patient label

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 has been 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 organ). 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 1-2 teespoons), 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. 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. Who can be contacted in case of remaining questions?

If you have further questions, please contact:

- Your treating physician: Telephone:

_____ _____

And/or

- CCI staff responsible for the ALPID study:

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Consent for healthy subjects

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

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 are used for research purposes and/or are 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 to genetic investigations:	yes ☐	no ☐
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 ☐	no ☐
I agree, that after double pseudonymisation, data and biomaterial can be used or passed on to cooperating research partners in Germany or abroad.	yes ☐	no ☐
I agree, that after double pseudonymisation, data and biomaterial may also be used for **commercial** purposes including pharmaceutical industry or patent development at the University Medical Center Freiburg.	yes ☐	no ☐
I agree, that in case of study withdrawal data and biomaterial acquired until this timepoint can be used for the study.	yes ☐	no ☐

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		signature of healthy subject	
	name of physician taking consent		
Datum		signature of physician	

Consent of underage and/or persons incapable of contracting

Date		signature of the legal representative of the healthy subject	
Date		where necessary signature of a second person having the care and custody of healthy subject	
Date		if applicable signature of the child, healthy subject	
	name of the physician taking consent		
Date		signature of physician	

AL - PID Study

Autoimmune lymphoproliferative primary immunodeficiency
Healthy probands / healthy family members

Information Sheet

Clinical contact person

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anne.rensing-ehl@uniklinik-freiburg.de

Shipment of blood samples

- Please send 10 ml - if acceptable - 15 ml EDTA blood and 4 ml serum.
- **Please announce any material > 3 days before sending it.**
  (via e-mail or phone, see Lab Contact)
- Send via express **(delivery until 8 am).**
- For healthy probands / healthy family members with German health insurance:
  please include transfer form (Überweisungsschein) for genetic analysis.
- Please also send signed consent form and the Healty probands information sheet.
  (IMPORTANT!)

Thank you for your cooperation!

Clinical contact person

Name _____

Phone _____ Fax _____

E-mail _____

Name of healthy proband / healthy family member

_____

Date of birth (day/month/year) | | | | | | |

Shipment of

Date of blood sample
day / month / year

	ml EDTA						
	ml serum						

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PROBAND / FAMILY MEMBER INFORMATION

Consent signed ○ yes ○ no

Name of healthy proband / healthy family member

Date of birth (day/month/year)

RELATIONSHIP TO THE AL-PID PATIENT

Relation - genetically related

○ mother ○ father ○ sister ○ brother

○ maternal grandmother ○ paternal grandmother

○ maternal grandfather ○ paternal grandfather

○ maternal aunt ○ paternal aunt

○ maternal uncle ○ paternal uncle

○ other relationship, please specify

if other, gender ○ female ○ male

INFORMATION OF THE AL-PID PATIENT

Patient label - if applicable

Name of patient

Date of birth (day/month/year)

Date Signature of Physician

Print form Remove all entries

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