this information (see below).

In case you do not wish to receive this type of feedback, please check the box containing “no” on the informed consent. Any time, you can change your decision for or against this feedback option by letting us know. However, please note that you may be obligated to disclose health related information that you receive through our registry, if you prefer this option, to other parties such as health- or life insurance companies. This may be a disadvantage for you.

The statement above is also relevant to genetic analyses and the discovery of genetic conditions. Therefore, this information may be relevant for your child’s family members and family planning.

In the long-term, biospecimen and data collected through our registry is meant eventually to improve the care of patients with cancer predisposition syndromes, which contains DNA repair defects (possibly including participants of the registry). For example, we would like to explore the role of regular evidence-based surveillance strategies.

General Benefit of the Registry:
Medical studies of this kind aim at a better understanding of the processes associated with disease development and improvement in diagnosis and care. Other patients with a cancer predisposition syndrome not participating in this research may benefit from our findings because our research aims at improving the care of all affected patients. Through the collection of biospecimen from individuals with a cancer predisposition syndrome, cancer research in general is advanced. There may be benefit for patients with cancer even in the absence of a cancer predisposition syndrome. We know that mechanism playing a role in individuals with a cancer predisposition syndrome may be relevant for cancer patients on the whole. In theory, it is possible that our research contributes to better therapy and prognosis of cancer patients.

Risks and Disadvantages of participation:
We would like to collect blood samples, bone marrow, tumor specimen, skin biopsies as well as cheek swabs from your child. Apart from the complications that may arise with a blood or bone marrow collection or skin biopsy, there are no other physical risks for your child.

Every ascertainment, storage, transfer of data is associated with the risk of breaching the confidentiality of the data (e.g. risk of identifying your child’s person/information), which may be especially relevant for genetic information. It is impossible to entirely exclude this type of risk. This risk increases with the amount of connected data, especially if you are publishing genetic information in the internet on your own. Please see below regarding data and material security.

Purpose of collecting biospecimen:
The biomaterials are either sent to the registry in Hannover or directly to one of the 9 ADDRess subgroups. The respective recipient is determined depending on the sample. For example, fresh tumor samples for subproject 9 are sent directly to Heidelberg. The skin samples will be sent directly to Würzburg for subproject 2. The further samples are collected in the registry in Hannover, coordinated and sent to the corresponding subgroups.

Protection of your child's biospecimen and data:
The biomaterials are either directly sent to the corresponding subgroups or coordinated by the CPS-registry in Hannover. Further Biospecimen will be stored in the biobank of Hannover Medical School of indefinite duration. Clinical data will be stored on a server of Medical School Hannover. The initials of the first name and surname, the quarter and year of birth, and the sex are recorded. Full names or dates of birth are not stored. However, through the link to the CPS register, it may be possible for the register team to identify your child. However, personal data can only be viewed by the collecting physician, the registry team and the staff of the individual subprojects. Your child's personal data will not be disclosed to third parties apart from ADDRess subprojects, the therapy study of the respective cancer and the Children's Cancer Registry. All identifying information of your child (name, date of birth, address, etc.) will be replaced by an identification code (pseudonymized).
Only after this process, biospecimen and data will be made available for research. Transfer of identifying information to researchers beyond the ADDRess subprojects or others such as insurances und employers does not occur.

The encoded biomaterials and medical data can be transferred to universities, research institutes and researching companies, possibly also abroad, for more precisely defined medical research purposes according to previously defined criteria. It is possible that our registry data will be connected to your data in other databases, in accordance with the law. When data is transferred abroad, it may not be possible to maintain the same high level of data protection as in Germany. Biomaterials and data issued to researchers may only be used for the predetermined research purpose and may not be passed on by the recipient for other purposes. Remaining material will be returned to the Hannover Unified Biobank or destroyed.
The prerequisite for the use of biomaterials and data for a concrete medical research project is, in principle, that the research project has been evaluated and approved by an ethics committee.
Publications are written in an anonymized fashion to prohibit identification of individual participants. This implies the situation, if data is entered into scientific online databases. A publication of your child's entire genetic information (genome) is impossible without your explicit written permission.

Financial benefits to you or the biobank:
You will not be paid for allowing us to collect and store your child's biospecimen and data. You will not receive financial or other compensation, should findings resulting from the research on your child's biospecimen become commercially valuable. With the transfer of the biomaterials to the ADDRess project within the CPS Registry, they become the property of the CPS-R01 Registry of the German Society of Pediatric Oncology and Hematology. You authorize the registry to use your data for research purposes. Your child's specimen and data will not be sold. However, the biobank can ask researchers for an expense allowance for providing specimen to collaborating researchers.

Other Questions and Concerns

Is it possible that you will be contacted regarding the registry?
On a regular basis, results from your medical visits are being forwarded to the registry team. In case of missing data, it could be useful that you are contacted at a later time point in order to request additional information or specimen. Also, this contact could occur to request your permission for connecting your child's data with other databases or in order to give feedback to you or your physician on findings that may be relevant to your child's health. You will not be contacted through the registry team directly but through your child's physician or the health care institution that cares for your child.

In case you do not wish to be contacted, please check the box containing “no” on the informed consent.

What is your right of withdrawal from the registry?
Any time and without justification and disadvantages you may withdraw your consent that allows us to use your child’s biospecimen and data. In case you withdraw your consent, you may decide whether your child’s specimen should be destroyed or be anonymized. In the latter situation, we delete the identification code that allows us to connect a specimen to your child. One has to keep in mind that such an anomymization process cannot entirely exclude the small chance that a specimen can be tracked back to your child. Deletion of data may be limited technically feasibility, however. You can also decide whether your child’s already collected data should be deleted or may be further used in anonymised form. Data can only be deleted under the conditions of Art. 17 DSGVO. As soon as the purchase of the biomaterials and other data relating to your child’s person has been deleted (anonymisation), destruction is no longer possible. In addition, data from analyses already carried out can no longer be removed.

In case you would like to withdraw your consent, please contact:

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Pediatric Hematology and Oncology
Hannover Medical School
Carl-Neuberg-Str. 1
30625 Hannover
Germany
Phone: +49 (0)511 532 6711
Fax: +49 (0)511 532 9120
Email: kratz.christian@mh-hannover.de

Is your participation voluntary?
Your participation in this registry is voluntary. In case you prefer not to participate, your child will experience no disadvantage.

Where can I get additional information?
Should you have additional questions, please contact your child’s physician prior to giving your consent. You can also contact Prof. Kratz or Prof. Pfister. Information regarding findings can be found on www.krebs-praedisposition.de.

We are happy to address your questions.

Sincerely

Christian Kratz, MD Stefan Pfister, MD

Krebsprädispositionssyndrom-Register 01

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Im Neuenheimer Feld 580, 69120 Heidelberg

Informed consent for parents/guardians

ADDRess project

As a part of Cancer-Predisposition–Syndrome-R01

Patient (Last Name, First Name) _____ Date of Birth (dd/mm/yy) _____

Treating Hospital _____

I have read the information sheet and have had the opportunity to ask questions. My questions were answered comprehensively and comprehensibly. I know that my child's participation is voluntary and that I can retract my consent any time without justification and without disadvantages. I had enough time to reconsider my decision to my child's participation and make my own decision.

I give my informed consent that my child's biospecimen as well as medical information as described in the information sheet are sent to the CPS-R01 to be used for medical research purposes especially for the ADDRess project.

I transfer ownership of the biospecimen to Medical School Hannover.

I approve that I may be contacted at a later time point for the following reasons, please check the boxes with “yes” or “no”:

- For the collection of additional medical information/biospecimen □ yes □ no
- If further consent is necessary for the use of your child’s medical information □ yes □ no
- If our research identifies actionable findings that may be relevant to your child’s health □ yes □ no

This contact will occur through the institution that collected my child’s biospecimen and data **or** by the following physician (please give this information to the physician if the latter is preferred):

Physician name and address: _____

Data Protection Statement

I approve that the registry team conducts the following actions (also described in the information sheet):

- Collects and stores the initials of my child’s first and last name as well as the quarter and year of birth,

- Collects and stores identifying materials and information related to my child’s health

- After the collection, the biospecimen and data will be coded to pseudonymised to be used for the ADDRess project

- Coded non-identifying information will be used for scientific publications and online databases

My child’s biospecimen and data may be used for medical research purposes for an unlimited time period.

In a non-identifiable manner, biospecimen and data may be transferred to universities, research institutes/companies for the purpose of medical research. This may include international research projects.

Identifying data can be exchanged with the ADDRess subprojects, the therapy study of the corresponding cancer and the children's cancer registry.

I was informed that I may withdraw my consent to my child’s participation in the registry/ ADDRess project any time without justification. In case of withdrawal, I may request that any remaining biospecimen and data be destroyed, deleted or anonymized.

Please note: If an analysis has been completed, the data cannot be removed.

I have the right to be informed about the stored personal data concerning my child (Art. 15 DS-GVO). If I discover that incorrect personal data of my child is being processed, I can demand correction (Art. 16 DS-GVO).

I have the right to demand the deletion of personal data if certain reasons for deletion exist. This is the case, for example, if the personal data are no longer necessary for the purpose for which they were

originally collected or processed, or if I revoke my consent and there is no other legal basis for the processing (Art. 17 DS-GVO). Furthermore, I have the right to limit the processing of my child's personal data (Art. 18 DS-GVO), to data transferability (Art. 20 DS-GVO) and a general right of objection (Art. 21 DS-GVO).

Data controller: Christian Kratz, MD
Pediatric Hematology and Oncology, OE 6780
Carl-Neuberg-Straße 1
30625 Hannover
Germany

If I have any questions or if I have the opinion that the processing of my child's personal data is not lawful, I have the option of contacting the MHH data protection officer:

Datenschutzbeauftragte der MHH
OE 0007
Carl-Neuberg-Straße 1
30625 Hannover
Germany

I have the right to complain at the supervisory authority if I believe that the processing of my child's personal data is not lawful.
The address of the supervisory authority responsible for the MHH is:

Die Landesbeauftragte für den Datenschutz Niedersachsen
Prinzenstraße 5
30159 Hannover
Germany

I am aware that the data protection regulations set out in the information letter also applies.

I have received a copy of the information sheet and the signed informed consent. The original is kept in the patient's medical record.

In addition, I was orally informed about the ADDRess project.

CONFIRMATION OF PARENTS/GUARDIANS

_____
Patient name (in block capitals)

_____ _____
Place, date Signature parents/guardians

CONFIRMATION FROM THE ATTENDING PHYSICIAN

I have discussed the ADDRess project and the accompanying research including the patient information and the declaration of consent with the custodians. All questions were answered comprehensively. I have explained to the parents/guardians that participation is voluntary.

_____

Name of physician (in block capitals)

_____ _____

Place, date Signature of attending physician