



AL-PID

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Information sheet for healthy subjects

Genetic and immunological variability in Autoimmune-Lymphoproliferative Primary Immunodeficiencies (AL-PID)

Short title: AL-PID

Dear relative/parent/legal representative,

Your child and you are being invited to take part in the study „**Genetic and immunological variability in Autoimmune-Lymphoproliferative Primary Immunodeficiencies “(AL-PID study)**. This is a research project of the Center for Chronic Immunodeficiencies (CCI) at the Medical Center - University of Freiburg, Germany and involves the collection of clinical data in a database and (long-term) storage of biological material (blood, tissue samples) of your child in a "biobank". Database as well as biobank (CCI-biobank) are located at the CCI. The AL-PID study has been approved by the Ethics Committee of the University Medical Center of Freiburg.

To be able to better understand or interpret the acquired data of your child and the results of our investigations we would like to ask you as parents and/or any healthy siblings for donation of biomaterial which can be stored and used for defined analyses (see Topic 1).

Apart from this written information your physician will talk to you about all procedures of the study. Study participation of you/your child is voluntary. Before you decide about your/your child's participation it is important for you to understand why the research is being done and which rights and obligations it involves. Please take time to read the following information and do not hesitate to ask for additional time or explanations if necessary.

1. What is the purpose/aim of the study?

Your child either suffers or is suspected to suffer from a rare disease of the immune system, which is associated with lymphoproliferation (enlargement of spleen and/or lymphnodes) and autoimmunity (caused by antibodies against blood cells and/or immune reactions in the gut, lung, liver or other organs). We have termed diseases characterized by these symptoms "Autoimmune Lymphoproliferative Immunodeficiencies" (AL-PID). Causes and consequences of many of these diseases are so far poorly understood and therapy is often not satisfactory. Further research is therefore urgently required to improve diagnostic and therapeutic options.

Your biomaterial and/or the biomaterial of your healthy child will be used as a control for samples of your diseased child. Comparing the results of genetic and immunological investigations in your diseased child to those of closely related healthy persons allows a better identification and evaluation of alterations/abnormalities in your diseased child.

2. What are the study procedures?

In case of study participation your treating physician will draw blood for storage in the CCI-biobank. It is a small amount of blood, approximately 5-10 ml (about 1-3 tablespoons), which will not lead to any symptoms

(see Topic 4). In your healthy child blood will only be taken for the CCI-biobank if blood is drawn for a medically required procedure anyway. No additional venous puncture of your child is required but in some cases we may need to draw additional blood tubes. However, the additional amount of blood is so small, that your child will not have any symptoms from it (see topic 4). In addition to the storage of your/your child's blood samples a few defined personal and/or clinical donor data will be saved.

3. How will data and biomaterial be used?

Data:

The data collected from you/your healthy child will be transferred to two databases, which are separately stored on different data drives/devices at the CCI. Identifying data (name, date of birth) of your child are transferred to the "identification database". Only a small number of the CCI staff, who are obliged to discretion have access to this database. Identifying data will never be handed out. The "identification database" will be saved for 10 years after study termination and will subsequently be destroyed.

The data generated from biomaterial will be captured in pseudonymised form in the "research database". Pseudonymisation means that identifying data of you/your child are replaced by a pseudonym, i.e. a combination of numbers, and are thus encrypted. Data can only be related to you/your child by persons who have access to the „identification data base“. The research database will be saved for unlimited time.

If data are transferred to cooperating institutions (scientists, pharmaceutical industry), this will occur after repeated encryption, thus double pseudonymised. Publication of scientific research only takes place in anonymous form, i.e. in a form that precludes identification of you/your child.

With the described measures everything with the currently available technology will be done to protect your privacy. Medical confidentiality and legal regulations for data privacy protection will be met (see also Topic 5).

Biomaterial:

Biomaterial is stored for an unlimited period of time in the freezers of the CCI. Investigations are carried out by scientists of the CCI or scientists from institutions that collaborate with the CCI. These investigations include characterization of hereditary material (genetic material, genome) through genome sequencing with current sequencing methods and methods that will be developed for this purpose in the future. Transfer of samples and data to scientific partners of the CCI takes place exclusively in encrypted form and according to relevant data protection regulations. Transfer of samples and data to unauthorized third parties is ruled out. If you do not agree to the use and storage duration of the samples described above you should mark the corresponding points in the consent form with "no". In this case, no biomaterial of you/your child will be stored in the CCI-biobank.

4. What personal benefits or risks are incurred from participation in the AL-PID study?

Study participation will not be of personal benefit to you/your healthy child. However, study results could contribute to better diagnostic and therapeutic options for future patients. Since your diseased child has a chronic disease, he/she may also benefit him/herself from the insights and experience gained from the research project.

Risks for you as a parent:

We cannot exclude small risks that are normally associated with drawing blood. In rare cases bleeding from the site of venous puncture or in very rare cases damage of blood vessels and neurons can occur.

Risks for your healthy child:

Donation of biomaterial does not entail any additional health hazard for your child since the only biomaterial used for the CCI-biobank are samples collected for anticipated diagnostic or therapeutic measures, which would otherwise be disposed of.

We cannot provide compensation for donated samples. You will not be involved in research endeavors with a commercial aim. Your consent involves waiver of commercial rights (particularly patents) to the samples donated, the data resulting from their investigation and the copyrights of research results.

The samples deposited at the CCI-biobank are considered property of the CCI-Biobank. With your consent you grant the CCI-biobank authority to process and use the data of you/your child.

Collection, storage and transmission of data from your/your child's biomaterial in research projects carry confidentiality risks (e.g. identification) particularly regarding information on the hereditary material. These risks cannot be fully excluded and increase when multiple data can be linked to each other. The risk of confidentiality breach is even greater if you yourself publish your genetic data on the internet (as in ancestry research). The CCI-biobank assures you that all technically feasible measures to protect your privacy will be undertaken, and that your/your child's samples and data will be transferred only to projects that can demonstrate application of adequate data protection procedures. (Topic 5)

5. Who has access to your/your child's data and biomaterial and how are they protected?

Your/your child's biomaterial and data will be saved for an unlimited period of time in the CCI-biobank under standardized quality and safety conditions. Upon request they will be handed out for medical research. According to the best available technology they will be protected from access by unauthorized persons. The CCI-biobank will provide biomaterial and data only to medical research projects that have been evaluated under ethical and judicial aspects and approved by an independent ethics committee.

- a) Samples are encrypted – pseudonymised - before they are stored or/and transferred. Each patient and participant receives a biobank identification number, which is used to identify samples and test results. Then the dataset will get a new code and will be saved. The biobank identification number will be connected to identifying data of your child in the above described „identification data base“ (topic 3). Transmission of biomaterial to cooperating researchers takes place exclusively with the biobank identification number precluding exposure of personal information. Tracing of data to your person/your child by a third party is ruled out. All persons who can access these data are obliged to maintain confidentiality and are under obligation of medical discretion (possible risks are described under topic 4).
- b) Twice encrypted biomaterial and medical data can be transferred on demand and after fulfillment of predetermined criteria to other universities, research institutions or industry, including abroad, for the purpose of medical research. Data as well as medical records can be linked to other databases under given circumstances as long as legal requirements are fulfilled.
- c) Biomaterial and data transferred to a third party can only be used for the determined research purpose. Recipients are not allowed to transfer biomaterial and data further. Biomaterial that is not used is returned to the CCI-biobank or is disposed of.

6. Can study participation be withdrawn at any time?

Study participation of you/your child is voluntary and requires your written consent. You/your child will not be at a disadvantage by refusing to take part. You may also withdraw your consent at any point in time without justification. In case of withdrawal of consent you are free to choose whether your/your child's biomaterial and associated data should be destroyed or further anonymously used for research purposes. However, completed research and publications cannot be reversed or withdrawn (topic 7). An association of genetic material with you/your child through other sources cannot be completely ruled out despite withdrawal of consent. Please inform your treating physician if you want to withdraw your consent.

If your child has completed the 18th year of life, your treating physician will contact you and give your adult child the opportunity to decide him/herself about further storage of data and biomaterial.

7. What other rights do you have in relation to your data?

The EU General Data Protection Regulation (EU-GDPR) ensures your and your child's personal rights and privacy; it enables more transparency and your active involvement. Of course, this also applies to the AL-PID study, whose internal processes follow the requirements of the GDPR and ensure the security of data processing. The GDPR demands extended information obligations: according to art.13 and 14 GDPR, we

are obliged to provide you with basic information on the property rights of the GDPR and the implementation of data protection at the Medical Center - University of Freiburg at the time of data collection. This information is provided (in German) on our website (www.uniklinik-freiburg.de) under the link "Datenschutz" and as written information at the following places: patient registration and waiting room of the outpatient clinics and other central locations within the Medical Center - University of Freiburg. Upon request you will receive information about the specific personal data that has been processed on the person of your child as a free copy (right to information on processed data, art. 15 GDPR). If necessary, you can correct or complete it (right to correct incorrect data, art. 16 GDPR). The right to deletion (art. 17 GDPR), to restriction of processing (art. 18 GDPR) and the right to object to the processing (art. 21 GDPR) have already been explained to you in topic 6: In the case of data processing based on a consent you have the right to withdraw the consent at any time with effect for the future! The legitimacy of the processing until the time of withdrawal remains unaffected. Please direct your inquiries as well as any objections to the processing of your/your child's data or a withdrawal of your consent to your child's participation in the AL-PID study to the persons responsible for data privacy in the study (topic 8).

8. Who can be contacted in case of remaining questions?

If you have further questions, please contact:

- your treating physician: Telephone:

- the investigators responsible for the ALPID study and the data privacy:

Medical Center – University of Freiburg
Department of Pediatric Hematology and Oncology
Center for Chronic Immundeficiency (CCI) and
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Dr. med. A. Rensing-Ehl
Tel. 0761/270 71080
anne.rensing-ehl@uniklinik-freiburg.de

- the data protection officer of Medical Center – University of Freiburg:

Medical Center – University of Freiburg
Data protection officer
Agnesenstraße 6-8
79106 Freiburg
E-Mail: datenschutz@uniklinik-freiburg.de

If you believe that the processing of your personal data is not legitimate, you have the right to complain to a regulatory authority (art. 77 GDPR). An overview of the German regulatory authorities is provided here: https://www.bfdi.bund.de/DE/Infothek/Anschriften_Links/anschriften_links-node.html

(patient label)

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Consent for healthy subjects **Genetic and immunological variability in** **Autoimmune-Lymphoproliferative Primary Immunodeficiencies (AL-PID))**

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I confirm that I have read and understand the information sheet for the AL-PID study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. I understand that my participation/the participation of my child is voluntary and that I am free to withdraw at any time, without giving any reason, without the medical care or legal rights of me/my child being affected. I am aware that my consent as a parent/legal representative must reflect the assumed will of my child and I confirm this with my signature.

I confirm that I was informed:

- that my/my child's biomaterial is stored in the CCI-biobank of the Medical Center – University of Freiburg for unlimited time together with few associated donor data.
- that my/my child's treating physician
.....(Name and city, physician) is released from medical confidentiality to pass on medical data to the University Medical Center Freiburg in the context of the AL-PID study.
- that stored biomaterial can be used for future medical research projects.
- that there is no financial reimbursement for participation or for any product that might result from this study.
- that participation is voluntary and I am free to withdraw at any time, without giving any reasons and without any disadvantage for me/my child.

Information and consent to data protection: I was informed and agree, that biomaterial are stored and personal and clinical data of me/my child are saved in pseudonymised form at the CCI, Medical Center – University of Freiburg and are subsequently analysed. When data is used for research purposes and/or is published in scientific journals it is impossible to trace my/my child's identity. Biomaterial can be used for unlimited time for research projects. If confirmed by crossing „yes“, biomaterial and data may be used and passed on to other research institutes or research industry for medical research purposes after double pseudonymisation. This may include commercial purposes (pharmaceutical industry, patent development at the University Medical Center Freiburg).

I understand that I can withdraw my consent at any time without justification. In case of study withdrawal I can ask for destruction of remaining biomaterial and deletion or anonymisation of collected data. Data of completed analyses cannot be withdrawn.

I agree, that biomaterial(s) is/are stored in the CCI-biobank:	yes <input type="checkbox"/>	no <input type="checkbox"/>
I agree to genetic investigations:	yes <input type="checkbox"/>	no <input type="checkbox"/>
I agree that I may be re-contacted at a later time point with possible information about results relevant for my/my child's health.	yes <input type="checkbox"/>	no <input type="checkbox"/>
I agree, that after double pseudonymisation, data and biomaterial can be used or passed on to cooperating research partners in Germany or abroad (EU countries to which GDPR applies, non-EU countries for which an adequacy decision by the EU commission or appropriate/adequate guarantees exists, as well as countries for which no such adequacy decision or appropriate/adequate guarantees exist).	yes <input type="checkbox"/>	no <input type="checkbox"/>
I agree, that after double pseudonymisation, data and biomaterial may also be used for commercial purposes, e.g. for the development of new medication for this disease in the pharmaceutical industry or for patent development at the Medical Center – University of Freiburg.	yes <input type="checkbox"/>	no <input type="checkbox"/>
I agree, that in case of study withdrawal data and biomaterial acquired until this timepoint can be used for the study.	yes <input type="checkbox"/>	no <input type="checkbox"/>

I have received a copy of this patient information and consent form. The original will be kept by my child's treating physician:

Consent adults

Datum	<input type="text"/>	signature of healthy subject	
		name of physician taking consent	
Datum	<input type="text"/>	signature of physician	

Consent of underage and/or persons incapable of contracting

Date	<input type="text"/>	signature of the legal representative of the healthy subject	
Date	<input type="text"/>	where necessary signature of a second person having the care and custody of healthy subject	
Date	<input type="text"/>	if applicable signature of the child, healthy subject	
		name of the physician taking consent	
Date	<input type="text"/>	signature of physician	