Press Release



CiRA Foundation is now accepting applications for the free provision of iPS cells made from COVID-19 convalescent patients

Kyoto, Japan, March 25th, 2021 –The CiRA Foundation® ("CiRA_F"; located in Kyoto, Japan), Center for iPS Cell Research and Application, Kyoto University ("CiRA"; located in Kyoto, Japan), Kyoto University Hospital ("KUHP"; located in Kyoto, Japan) and Rinku General Medical Center ("RGMC"; located in Osaka, Japan) today have started accepting applications for the free provision of induced pluripotent stem cell (iPS cells) made from blood samples of COVID-19 convalescent patients.

1. Overview

Four organizations – CiRA_F, CiRA, KUHP, RGMC - have been collaborating on COVID-19 research since April 2020 for the purpose of distributing patient iPS cells.

Specifically, the collaboration has established iPS cells from the peripheral blood of six patients who have recovered from SARS-CoV-2 infection. We will distribute these iPS cell lines free of charge to companies and research institutes that study the onset mechanism of COVID-19 and the causes of the different severities seen in patients. The ultimate goal of research using these iPS cells is to contribute to new diagnostic and therapeutic methods for COVID-19.

2. Background

The first human infection of SARS-CoV-2 occurred in November 2019, and the subsequent global spread of the virus has caused enormous damage to humanity, with more than 2.4 million deaths worldwide as of February 2021.

In many cases, this virus does not cause symptoms even when it infects humans. However, in some patients, the symptoms are severe and include acute respiratory disease. For this reason, prediction of the severity risk and appropriate treatment based on this prediction are very important to reduce burden on the medical field and to save the maximum number of patients. Smoking, age, and underlying diseases such as cardiomyopathy are all risks for severe cases of COVID-19 infection. Another hypothesized factor is congenital differences in alveolar epithelial cells and cardiomyocytes. However, it is very difficult to collect these cells from live patients. Instead, by collecting and reprogramming easily accessible blood cells to iPS cells, we can study lung and heart cells that have the same genetic background as the patient.

Press Release

Despite the attraction of iPS cells for COIVD-19 research, their manufacturing requires contacting and obtaining consent from the patients and then manufacturing and confirming the quality of the iPS cells. These efforts take extraordinary time, delaying research progress. The provision of COVID-19 patient iPS cells through this collaboration is intended to resolve this bottleneck in order to develop new diagnostics and treatments faster.

3. Summary of the iPS cell establishment and distribution

<Establishment and distribution of iPS cells derived from COVID-19 convalescent patients>

1) Recruitment of donors

RGMC and KUHP have invited patients who have been diagnosed with COVID-19, hospitalized and met the criteria for discharge with negative PCR test for SARS-CoV-2 or patients who had been previously diagnosed with COVID-19 but now convalesced to hear an explanation about the research. All cells used in the research are from patients who provided voluntary consent after hearing the explanation.

2) Cell collection

 $20\mathchar`-30$ mL of peripheral blood at RGMC or KUHP.

3) Genome analysis

At RGMC or KUHP, the peripheral blood samples were anonymized to prevent the identification of individual donors before the collected peripheral blood and medical information (gender, age, preexisting medical conditions, severity of the COVID-19 infection, etc.) were provided to CiRA for the iPS cell establishment.

4) Establishment of iPS cells

CiRA isolated and reprogrammed blood cells from the peripheral blood collected in (2) into iPS cells.

5) Genome analysis

CiRA_F conducted whole genome analysis of the iPS cells established in (4) to confirm quality. In addition, it received some medical information from CiRA.

6) Distribution of research samples and provision of accompanying information

CiRA_F provides the iPS cells established for this project to researchers around the world free of charge. In addition, it will provide the obtained analysis data and, if necessary, medical information (gender, age, previous medical conditions, severity of COVID-19 infection, etc.) and other information that may be useful for the research.

< About the convalescent patients >

We received blood samples from 12 people who met all of the following criteria and selected samples from 6 of them to establish iPS cells.

- Those who have recovered from COVID-19 infection.
- Those who have received a medical examination at KUHP or RGMC.
- Those who have given their free and voluntary consent.

4. About the cell donation

CiRA_F is providing free of charge three iPS cell lines made from three patients that have passed all quality and other tests. Ultimately, a total of six lines will be available for distribution as soon as the tests are completed.

Press Release

Researchers who wish to receive these iPS cells should download the application form from <u>the CiRA_F website</u> and send a completed version to <u>minnano-saibou@cira-foundation.or.jp</u> Fees : Free

* In principle, transportation costs to domestic companies and overseas institutions are borne by the requester, while transportation costs to domestic academia are borne by CiRA.

5. Background

1) 16 April 2020: The project was launched by CiRA_F, CiRA, KUHP and RGMC.

2) 28 April 2020: Permission from the Ethics Committee for this project was granted. Contact to COVID-19 convalescent patients for cooperation was initiated.

3) June to September 2020: Received blood samples from 12 convalescent patients who had suffered from varying degrees of COVID-19 severity.

4) 20 September 2020: Establishment of iPS cells from one person.

5) Late February 2021: Establishment of iPS cells from three people, with completion of all quality and other tests.

6) 25 March 2021: Start accepting applications for the free provision of iPS cells.

6. Future plans

We will contact institutions that have requested provision of these iPS cells in order to prepare for the cell shipment, including the contract agreement.

7. Support for this research

This research was made possible by donations to CiRA.

8. Message from Shinya YAMANAKA - Representative Director of CiRA_F and Director of CiRA

In response to the pandemic caused by COVID-19, we have formed a special research project team. At this time, we have started accepting applications for the distribution of iPS cells produced by the project so that other researchers can use them. The iPS cells to be distributed were established from convalescent patients who were infected with SARS-CoV-2 and recovered from mild, moderate, or severe disease. We have confirmed that SARS-CoV-2 efficiently infects both lung tissue cells differentiated from iPS cells and undifferentiated iPS cells in which the ACE2 gene is forcibly expressed. We hope that more researchers will use this system to contribute to the study of COVID-19 infections.

Contacts :

For inquiries about the iPS cells : Emiri NAKAUE (Ms.) Public Relations Office, CiRA Foundation (CiRA_F) TEL: +81-75-761-3363 Email: <u>contact@cira-foundation.or.jp</u> For inquiries about the research : Hiroyuki WADAHAMA (Mr.) International Public Communications Office, Center for iPS Cell Research and Application, Kyoto University (CiRA) TEL: +81-90-6982-5882 Email: media@cira.kyoto-u.ac.jp