Version Nov 2013

Consent Form for Gene Sequencing and Immunological Characterisation in Patients with Haemophagocytic Lymphohistiocytosis

Patient..... **Date of Birth.....**

Dear parents, dear patients,

Several different genetic defects are known to be associated with Haemophagocytic Lymphohistiocytosis (HLH). Currently, defects in the following genes are known: *PRF1, UNC13D, STX11* and *STXBP2*. In other immunodeficiencies a propensity to develop HLH is described as well (Chediak-Higashi-Syndrome (*LYST*), Griscelli syndrome type II (Rab27a), XIAP deficiency *RAB27A*), XIAP deficiency (*BIRC4/XIAP*), X-chromosomal lymphoproliferativ syndrom (XLP*, SH2D1A*), Hermansky-Pudlak-Syndrom Typ II (*AP3B1*), ITK-Deficiency (*ITK*).

These gene defects can be analyzed at the reference center at the university hospital Hamburg Eppendorf. In most cases of HLH with a proven genetic defect a stem cell transplantation is necessary to cure the disease and prevent relapses. A known genetic defect may as well be used for prenatal testing.

In less than 10 % of patients with assumed genetic HLH, no defects can be identified with regular testing. It is the aim of the Centre of Chronic Immundeficiency (CCI, University Hospital Freiburg), the Cologne Center for Genomics (University Hospital Köln), the university hospital Hamburg Eppendorf and cooperating scientists worldwide to identify further genes associated with HLH. For this study we use exome sequencing. This will be the basis for a better understanding and treatment of the disease and will make the decision for or against stem cell transplantation easier. However, the result may take several months or years in individual cases with unknown genetic defects. For the genetic analysis we need about 5ml EDTA blood.

In addition, further investigations will be done to characterize certain properties of cells of the human immune system. If these investigation show abnormal results conclusions can be drawn which genetic defect may be present. The investigation requires 10-15 mL of blood, in infants 5mL. The analyses will be performed at the immunological HLH reference center CCI at Freiburg University Hospital.

We ask for your permission to keep remaining material of the sample that is sent to us to potentially identify genetic defects in the future by the research groups in Freiburg or Hamburg or other researchers. The samples and clinical data of you / your child will be stored in a pseudonomised fashion at the study center. Only the study center with the collaborating laboratories in Freiburg, Hamburg or Cologne can assign a name to each sample. No third parties may be informed of any aspects of your samples without your consent. You may withdraw your consent and ask for the elimination of the respective samples and data at any time.

Consent form

I agree that investigations will be performed that can identify known genetic defects associated with HLH. For this purpose, methods may be applied that make the analysis of a large number of genes possible. Additionally, I agree with the immunological characterization which helps to identify the presence of a genetic disease. **YES** □ **NO** □

I agree that the result will be transmitted to the following physician(s)/person(s) **YES** □ **NO** □

_____

Name (e.g. treating physician)

I want to be informed about the results. **YES** □ **NO** □

I agree that the samples will be kept for 30 years, to be able to identify not yet discovered genetic defects in the future. . **YES** □ **NO** □

I agree that the samples and the obtained data will be made available to other physicians involved in HLH research in a pseudonomised form and may be published in scientific journals. **YES** □ **NO** □

By law data must be deleted after 10 years. However, they may be of relevance for you or your family later. If you agree we may keep them for 30. I agree that the data obtained may be kept for 30 years in Hamburg and Freiburg. **YES** □ **NO** □

If exome sequencing will be performed for your sample, we may find genetic mutations which are not related to HLH, even though we do not specifically look for them. Most variants are not harmful and represent the genetic variability of the human genome. However, we may also find a serious and disease causing mutation not related to HLH. If you agree we will inform you about the mutation in the setting of a genetic consultation, if there are methods to prevent or treat the disease or if it has any other medical importance for your health.

I agree that I / my child will be analyzed for so far unknown gene defects in the context of HLH. To this end, we can use a method analyzing many genes at the same time. **YES** □ **NO** □

I agree that I will be informed during a genetic consultation about any additional result not related to HLH, but with clinical relevance or relevance for family planning. **YES** □ **NO** □

I am aware that I can withdraw my consent and can demand the elimination of the study samples and personal data at any time without explanation, which will not have any negative effects for me. I am aware of the right to not be informed about the results. All my questions have been answered.

....
Date **Father**

....
Date **Mother**

....
Date **Patient** (if appropriate)

....
Date **Physician**