Krebsprädispositionssyndrom-Register 01

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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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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