

Informed Consent Form

Study Title: Patient-derived iPS cells for the study of the new coronavirus infection (COVID-19)
Version 1 (prepared June 25, 2020)

This document provides information for how to participate in research on the new coronavirus to people who have been diagnosed with its infection and who have provided blood and other medical information.

Please read it carefully before deciding whether you want to participate in this study.

If you are willing to participate, please sign the attached consent form and hand it to the person in charge.

1. Background and purpose of the study

Coronavirus disease 2019 (COVID-19) is a respiratory disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. The infection was first reported in Wuhan, China, November 2019, but has spread to a global pandemic, and by June 2020 was responsible for the death of over 400,000 people. The majority of infected patients show only mild symptoms, but severe symptoms are also reported, as the number of deaths would indicate. Understanding the reasons for the mild and severe symptoms would contribute greatly to treatments. Certain demographics seem more at risk of infection, including the elderly, smokers, and people with chronic diseases. A genetic risk may also exist.

Lung cells are one of the most vulnerable cell types to the infection, but taking lung samples from patients is difficult. Alternatively, blood from patients that is reprogrammed to induced pluripotent stem (iPS) cells is a safer way to study the disease. iPS cells were invented by Dr. Shinya Yamanaka, Director of the Center for iPS Cell Research and Application (CiRA), Kyoto University. iPS cells can be differentiated into lung cells or other cell types without changing the genetic makeup of the cells. Thus, the goal of this project is to generate iPS cells from COVID-19 patient and differentiate the cells to lung, heart and other cell types for study of the disease, including differences between cells prepared from patients with mild and severe symptoms, and new therapies. We are therefore asking you to donate your blood and relevant medical records (test results, etc.).

The iPS cells generated from your blood will be shared with researchers around the world investigating COVID-19 and SAR-CoV-2. This research will contribute to our understanding of how the virus infects human cells, causes respiratory failure, and the development of new diagnostics and drugs. Finally, because the type of cells and microorganisms correlate with the infection, we will also use other samples such as sputum, saliva and mucous for this study.

The research will follow ethical guidelines set by the Japan Ministries of Health,

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Labour and Welfare, of Economy, Trade and Industry, and of Education, Culture, Sports, Science and Technology. An Ethics Review Committee* has confirmed the conditions for using human samples in this project and that the burden and risk to the donor is negligible.

- * Ethics Review Committees examine the appropriateness of a research plan from scientific and ethical perspectives based on guidelines set by the government.

2 Research period and number of participants

This study will continue until March 31, 2025, and will include approximately 30 participants.

3 Why we need your help

With regards to our purpose explained in Article 1, we are collecting blood samples from both COVID-19 patients and people who have recovered from COVID-19 and reprogramming these samples to iPS cells. Using the iPS cells, we will produce lung cells and other cell types relevant for study of the disease including how the virus infects and affects the cells.

Along with blood samples, we will need access to your medical records for information about COVID-19 tests and treatments.

4 Procedures for donating blood

Besides your consent to donate blood samples, several conditions must be met in order for us to use your samples in this project:

(1) Provision of medical records

We require records that include medical information about the severity of the SARS-CoV-2 infection, CT images, the test results for several infectious diseases (HIV, HBV, HCV, HTLV1/2), and how your condition changed during the COVID-19 treatment. We will also need records about your lifestyle habits such as smoking. The information you provide will be anonymized so that no one will be able to identify your name or contact information.

(2) Provision of blood

Blood will be collected using a standard method. No more than 50 mL will be acquired. However, if the medical records provided in Article 4.1 do not include test results for infectious diseases, then an additional 10 mL of blood will be taken. In this case, a maximum of 60 mL will be taken.

(3) Provision of sputum, saliva and mucous

We will not collect new samples of sputum or mucous for this project. If previously taken samples are stored, we ask for access to them. We will collect saliva. These samples will be transported to and stored at CiRA. If they are used, it will be for genetic information on pathogens such as the viruses and bacteria they contain.

We understand if some participants cannot contribute to Article 4.3, but ask all participants contribute to Article 4.1 and 4.2.

5 Research method

(1) Infectious Agents and Viral Testing

Part of your blood sample will be used for a new SARS-CoV-2 test at Kyoto University. We will also test for the following infectious diseases.

Testing will be done for the following.

- SARS-CoV-2 (by PCR, antibody tests, antigen tests, etc.).

If there is no medical history of testing, then the following infectious diseases will also be

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tested for

- HIV
- HBV
- HCV
- HTLV1/2

If any test is positive, then you will not be able to participate further in this study, and your entire blood sample will be discarded. Test results will not be reported directly to you. However, they will be provided to your doctor if follow-up is deemed necessary.

(2) Virus infection experiments and iPS cell generation

Except for the antibody test, if the test results in Article 5.1 are negative, blood cells from the blood sample will be frozen and stored for later experiments. Serum will also be isolated and used to infect some of the stored cells with the virus or virus-like particles. Other stored cells will be used to produce iPS cells and to study the immune response to the virus.

(3) Genome editing and differentiation of iPS cells

Some of the iPS cells will be differentiated to cell types of high interest for COVID-19 study, such as lung cells and heart cells. In addition, genes thought to have a role in SARS-CoV-2 infection or resistance will be modified by gene editing in some iPS cells, which will also be differentiated to the above cell types. The differentiated cells will be used to model how the virus affects these cells and related tissues and organs in the human body in order to understand how the disease develops and to develop new therapies for the disease.

(4) Genome analysis

The genome[※] of the blood cells in your sample and the iPS cells made in Article 5.2 will be analyzed.

✂The genome describes an organism's complete set of DNA and carries all the genetic information needed to build and maintain that organism. Each cell with a nucleus in the organism has the same genome.

The purpose of the genome analysis is to investigate the function of all genes and determine their functions in inflammation and how their behavior changes upon SARS-CoV-2 infection. The analysis will be done by Kyoto University and the CiRA Foundation.

In principle, we will not inform you the results of the analysis. Genome analysis is mostly used for basic research and not health, because it is difficult to interpret the results and because of limitations in genome analysis techniques, which can make the data unreliable. However, if there are health concerns that emerge from the analysis, we may inform you after consulting your doctor. If you would like to discuss any concerns about the analysis, we can also introduce you to a genome counsellor.

Furthermore, part of the genome analysis may be outsourced to an external organization. If so, your information will be sent satisfying Article 6 so that your identity is kept anonymous. Additionally, the organization will destroy any data or results in its possession after a certain time.

6 Confidentiality

Any personal information you provide, such as your name, age, and gender, and all samples you donate and anything made from those samples, including blood, sputum, saliva mucous, medical records, iPS cells and cells differentiated from those iPS cells, will be assigned a number so that they cannot be used to deduce your identity. The number and your name will be put into a correspondence list that

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will be highly protected and only accessible to a Privacy Officer who is not directly involved in the research. Therefore, even the researchers will not know whose samples they are handling. Further, when the research results are publicized, people accessing the data will also be unable to trace any of the information to you.

【Privacy Officer】

Name: ※各医療機関ごとに記入

Job Title: ※各医療機関ごとに記入

Organization: ※各医療機関ごとに記入

The following collaborating institutes will have access to your samples and medical information.

- Kyoto University, Center for iPS Cell Research and Application (CiRA; Director: Shinya Yamanaka)
- Kyoto University, Center for iPS Cell Research and Application Foundation (CiRA Foundation; Manager: Masayoshi Tsukahara)
- National Institute of Infectious Disease (Principle Investigator: Kouji Sakai)

7 Benefits for participating

There are no direct benefits to you for participating in this study. However, your contribution will help in understanding how SARS-CoV-2 infection causes COVID-19 and the development of therapies against the virus and disease.

8 Risks and burdens to the donor

(1) Risks associated with donating blood, sputum, mucous and saliva

The method for the blood collection is the same as blood collections taken at medical institutions for typical health checks and pose no particularly high risks,

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although serious side effects are rare. Only previously collected sputum and mucous will be used. Saliva can be collected by yourself with a special container we provide.

(2) Risk about private information

High security measures will be taken to protect your identity and information so that only authorized people will have access. Further, your samples and information will be stored so that there is no direct way of associating them to you. However, while we will take every reasonable precaution to protect your personal information, we cannot absolutely guarantee the prevention of a leak.

(3) Other burdens

You will not be charged for participating in this study. You will be compensated 5000 yen for your participation to assist for travel costs to and from the clinic and other costs. In exceptional circumstances, where participants are traveling long distances, we will consider increasing the compensation. Please ask for more details if you have questions.

9 Storage and management of cells and information

The samples you provide, including blood, sputum, mucous and saliva, and the iPS cells made from these samples have extraordinary research value and so will be kept even after completion of this project at Kyoto University and other collaborating institutes for future research projects. So too will your medical and personal information. All will be stored with high security measures and will be inaccessible except to a small number of people who will have exclusive authorization to protect your identity.

Future research projects may involve collaborating parties such as universities and private companies, both domestically and overseas, not involved in the current project.

In such cases, we generally will not seek your consent again. However, no samples or information will be shared until an Ethics Review Committee approves the research plan.

If a new research plan is approved, it will be publicly disclosed on the websites of CiRA or the CiRA Foundation. You will not be contacted directly about such announcements. If, after reading the website, you have concern and would prefer not to have your samples or information contribute to the new research, please contact the appropriate authority on the website.

Similar to the above, some of the data acquired from the genome analysis may be shared with other domestic and overseas organizations, but only in a manner that protects your identity.

10 Withdrawing consent

Your consenting to participate in this study is completely at your discretion. Furthermore, if after consenting you prefer to withdraw, you are free to stop in the participation without punishment or penalty. In this case, you will be asked to sign a form that declares your withdrawal. The cells and samples you provided will be discarded. However, there may be some exceptions depending on the progress of the research.

11 Ownership of intellectual property

New discoveries are expected from this research that will lead to patents and other intellectual property awarded to the researchers and research institutes. You will not be entitled to any intellectual property that comes from discoveries using your cells

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or samples.

Furthermore, once you have donated blood and samples and provided your medical information, those items along with the data gained from them or other materials produced from them, such as iPS cells and DNA, are the property of Kyoto University and other participating research institutes.

12 Participating institutes

The following institutes are participating in this project. The current structure is not permanent and could change in the future.

〈Primary research institute〉

Center for iPS Cell Research and Application (CiRA; Director, Shinya Yamanaka)

〈Other participating institutes〉

Department of Parasitology, Osaka City University (Associate Professor, Yasutoshi Kido)

Osaka City Juso Hospital, Department of Respiratory Medicine (Chief, Satoshi Shiraishi)

Japan Red Cross Medical Center, Department of Respiratory Medicine (Chief, Takehiro Idumo)

The University of Tokyo, Institute of Medical Science, Division of Infectious Disease and Applied Immunology (Assistant Professor, Eisuke Adachi)

Rinku General Medical Center, General Internal Medicine and Infectious Disease (Director, Masaya Yamato)

National Institute of Infectious Disease (Chief of Research, Kouji Sakai)

CiRA Foundation (General Manager, Masayoshi Tsukahara)

13 Research funding and conflicts of interest

(1) Research funding for the project is as follows

Private donations to CiRA will be used. None of the donors will influence the research. The appropriate committees at each participating institute have verified that the funding does not cause any conflicts of interest.

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(2) Conflicts of interest

To protect the research and the results obtained from any improper financial influence, conditions consistent with the conflict of interest guidelines set by the federal government will be met.

14 Inquiries

For more information about this project, please contact and provide your contact information as explained below.

【Contact information】

※各医療機関で記載

住所：〒

TEL：

★担当医師：

★担当コーディネーター：

※京大病院の患者様※

京都大学医学部附属病院 相談支援センター

(Tel)075-751-4748 (E-mail) ctsodan@kuhp.kyoto-u.ac.jp

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Certificate of Consent

[Name of head of the medical institution, etc.]

Director, Center for iPS Cell Research and Application, Kyoto University
Representative Director, CiRA Foundation

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I have been given information about this study. I have had the opportunity to ask questions about it and any questions I have asked have been answered to my satisfaction. I consent voluntarily to be a participant in this study.

Signature of participant: _____

Signature of representative of the participant: _____

(Relationship of the legal representative to the participant: _____)

Date _____

day/month/year

Statement by the researcher/person taking consent

I have accurately read the information sheet to the potential participant and to the best of my ability have made sure that the participant understands that the following will be done:

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3 Why we need your help	4 Procedures for donating blood
5 Research method	6 Confidentiality
7 Benefits for participating	8 Risks and burdens to the donor
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11 Ownership of intellectual property	12 Participating institutes

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I confirm that the participant was given an opportunity to ask questions about the study, and all the questions asked by the participant have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.

A copy of this ICF has been provided to the participant.

Institution (Name)/Department (Name) _____

Signature of Researcher /person taking the consent _____

Date _____

day/month/year

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Consent Withdrawal Notification

[Name of head of the medical institution, etc.]

Director, Center for iPS Cell Research and Application, Kyoto University
Representative Director, CiRA Foundation

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I, the undersigned, hereby withdraw the consent I granted at an earlier date by signing the Informed Consent Form regarding the participation in this study.

I ask that the specimen I have donated, the iPS cells or other materials derived from the specimen, and medical information associated with the donated specimen be destroyed and no longer be used.

Print Name of Person Withdrawing Consent _____	Date _____
(Signature)	
Print Name of Legal Representative _____	Date _____
(Signature)	
(Relationship of the legal representative to above person)	_____

Receipt of consent withdrawal notification

I have received notification of withdrawing consent to the participation in this study as above.

Print Name of Person at hospital Name of hospital Department	Date of receipt _____
Memo :	