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Collaborative Transplant Study | INF 305 | 69120 Heidelberg

Patient-ID

**Collaborative Transplant Study Covid-19 Serum Study**

**“Antibody formation against the transplant after SARS-CoV-2 infection”**

***Study Handout***

***for legal representatives of transplanted patients with SARS-CoV-2 infection***

Dear Ms. \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_, Dear Mr. \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

By this information document, we invite you, as the legal representative of a transplanted patient, to review the participation of the patient you represent in the above mentioned multicenter study. Please read the following information carefully. On this basis, you can decide whether or not the patient you represent will participate. Take your time for the decision and ask the study staff any question that is important for you. The study is funded by the Institute of Immunology in Heidelberg. In addition, project funding from third parties is sought. There are no conflicts of interest (both financial and personal) for any department or individual involved in the study.

**What is the aim of the study?**

In this study, we would like to investigate whether

a) patients who had a Corona virus (SARS-CoV-2) infection before or after organ transplantation are more likely to develop antibodies against their transplant than control patients without SARS-CoV-2 infection depending on the severity of the disease

b) the formation of such graft-damaging antibodies affects graft function.

Furthermore, we would like to analyze how the subsets of antibodies that patients with SARS CoV-2 infection form against the Corona virus change during the course of the infection and whether these changes have an impact on the further course of the disease.

After transplantation, new formation of graft-damaging antibodies may occur. It has been shown that this increases the risk of rejection. We would like to investigate whether transplanted patients with SARS-CoV-2 infection are more likely to form such graft-damaging antibodies.

Other aspects we would like to analyze include the influence of blood group and tissue antigens on the frequency of occurrence (incidence) and severity of Covid-19 as well as the influence of the decrease of the SARS-CoV-2 antibody strength on the severity of Covid-19 in transplanted patients. The question is whether there are genetically determined factors (such as blood type or particular tissue antigens) that influence the occurrence and severity of Covid-19. Therefore, in order to answer the aforementioned questions, specific testing of genetic material (blood) is necessary. At this time, it is not possible to predict which genetic variants might influence the occurrence and progression of Covid-19; thus, it is difficult to narrow down the scope of genetic testing. We would also like to investigate whether specific subsets of SARS-CoV-2 antibodies correlate with better control (neutralization) of the virus.

Until now, studies on these questions regarding transplanted patients have either not been performed at all or did not meet the necessary numerical requirements. The international Collaborative Transplant Study, which we are coordinating and in which more than 150 liver and kidney transplant centers from around the world are actively participating, offers a unique opportunity to gather reliable information on the effects of Corona infection on organ transplantation outcome in a relatively short time. We would then like to make these results available to transplant centers for the benefit of transplanted patients.

**How does the study work?**

Patients legally represented by you will have two additional blood samples (approximately 15 – 20 ml) taken on the day of hospitalization due to SARS-CoV-2 infection for testing of the immune activation marker sCD30, graft-damaging and SARS-CoV-2 antibodies as well as accurate typing of tissue characteristics (HLA antigens).

60 – 90 days after hospitalization, an additional blood sample (approximately 10 ml) will be taken from the patient you represent as part of the routine follow-up at the transplant center to again evaluate the development of the above mentioned immune parameters (sCD30, graft-damaging antibodies and SARS-CoV-2 antibodies). At this time, the attending physician will also fill out a questionnaire about the course of SARS-CoV-2 infection of the patient you represent.

One year after hospitalization, an additional blood sample will be taken (approximately 10 ml) from the patient you represent to evaluate the development of immune parameters in response to SARS-CoV-2 infection.

According to our experience, the collection of additional blood tubes requires less than 1 minute in addition. Information about the study and discussing participation and consent is expected to take 15 minutes depending on the amount of required information. The study-related additional collection of approximately 10 to a maximum of 20 ml of blood will have only a minor impact on the total blood volume and your general condition.

**Is there any personal benefit for the person I legally represent?**

Since the findings will only be elaborated in the course of the study and the examination will be pseudonymized[[1]](#footnote-1), there will be no direct individual benefit for the patient you represent. It is planned to publish the results in medical or biological journals and to present the study at national and international congresses for further discussion of the results.

**What are the risks associated with participation?**

A small amount of blood will be taken three times at the most from the patient you represent. Adverse effects or risks are not expected as a result of the blood collection and the amount of blood taken. All blood collections will be obtained as part of routine care. No additional study-related punctures will be performed. In addition to mild pain from the puncture, local irritation, infection, bleeding, and bruising may occur in rare cases during blood sampling. There is also a risk of nerve injury with superficial numbness. All of these risks have nothing to do with this study, but represent general risks of blood collection.

According to the current state of science, the occurrence of incidental findings is unlikely. Nevertheless, incidental findings may occur in the course of the examinations of the material obtained. They may provide evidence of already existing or future diseases that are not related to the objectives of the study (incidental findings). We will inform you about such findings upon request. However, the notification of incidental findings may have far reaching, even negative consequences for the patient you represent and his or her further life and the life of his or her blood relatives. For example, the patient may be required to provide this information when taking out an insurance policy or during a health examination with the aim of obtaining a civil service position. Not least because of these potentially negative consequences, but also because of the constitutionally guaranteed right not to know, the decision on how to deal with related findings is left up to you. Therefore, if you do not wish to be informed about incidental findings or only those that are likely to have the potential to prevent or treat disease at an early stage, please tick the appropriate option on the consent form. All data will be treated strictly confidentially and will only be evaluated in pseudonymized form.

**Information on data protection**

General information:

Medical confidentiality and data protection regulations will be observed. During the study, medical findings and personal information will be collected from you and written down in your personal file at the test center or stored electronically. Data important for the study will additionally be stored in pseudonymized (encrypted) form, evaluated and, if necessary, passed on to university clinics and cooperation partners, possibly also in countries where data protection requirements are lower than in the European Union.

The study management will take all reasonable steps to ensure the protection of the data in accordance with the data protection standards of the European Union. The data is secured against unauthorized access. Decryption will only occur upon withdrawal from the study for the purpose of data destruction. As soon as possible according to the research or statistical purpose, the personal data will be anonymized[[2]](#footnote-2). Data collected during the study will be kept indefinitely in the Collaborative Transplant Study database in Heidelberg for use in future scientific studies. Any biological material from you that is not needed will also be asserved indefinitely under a pseudonym at the study center after the study is completed in order to evaluate further biomarkers in Covid-19 research in the future. These include, for example, studies of tissue characteristics, blood group and genetic information important for organ transplantation. As soon as possible according to the research purpose, the samples will be pseudonymized. If you do not agree to the use of data for future research purposes, you may restrict your declaration of consent. The retention period of the biomaterials and data cannot be stated precisely, as it is currently not foreseeable which further investigations on the study blood might be relevant in the future regarding organ transplanted patients with SARS-CoV-2 infection. Therefore, biomaterials will be kept until further notice and made available for further medical research regarding transplanted patients with SARS-CoV-2 infection. We will review every five years whether further retention of the biomaterials and data is still necessary. Personal data will be anonymized as soon as feasible according to the research purpose.

The data and samples may also be shared with recipients in countries outside the EU (clinics, collaborators) if one of the following conditions is met:

a) The European Commission has established an adequate legal level of data protection in the country.

b) On the part of the study director, contractual data protection clauses have been concluded with the research partners which have been adopted or approved by the European Commission or the competent supervisory authority. You may obtain a copy of these data protection clauses from the responsible study physician (see below).

In addition, however, there may be occasions when data and samples will be shared with research partners in third countries for which neither of these requirements is met. **These countries may have a lower level of data protection than the EU.** The study directors mentioned below assure that, also in these cases, the research partners will be contractually obliged, as far as legally possible, to comply with the EU data protection level. Nevertheless, there is a risk that government or private agencies may access your data even though this would not be permitted under European data protection law. In addition, you may be subject to fewer or less enforceable data subject rights in these countries and there may be no independent supervisory authority to assist you in exercising your rights. **In this case, your samples and data can only be shared if you have given your explicit consent. If you do not agree, you may delete the respective marked paragraph on the “Declaration of Consent” form.**

We would like to point out that there is currently a high and also legitimate interest in Covid-19 research. Through good cooperation with other transplant centers, we hope to obtain as much data as possible regarding Covid-19 infections in transplanted patients as soon as possible. This requires an exchange of data between different transplant centers. We would like to point out again that the data important for the study will be stored in pseudonymized (encrypted) form, evaluated and, if necessary, passed on to university clinics and cooperation partners, possibly also in countries where data protection requirements are lower than in the European Union.

You have the right to request information from the persons responsible (see below) about the stored personal data of the patient you represent. Likewise, you may request the correction of inaccurate data as well as the deletion of data or restrictions on their processing.

The persons responsible for the study-related collection of personal data are:

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[christian.morath@med.uni-heidelberg.de](mailto:christian.morath@med.uni-heidelberg.de)

If you have any concerns about data processing and compliance with data protection requirements, you may contact the following data protection officer at the facility:

Dr. jur. Regina Mathes

Im Neuenheimer Feld 672

69120 Heidelberg

Tel.: +49 (0) 6221 56 7036

[datenschutz@med.uni-heidelberg.de](mailto:datenschutz@med.uni-heidelberg.de)

In the event of unlawful data processing, you have the right to lodge a complaint with the following supervisory authority:

The State Commissioner for Data Protection and Freedom of Information of Baden-Württemberg

P.O. Box 10 29 32, 70025 Stuttgart

Königstrasse 10a, 70173 Stuttgart

Tel.: +49 (0) 711 61 55 41 - 0

Fax: +49 (0) 711 61 55 41 - 15

E-mail: poststelle@lfdi.bwl.de

Internet: <http://www.baden-wuerttemberg.datenschutz.de>

For the purposes of the study, it is useful to also include data from the medical records of the patient you represent collected by their physicians in charge. We would like to ask you to agree to passing on of transplantation-relevant data to the study management and to release the physicians in charge from medical confidentiality in this respect.

There are confidentiality risks associated with any collection, storage, and transmission of biomaterial data in the context of research projects (e.g., the possibility of identifying the patient you represent), especially with regard to information on the patient's genetic material. These risks cannot be completely excluded and increase according to the volume of data that can be linked, especially if the patient you represent himself or herself publishes genetic data on the Internet (e.g. for genetic research). The study management assures that it will do everything possible according to the state of the art to protect privacy and that samples and data will only be passed on to projects that can demonstrate a suitable data protection concept.

**Voluntariness / Withdrawal**

Participation in the study is voluntary. If you agree to the participation of the patient you represent, we ask you to sign the enclosed consent form. You may withdraw this consent at any time in writing or verbally without giving reasons and without any disadvantages for the patient you represent. If you wish to withdraw your consent, please contact the study director or the staff treating you. In the event of revocation, you may decide whether the data collected for study purposes should be deleted and the samples obtained destroyed or whether they may continue to be used for the purposes of the study. Even if you initially agree to further use, you may still change your mind later and request deletion of the data or destruction of the samples; to do this, please also contact the study management or the staff treating you.

Please note that data that have already been included in scientific evaluations or data or samples that have already been anonymized can no longer be deleted or destroyed at your request or at the request of the patient you represent.

**Will the person I legally represent incur any costs as a result of participation? / Is there any payment or reimbursement of expenses?**

Participation in the study is free of charge. However, there is no reimbursement either, since the study participation takes place in the context of your regular transplant aftercare.

**Further information**

For further information as well as for information on general results and the outcome of the study, please contact the following persons:

Responsible Study Physician:

Dr. med. Louise Benning

Kidney Center Heidelberg

Im Neuenheimer Feld 162

69120 Heidelberg, Germany

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**Your support of this research project is greatly appreciated!**

1. "Pseudonymization" means the processing of personal data in such a way that the personal data can no longer be attributed to a specific data subject without the use of additional information ("key"). This additional information is kept separately and is subject to technical and organizational measures that ensure that the personal data cannot be assigned to an identified or identifiable natural person [↑](#footnote-ref-1)
2. "Anonymization" is the alteration of personal data in such a way that the data subject can no longer be identified or can only be identified at a disproportionate cost or time. [↑](#footnote-ref-2)